

ANTIBACTERIAL METHODS & CELLS

TECHNICAL FIELD

The invention relates to methods of killing bacterial target cells comprising Resistance-Nodulation-Cell Division (RND)-efflux pumps, as well as carrier cells useful for this purpose wherein the carrier cells comprise a conjugative plasmid encoding an antibacterial-microbial agent that is toxic to target cells. A carrier bacterium is capable of conjugative transfer of plasmid DNA encoding the agent to a target cell.

BACKGROUND

Bacterial efflux systems as determinants of multidrug resistance

Efflux pumps are bacterial transport proteins which are involved in extrusion of substrates from the cellular interior to the external environment. These substrates are often antibiotics, imparting the efflux pump expressing bacteria antibiotic resistant phenotype. From the first drug-resistant efflux pump discovered in the 1990s, the development in molecular microbiology has led to the characterization of many efflux pumps in Gram-positive bacteria (GPB) including methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae*, *Clostridium difficile*, *Enterococcus* spp. and *Listeria monocytogenes* and Gram-negative bacteria (GNB) such as *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Stenotrophomonas maltophilia*, *Campylobacter jejuni*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Vibrio cholerae* and *Salmonella* spp. Since these transport substrates against a concentration gradient, these efflux pumps are energy dependent. Based on the mechanism by which these derive this energy, the efflux pumps are broadly classified into two categories. The primary efflux pumps draw energy from active hydrolysis of ATP, whereas the secondary efflux pumps draw energy from chemical gradients formed by either protons or ions such as sodium. Five major families of efflux pumps have been described in the prokaryotes, namely: (i) ATP binding cassette (ABC), which are primary active transporters, (ii) small multidrug resistance family, (iii) multidrug and toxin extrusion (MATE) family, (iv) major facilitator superfamily (MFS) and (v) resistance nodulation cell division (RND) family. RND family efflux pumps have tripartite organization and are the major contributors to intrinsic antibiotic resistance, which expel a broad spectrum of antibiotics and biocides, including fluoroquinolones, β -lactams, tetracycline and linezolid. Apart from drug resistance, the physiological role of efflux pumps in bacteria extends to bile tolerance in enteric bacteria, leading to colonization, increase in virulence, biofilm secretion and bacterial survival in the host.

Biofilms are complex microbial associations anchored to abiotic or biotic surfaces, embedded in extracellular matrix produced by the biofilms themselves where they interact with each other and the

environment. One of the main properties of biofilms is their capacity to be more resistant to antimicrobial agents than planktonic cells. Efflux pumps have been reported as one of the mechanisms responsible for the antimicrobial resistance in biofilm structures. Evidence of the role of efflux pump in biofilm resistance has been found in several microorganisms such as *Pseudomonas*

5 *aeruginosa*, *Escherichia coli* and *Candida albicans*.

RND efflux pumps

Multidrug efflux pumps belonging to the resistance-nodulation cell division (RND) family have major roles in the intrinsic and elevated resistance of Gram-negative bacteria to a wide range of compounds.

10 RND efflux pumps require two other proteins to function: a membrane fusion protein (MFP) and an outer membrane protein. It has been demonstrated that *Salmonella enterica* serovar *Typhimurium* has five RND efflux systems: AcrAB, AcrD, AcrEF, MdtABC and MdsABC. Most RND efflux system genes also code for an MFP in the same operon.

15 Efflux pumps belonging to the resistance-nodulation-division (RND) family of transporters are the major multi-drug efflux (Mex) mechanism in both *E. coli* and *P. aeruginosa*. The pumps in this family consist of three components that function via active transport to move numerous molecules, including antibiotics, out of the cell: an antiporter that functions as a transporter (e.g., MexB, MexD, MexF, MexY), an outer membrane protein that forms a surface-exposed channel (e.g., OprC, OprB, OprG, OprD, OprI, OprH, OprP, OprO, OprM, OprJ, OprN), and a periplasmic membrane fusion protein that links the two proteins (e.g., MexA, MexC, MexE, MexH, MexX). This system is the major efflux pump associated with intrinsic resistance among 17 possible RND efflux pumps in *P. aeruginosa*. *P. aeruginosa* is more resistant than *E. coli* due to a highly impermeable OM and the presence of multiple efflux systems. Inactivation of the Mex efflux pump renders *P. aeruginosa* more vulnerable to antibiotics than the average *E. coli* strain.

20

25

The flavonoid-responsive RND family of efflux pumps includes several members, such as AcrAB from *Erwinia amylovora*, IfeAB from *Agrobacterium tumefaciens*, MexAB-OprM from *Pseudomonas syringae*, BjG30 from *Bradyrhizobium japonicum*, and EmrAB in *Sinorhizobium meliloti*, among others. Further supporting the role of this efflux pump in bacteria/plant interactions, it has been reported that *E. amylovora*, an enterobacterium that causes fire blight on species of the Rosaceae family, has an AcrAB efflux pump, which confer resistance to phytoalexins, and that is required for successful colonization of the plants and for bacterial virulence. This finding is in agreement with the idea that the ability export toxic compounds is one of the key traits for survival in the rhizosphere, and efflux pumps may have a relevant role for achieving resistance to these toxic compounds.

30

35

- Phylogenetically close to *E. coli*, the enterobacterial pathogen *Salmonella enterica* serovar Typhimurium presents at least nine multidrug efflux pumps. Among these pumps, AcrAB, the orthologue of the *E. coli* efflux pump with the same name, contributes to antimicrobial resistance and has a wide substrate spectrum that includes antibiotics, dyes, and detergents. Another important gut
- 5 pathogen is *Campylobacter jejuni*. Among the known antibiotic resistance mechanisms of this microorganism, the CmeABC efflux pump is a relevant player and confers resistance to structurally-diverse antibiotics and toxic compounds, including those naturally present in its animal host, as bile salts. CmeABC belongs to the RND family of efflux transporters and its expression is regulated by the transcriptional repressor CmeR, which binds to a specific site in the promoter region of *cmeABC*.
- 10 Free-living bacteria, including opportunistic pathogens with an environmental origin, should respond to different signals and this may impact their behaviour in clinical and non-clinical ecosystems. For instance, *Pseudomonas aeruginosa* express several RND-type efflux systems, among which four, MexAB-OprM, MexCD-OprJ, MexEF-OprN, and MexXY-OprM are reported to be significant determinants of multidrug resistance.
- 15
- The fact that the expression of MDR efflux pumps is induced by host-produced compounds suggests that they can play a role in the virulence of bacterial pathogens. Indeed, it has been shown that the *Vibrio cholerae* efflux pump VexB is the primary efflux system responsible for resistance to bile salts in this microorganism. Since bile salts are present at the human gut, the activity of this efflux
- 20 pump is a pre-requisite for *V. cholerae* infection. A similar situation happens with AcrAB, the main pump responsible for bile salts resistance in *Enterobacteriaceae*, which is required for the pathogenesis of *Salmonella enterica* serovar Typhimurium. Notably this efflux pump is involved as well in the bacterial capability for forming biofilms. A protective role to host antibacterial compounds has also been described in the case of *Neisseria gonorrhoeae*. In this organism, the MtrCDE efflux
- 25 pump contributes to resistance to vertebrate antibacterial peptides, and FarAB is involved in resistance to long-chain fatty acids. The activity of these efflux pumps contributes to the pathogenesis of *N. gonorrhoeae*. Similarly, the *Campylobacter jejuni* CmeABC efflux pump confers resistance to bile salts, fatty acids, and detergents, and is needed for the colonization of the intestinal tract.
- 30 Together with their role in modulating the quorum-sensing response, and consequently bacterial virulence, these results support the notion that MDR efflux pumps, besides contributing to the resistance of bacterial pathogens, are major contributors to their pathogenicity.

- Pseudomonas syringae* pv. *tomato* DC3000 (*PsPto*) is a phytopathogenic bacterium that infects tomato
- 35 (causing bacterial speck) and *Arabidopsis thaliana*. *PsPto* can grow epiphytically and endophytically on plant foliage without causing disease symptoms. In the early stages of the infective

phase, *PsPto* enters the plant through wounds and natural openings (such as stomata) and multiplies in the apoplastic space by exploiting live host cells. In this scenario, bacterial survival in the apoplast is one of the key factors for the establishment of a bacterial density large enough to further infect adjacent plant tissues. However, plant apoplast represents a harsh environment for bacteria since it is

5 laden with antimicrobial compounds, both preformed (phytoanticipins) and inducible (phytoalexins), which constitute chemical barriers capable of inhibiting the growth of the pathogen. In fact, plants produce antimicrobial peptides and a variety of secondary metabolites such as phenylpropanoids, isoprenoids, and alkaloids, that are generally accepted to play a role in protecting plants against pathogens. Using the tomato-*PsPto* pathosystem, an increased expression of phenylpropanoid

10 biosynthetic genes has been detected upon bacterial infection, with specific accumulation of different phenylpropanoids such as hydroxycinnamic acid amides conjugated to alkaloids, chlorogenic acid (CGA), and the flavonoid rutin. Tomato plants have also been reported to produce other number of flavonoids like chalconaringenin, rutin, quercetin 3-O-(2"-O- β -apiosyl-6"-O- α -rhamnosyl- β -glucoside) or phloretin 3', 5'-di-C- β -glucoside. To overcome the effect of these potentially toxic

15 compounds, plant-associated bacteria have in turn evolved different defense strategies, among which multidrug resistance (MDR) efflux pumps are the most widespread. MDR transporters can recognize and pump out many different organic compounds (often structurally dissimilar), providing resistance to antibiotics and many other antimicrobial compounds. Microorganisms with the largest number of MDR pumps are found in the soil or in association with plants. Although still scarce, several studies

20 on plant-pathogen interactions with bacteria from the genera *Xanthomonas*, *Ralstonia*, *Erwinia* and *Dickeya* have shown that efflux pumps can contribute to bacterial virulence, bacterial fitness, resistance to plant antimicrobials, or competition with epiphytic bacteria.

Regarding *P. syringae*, most studies have been focused on MexAB-OprM, an efflux pump from the

25 resistance-nodulation-cell division (RND) family. It has been shown that the *P. syringae* MexAB-OprM system is involved in the tolerance to a broad range of toxic compounds, including some plant-derived antimicrobials, and that a mutant in this system showed a reduced ability to multiply *in planta*. A recent study on the *Arabidopsis-PsPto* pathosystem has identified three RND efflux pumps (one of them the MexAB-OprM system) which are required to overcome the isothiocyanate-based

30 defenses of *Arabidopsis*.

PSPTO_0820 is a predicted multidrug transporter from the phytopathogenic bacterium *Pseudomonas syringae* pv. tomato DC3000. Orthologs of this protein are conserved within many *Pseudomonas* species that interact with plants. Reference is made to PLoS One, 2019 Jun

35 25;14(6):e0218815. doi: 10.1371/journal.pone.0218815. eCollection 2019, "The *Pseudomonas syringae* pv. tomato DC3000 PSPTO_0820 multidrug transporter is involved in resistance to plant

antimicrobials and bacterial survival during tomato plant infection”, Saray Santamaría-Hernando *et al*: To study the potential role of *PSPTO_0820* in plant-bacteria interaction, a mutant in this gene was isolated and characterized. In addition, with the aim to find the outer membrane channel for this efflux system, a mutant in *PSPTO_4977*, a TolC-like gene, was also analyzed. Both mutants were more
 5 susceptible to *trans*-cinnamic and chlorogenic acids and to the flavonoid (+)-catechin, when added to the culture medium. The expression level of both genes increased in the presence of (+)-catechin and, in the case of *PSPTO_0820*, also in response to *trans*-cinnamic acid. *PSPTO_0820* and *PSPTO_4977* mutants were unable to colonize tomato at high population levels. This work evidences the involvement of these two proteins in the resistance to plant antimicrobials, supporting also the
 10 importance of chlorogenic acid, *trans*-cinnamic acid, and (+)-catechin in the tomato plant defense response against *P. syringae* pv. tomato DC3000 infection.

Bacterial Conjugation

DNA sequences controlling extra-chromosomal replication (ori) and transfer (tra) are distinct from
 15 one another; i.e., a replication sequence generally does not control plasmid transfer, or vice- versa. Replication and transfer are both complex molecular processes that make use of both plasmid- and host-encoded functions. Bacterial conjugation is the horizontal transmission of genetic information from one bacterium to another. The genetic material transferred may be a plasmid or it may be all or part of a chromosome if a functional origin of transfer is within the chromosome. Bacterial cells
 20 possessing a conjugative plasmid contain a surface structure (the sex pilus) that is involved in the coupling of donor and recipient cells, and the transfer of the genetic information. Conjugation involves contact between cells, and the transfer of genetic traits can be mediated by many plasmids. Among all natural transfer mechanisms, conjugation is the most efficient. For example, F plasmid of *E. coli*, pCF10 plasmid of *Enterococcus faecalis* and pXO16 plasmid of *Bacillus*
 25 *thuringiensis* employ different mechanisms for the establishment of mating pairs, the sizes of mating aggregates are different, and they have different host ranges within gram-negative (F) as well as gram-positive (pCF10 and pXO16) bacteria. Their plasmid sizes are also different; 54, 100 and 200 kb, respectively. Remarkably, however, those conjugation systems have very important characteristics in common: they are able to sustain conjugative transfer in liquid medium and high transfer
 30 efficiencies are often reached in a very short time. Thus, the conjugative process permits the protection of plasmid DNA against environmental nucleases, and the very efficient delivery of plasmid DNA into a recipient cell. Conjugation functions are naturally plasmid encoded. Numerous conjugative plasmids (and transposons) are known, which can transfer associated genes within one species (narrow host range) or between many species (broad host range). Typically a range of
 35 effecincy is observed that is dependant on the incompatilty group of the plasmid conjugative system and the conditions and environment where conjugation occurs (Alderliesten, J.B., Duxbury,

S.J.N., Zwart, M.P. *et al.* Effect of donor-recipient relatedness on the plasmid conjugation frequency: a meta-analysis. *BMC Microbiol* **20**, 135 (2020). <https://doi.org/10.1186/s12866-020-01825-4>.

Transmissible plasmids have been reported in numerous Gram-positive genera, including but not limited to pathogenic strains of *Streptococcus*, *Staphylococcus*, *Bacillus*, *Clostridium* and *Nocardia*.

- 5 The early stages of conjugation generally differ in Gram-negative and Gram-positive bacteria. The role of some of the transfer genes in conjugative plasmids from Gram-negative bacteria are to provide pilus-mediated cell-to-cell contact, formation of a conjugation pore and related morphological functions. The pili do not appear to be involved in initiating conjugation in Gram-positive bacteria.

10 SUMMARY OF THE INVENTION

The also invention provides the following configurations:-

In a First Configuration

In one Aspect:

- 15 A method of killing a bacterial target cell, the cell comprising at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, the method comprising contacting the target cell with a carrier bacterial cell, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent that is toxic to the target cell, wherein the carrier cell conjugates to the target cell and the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the
20 target cell is killed.

In another Aspect:

- A method of modifying the genome of a bacterial target cell, the cell comprising at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, the method comprising contacting the
25 target cell with a carrier bacterial cell, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an agent that capable of modifying the genome of the target cell, wherein the carrier cell conjugates to the target cell and the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell genome is modified.

30 In a First Aspect of the First Configuration

- The method is a method of increasing the biomass of a plant or part thereof, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the
35 second population are killed, wherein the plant comprises said target cells (optionally on leaves and/or

stems thereof or comprised by the apoplast of the plant), whereby target cells are killed and said biomass is increased.

In a Second Aspect of the First Configuration

- 5 The method is a method of promoting germination of a plant seed, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the seed comprises said target cells, whereby target cells are killed and
10 germination is promoted.

In a Third Aspect of the First Configuration

- The method is a method of increasing leaf chlorophyll production in a plant, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a
15 second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the plant comprises said target cells (optionally on leaves and/or stems thereof, or comprised by the apoplast of the plant), whereby target cells are killed and chlorophyll is increased in the plant.

20

In a Fourth Aspect of the First Configuration

- The method is a method of reducing a biofilm comprised by a subject or comprised on a surface, wherein the biofilm comprises target cells, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population
25 comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, thereby killing the target cells in the biofilm or reducing the growth or proliferation of target cells, optionally wherein the method is carried out ex vivo or in vitro.

In a Second Configuration

- 30 A carrier bacterial cell for use in a method of killing a bacterial target cell according to the first configuration, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent that is toxic in the target cell, wherein the carrier cell is capable of conjugating to the target cell wherein the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell is killed.

35

In a Third Configuration

A pharmaceutical composition comprising a plurality of carrier cells of the second configuration for administration to a human or animal subject for killing a plurality of bacterial target cells comprised by the subject, wherein each target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump whereby each target cell is an antibiotic resistant cell, wherein plasmids encoding the antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and an antibiotic resistant infection of bacterial target cells is treated or prevented in the subject.

10 In a Fourth Configuration

A method of treating or preventing a disease or condition in a plant, the method comprising contacting the plant (eg, one or more stems and/or one or more leaves of the plant) with a composition comprising a plurality of carrier cells of the second configuration, wherein the plant comprises target bacterial cells that mediate the disease or condition, wherein each target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein plasmids encoding the antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and the disease or condition is treated or prevented.

20 In a Fifth Configuration

Use of a carrier cell of the second configuration in the manufacture of a composition, for killing a bacterial target cell ex vivo or wherein the target cell is not comprised by a human or animal (eg, the target cell is comprised by a plant or soil), wherein the target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein the target cell is contacted with the carrier cell and the carrier cell conjugates to the target cell, whereby the plasmid is introduced into the target cell, wherein the antibacterial agent is expressed in the target cell and the target cell is killed.

Optionally, the target bacteria are *Pseudomonas* bacteria, such as *P syringae* or *P aeruginosa* bacteria or any other *Pseudomonas* bacteria disclosed herein. For example, the *P syringae* is *P. syringae* pv. tomato DC3000 and/or the target cells are comprised by a tomato plant, eg, *Lycopersicon esculentum* cultivar (cv.) MoneyMaker.

Optionally, the agent is a guided nuclease system or a component thereof, eg, any such system or component disclosed herein for modifying (eg, cutting) a target nucleic acid sequence comprised by target bacteria.

Optionally, the plant is any plant disclosed herein.

Optionally, the chlorophyll is a chlorophyll a and/or chlorophyll b.

5

BRIEF DESCRIPTION OF FIGURES

Figure 1A-C. The three biological replicates (in the order as labelled) of the protection assay using the plant control GBTM 1 and the plant active GBTM 1. In the biological replicate # 2, the CFU/cm² of *Pto* DC3000 was 0, for the plant active GBTM 1, at the timepoints 48 hrs and 7 days;

10

Figure 2A-C: The three biological replicates (in the order as labelled) of the protection assay using the plant control GBTM 2 and the plant active GBTM 2; and

Figure 3. The Moneymaker tomato plants treated with the plant control GBTM 1 or the plant active GBTM 1 and spray challenged with *Pto* DC3000. (A and B). Plant control GBTM 1 + *Pto* DC3000 (C and D). Plant active GBTM 1 + *Pto* DC3000.

15

DETAILED DESCRIPTION

The invention relates to methods of killing bacterial target cells comprising Resistance-Nodulation-Cell Division (RND)-efflux pumps, as well as carrier cells useful for this purpose wherein the carrier cells comprise a conjugative plasmid encoding an antibacterial-microbial agent that is toxic to target cells. A carrier bacterium is capable of conjugative transfer of plasmid DNA encoding the agent to a target cell.

20

Reference is made to mBio, 2015 Mar 24;6(2):e00309-15. doi: 10.1128/mBio.00309-15,

25

“Contribution of resistance-nodulation-cell division efflux systems to antibiotic resistance and biofilm formation in *Acinetobacter baumannii*”, Eun-Jeong Yoon *et al*, which studied the expression of RND efflux pumps in *A. baumannii*. The authors observed that in two types of plasmid transfer, mobilisation and conjugation, high expression of *adeABC* and *adeIJK* RND pumps by the recipient bacteria resulted in reproducible reduction of transfer frequencies (see figure 4 in Yoon *et al*). The authors concluded that it thus appears that, if high expression of pumps contributes to multi-drug resistance (MDR) by efflux, it decreases acquisition of foreign DNA by both transformation and conjugation. This suggests that upregulation of expression of RND pumps (such as in response to antibiotics and other antibacterial agents in the environment of the bacteria) can reduce the chances of DNA entry by conjugation. For example, several studies have reported that *E. coli* biofilms have higher antibiotic resistance than planktonic cells and that expression of several gene-encoded efflux pumps was increased in biofilms (eg, see Ito A, Taniuchi A, May T, Kawata K, Okabe S. Increased antibiotic resistance of *Escherichia coli* in mature biofilms. *Appl Environ Microbiol*. 2009;75:4093–100. doi:

30

35

10.1128/AEM.02949-08). Hyperexpression of efflux pumps of the RND type in *Pseudomonas aeruginosa* (e.g., MexAB-OprM), chromosomally encoded by *mexAB-oprM*, *mexCD-oprJ*, *mexEF-oprN*, and *mexXY (-oprA)*, is often detected in clinical isolates and contributes to worrying multi-drug resistance phenotypes. By monitoring the amount of extracellular DNA (eDNA) released by strains overexpressing *pmt*, Sahu *et al* ("Characterization of eDNA from the clinical strain *Acinetobacter baumannii* AIIMS 7 and its role in biofilm formation", Sahu PK *et al*, *Scientific World Journal*. 2012; 2012:973436) proposed the involvement of the Pmt efflux pump (a MFS pump) in nucleic acid transport. Since DNA and RNA are well-known scaffolding components of the biofilm matrix, the authors have inferred that an increase in eDNA supports a more abundant development of the bacterial biofilm.

In view of the art, such as these teachings, it is surprising that the inventors could successfully deliver a plasmid-borne antibacterial agent using conjugation into bacteria comprising RND efflux pumps (see Examples). Targeted killing of the desired bacteria was surprisingly and advantageously achieved. The invention will, for example, be particularly useful for targeting bacteria in biofilms.

In particular, very high rates of target cell killing were surprisingly observed using plasmid conjugation and CRISPR/Cas killing as shown in the Examples. Killing of more than 90% of target cells was reproducibly and advantageously achieved despite the presence of RND efflux pumps in target strains.

In addition, we could surprisingly achieve maintenance of bacteriocidal effect on surfaces (as exemplified by leaf surfaces, Example 1).

Thus, there is provided:-

A method of killing a bacterial target cell, the cell comprising at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, the method comprising contacting the target cell with a carrier bacterial cell, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent that is toxic to the target cell, wherein the carrier cell conjugates to the target cell and the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell is killed.

In an alternative, instead of bacterial cells, the carrier and target cells may be archaea.

In another alternative, instead of killing the target cell, the method modifies the genome of the cell, eg, modifies a chromosome or episome (eg, a plasmid) of the cell. Modification may be cutting of the chromosome or episome, for example, such as where the agent is a guided nuclease. An example of such a nuclease is a Cas, meganuclease, TALEN or zinc finger nuclease. Thus, there is also

5 provided:-

A method of modifying the genome of a bacterial target cell, the cell comprising at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, the method comprising contacting the target cell with a carrier bacterial cell, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an agent that capable of modifying the genome of the target cell, wherein the carrier
10 cell conjugates to the target cell and the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell genome is modified.

Optionally, the target cell is resistant to one or more antibiotics. The target cell may comprise an efflux pump may mediate antibiotic resistance in the target cell. The target cell may comprise an
15 efflux pump may mediate resistance of the target cell to one or more antibacterial agents.

The carrier cell and target cell may be cells of the same order, family or genus, such as shown in the Examples.

20 Preferably, the agent comprises a CRISPR/Cas system or component thereof. The agent may be a crRNA or guide RNA that guides a Cas nuclease in the target cell to a target protospacer sequence, wherein the Cas cuts the target sequence and the target cell is killed. For example, the plasmid may encode a plurality of different crRNAs or guide RNAs, such as a first crRNA or gRNA that comprises a spacer sequence that is capable of guiding a Cas in the target cell to a first protospacer sequence and
25 a second crRNA or gRNA that comprises a spacer sequence that is capable of guiding a Cas in the target cell to a second protospacer sequence wherein the protospacer sequences are different (eg, different chromosomal sequences of the target cell). Each protospacer may be comprised by an essential gene, virulence gene or antibiotic resistance gene of the target cell genome. Each protospacer sequence may be from 10 to 60 nucleotides in length, eg, 15 to 50, 15 to 40, 15 to 30 or
30 15 to 20 nucleotides in length. The target sequence may be a chromosomal sequence of the target cell. The target sequence may be an episomal sequence of the target cell. The plasmid may encode a or said Cas nuclease, optionally a Cas9, Cas3 or Cpf1.

In an example, the target cell comprises an RND efflux pump of a strain selected from
35 (i) *Azotobacter chroococcum* NCIMB 8003, *Azotobacter chroococcum* strain B3, *Azotobacter salinestris* strain KACC 13899, *Burkholderia ambifaria* MC40-6,

- Burkholderia cenocepacia AU 1054 chromosome 1, Burkholderia cenocepacia HI2424 chromosome 3, Burkholderia cenocepacia MC0-3, Burkholderia cenocepacia strain CR318 chromosome 3, Burkholderia cenocepacia strain FDAARGOS_720, Burkholderia lata strain A05, Burkholderia pyrocinia strain mHSR5, Cupriavidus basilensis strain 4G11, Cupriavidus necator N-1 plasmid pBB1, Cupriavidus taiwanensis STM 3679, Lysobacter gummosus strain 3.2.11, Paraburkholderia sprengiae WSM5005, Paraburkholderia terricola strain mHS1, Ralstonia pseudosolanacearum strain CRMRS218, Ralstonia solanacearum strain UA-1591, Variovorax paradoxus S110, Variovorax sp. PBL-H6, Xanthomonas arboricola pv. juglandis strain Xaj 417, Xanthomonas arboricola pv. pruni strain 15-088, Xanthomonas arboricola strain 17, Xanthomonas axonopodis pv. dieffenbachiae LMG 695, Xanthomonas axonopodis pv. phaseoli strain ISO18C8, Xanthomonas axonopodis pv. phaseoli strain ISO98C12, Xanthomonas campestris pv. campestris MAFF302021, Xanthomonas citri pv. glycines strain 2098, Xanthomonas euvesicatoria strain LMG930, Xanthomonas perforans strain LH3 and Xanthomonas sp. ISO98C4, which strains have NCBI Accession Numbers respectively of CP010415.1, CP011835.1, CP045302.1, CP001027.1, CP000378.1, CP000460.1, CP000960.1, CP017240.1, CP050980.1, CP024945.1, CP024903.1, CP010537.1, CP002879.1, LT984803.1, CP011131.1, CP017561.1, CP024941.1, CP021764.1, CP034195.1, CP001636.1, LR594659.1, CP012251.1, CP044334.1, CP011256.1, CP014347.1, CP012063.1, CP012057.1, AP019684.1, CP041965.1, CP018467.1, CP018475.1 and CP012060.1, or an orthologue or homologue of such a pump;
- (ii) *Pseudomonas aeruginosa* strain: IOMTU 133, *Pseudomonas aeruginosa* DSM 50071, *Pseudomonas aeruginosa* genome assembly NCTC10332, *Pseudomonas aeruginosa* isolate B10W, *Pseudomonas aeruginosa* isolate PA14Or, *Pseudomonas aeruginosa* NCGM2.S1, *Pseudomonas aeruginosa* PAK, *Pseudomonas aeruginosa* strain 243931, *Pseudomonas aeruginosa* strain 24Pae112, *Pseudomonas aeruginosa* strain 268, *Pseudomonas aeruginosa* strain 60503, *Pseudomonas aeruginosa* strain AR_0095, *Pseudomonas aeruginosa* strain AR_0353, *Pseudomonas aeruginosa* strain AR_0354, *Pseudomonas aeruginosa* strain AR_455, *Pseudomonas aeruginosa* strain BAMCPA07-48, *Pseudomonas aeruginosa* strain CCUG 51971, *Pseudomonas aeruginosa* strain E90, *Pseudomonas aeruginosa* strain FDAARGOS_571, *Pseudomonas aeruginosa* strain GIMC5002: PAT-169, *Pseudomonas aeruginosa* strain H26023, *Pseudomonas aeruginosa* strain L10, *Pseudomonas aeruginosa* strain M1608, *Pseudomonas aeruginosa* strain M37351, *Pseudomonas aeruginosa* strain MRSN12280, *Pseudomonas aeruginosa* strain NCTC13715, *Pseudomonas aeruginosa* strain Pa58, *Pseudomonas aeruginosa* strain

PABL048, *Pseudomonas aeruginosa* strain PAK, *Pseudomonas aeruginosa* strain
 PASGNDM345, *Pseudomonas aeruginosa* strain PASGNDM699, *Pseudomonas*
aeruginosa strain PA-VAP-3, *Pseudomonas aeruginosa* strain PB368, *Pseudomonas*
aeruginosa strain PB369, *Pseudomonas aeruginosa* strain S04 90, *Pseudomonas*
 5 *aeruginosa* strain ST773, *Pseudomonas aeruginosa* strain T2436, *Pseudomonas aeruginosa*
 strain W60856, *Pseudomonas aeruginosa* strain WPB099, *Pseudomonas aeruginosa* strain
 WPB100, *Pseudomonas aeruginosa* strain WPB101, *Pseudomonas aeruginosa* UCBPP-
 PA14, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* VRFPA04,
Pseudomonas amygdali pv. *lachrymans* str. M301315, *Pseudomonas amygdali* pv.
 10 *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244,
Pseudomonas amygdali pv. *tabaci* str. ATCC 11528, *Pseudomonas avellanae* strain
 R2leaf, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas*
coronafaciens pv. *oryzae* str. 1_6, *Pseudomonas coronafaciens* strain X-1, *Pseudomonas*
otitidis MrB4, *Pseudomonas salegens* strain CECT 8338, *Pseudomonas savastanoi* pv.
 15 *phaseolicola* 1448A, *Pseudomonas savastanoi* pv. *savastanoi* NCPPB 3335, *Pseudomonas*
sp. KBS0707, *Pseudomonas sp.* LPH1, *Pseudomonas syringae* CC1557, *Pseudomonas*
syringae group genomosp. 3 isolate CFBP6411, *Pseudomonas syringae* isolate
 CFBP3840, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae*
 pv. *actinidiae* ICMP 18884, *Pseudomonas syringae* pv. *actinidiae* ICMP 9853,
 20 *Pseudomonas syringae* pv. *actinidiae* str. Shaanxi_M228, *Pseudomonas syringae* pv.
actinidiae strain CRAFRU 12.29, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU
 14.08, *Pseudomonas syringae* pv. *actinidiae* strain MAFF212063, *Pseudomonas syringae*
 pv. *actinidiae* strain NZ-45, *Pseudomonas syringae* pv. *actinidiae* strain NZ-47,
Pseudomonas syringae pv. *actinidiae* strain P155, *Pseudomonas syringae* pv. *avii* isolate
 25 CFBP3846, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas*
syringae pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *tomato* str. DC3000,
Pseudomonas syringae pv. *tomato* strain B13-200, *Pseudomonas syringae* pv. *tomato*
 strain delta IV/IX, *Pseudomonas syringae* pv. *tomato* strain delta VI, *Pseudomonas*
syringae pv. *tomato* strain delta X, *Pseudomonas syringae* strain CFBP 2116 and
 30 *Pseudomonas syringae* strain Ps25, which strains have NCBI Accession Numbers
 respectively of AP017302.1, CP012001.1, LN831024.1, CP017969.1, LT608330.1,
 AP012280.1, CP020659.1, CP041772.1, CP029605.1, CP032761.1, CP041774.1,
 CP027538.1, CP027172.1, CP027171.1, CP030328.1, CP015377.1, CP043328.1,
 CP044006.1, CP033833.1, CP043549.1, CP033685.1, CP019338.1, CP008862.2,
 35 CP008863.1, CP028162.1, LR134330.1, CP021775.1, CP039293.1, LR657304.1,
 CP020703.1, CP020704.1, CP028330.1, CP025050.1, CP025049.1, CP011369.1,

- CP041945.1, CP039988.1, CP008864.2, CP031878.1, CP031877.1, CP031876.1, CP034244.1, CP000438.1, CP008739.2, CP031225.1, CP020351.1, CP026558.1, CP042804.1, CP026562.1, CP046441.1, CP046035.1, CP050260.1, AP022642.1, LT629787.1, CP000058.1, CP008742.1, CP041754.1, CP017290.1, CP007014.1, LT963408.1, LT963409.1, CP012179.1, CP011972.2, CP018202.1, CP032631.1, CP019730.1, CP019732.1, CP024712.1, CP017007.1, CP017009.1, CP032871.1, LT963402.1, LT963391.1, CP047260.1, AE016853.1, CP019871.1, CP047072.1, CP047071.1, CP047073.1, LT985192.1 and CP034558.1, or an orthologue or homologue of such a pump;
- (iii) *Stenotrophomonas rhizophila* strain GA1, *Enterococcus faecalis* strain V583 and *Paucimonas lemoignei* strain NCTC10937, which strains have NCBI Accession Numbers respectively CP031729.1, CP022312.1 and LS483371.1, or an orthologue or homologue of such a pump; or
- (iv) *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas asturiensis* strain CC1524, *Pseudomonas avellanae* strain R2, *Pseudomonas cerasi* isolate PL963, *Pseudomonas chlororaphis* strain PCL1606, *Pseudomonas chlororaphis* subsp. *aurantiaca* strain JD37, *Pseudomonas chlororaphis* subsp. *aureofaciens* strain ChPhzTR36, *Pseudomonas chlororaphis* subsp. *chlororaphis* strain DSM 50083, *Pseudomonas chlororaphis* subsp. *piscium* strain DSM 21509, *Pseudomonas cichorii* JBC1, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas putida* GB-1 chromosome, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas* sp. 09C 129, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *lapse* strain ATCC 10859, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *pisi* str. PP1, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* UMAF0158 and *Pseudomonas viridiflava* strain CFBP 1590, which strains have NCBI Accession Numbers respectively of CP020351.1, CP026558.1, CP042804.1, CP047265.1, CP026562.1, LT963395.1, CP011110.1, CP009290.1, CP027721.1, CP027712.1, CP027707.1, CP007039.1, CP046441.1, CP000926.1, CP000058.1, CP025261.1, CP007014.1, CP012179.1, LT963391.1, CP013183.1, CP047260.1, CP034078.1, CP005969.1, AE016853.1, CP005970.1 and LT855380.1, or an orthologue or homologue of such a pump.

The RND efflux pump of the target cell may comprise a protein produced by any of these strains. The target cell may be a cell of any of these strains. Any NCBI database and related Accession numbers are, for example, those publicly available on 27.04.2020.

- 5 The efflux pump may comprise a protein encoded by a *Pseudomonas syringae* gene selected from PSPTO_0820, PSPTO_4977, PSPTO_02375, PSPTO_1308, PSPTO_2592, PSPTO_2755, PSPTO_3100, PSPTO_3302, PSPTO_430 or PSPTO_5191, or an orthologue or homologue thereof.
- 10 The efflux pump may comprise a protein encoded by
 - (a) *Pseudomonas syringae* PSPTO_0820 or PSPTO_4977 gene or an orthologue or homologue thereof; or
 - (a) A nucleotide sequence selected from SEQ ID NO: 1 and 3, or a nucleotide sequence that is at least 70% identical (eg, at least 80, 85, 90, 95, 96, 97, 98 or 99% identical) to SEQ
 - 15 ID NO: 1 or 3.

The efflux pump may comprise a protein comprising the amino acid sequence of SEQ ID NO: 2 or 4, or an amino acid sequence that is at least 70% identical (eg, at least 80, 85, 90, 95, 96, 97, 98 or 99% identical) to SEQ ID NO: 2 or 4.

20

- The efflux pump may be a Mex efflux pump (optionally a MexAB-OprM efflux pump, MexCD-OprJ efflux pump, MexEF-OprN efflux pump or MexXY efflux pump), AdeABC efflux pump, AcrAD-TolC efflux pump, AcrAB-TolC efflux pump, AcrABZ-TolC efflux pump, AcrA efflux pump, ArcB efflux pump, AcrC efflux pump, AcrD efflux pump, AcrAB efflux pump, AcrEF efflux pump, AcrF
- 25 efflux pump, CmeABC efflux pump, VexB efflux pump, VexD efflux pump, VexK efflux pump, adeABC efflux pump, adeIJK efflux pump, MdsABC efflux pump or MdtABC efflux pump. Preferably, the pump is an AcrAD-TolC efflux pump.

- The carrier cell may be a *Pseudomonas* cell, optionally a *P fluorescens* cell. Optionally, the carrier and target cells are cells of the same genus or species, optionally both are *Pseudomonas* cells. For example, the target cell is a *P syringae* or *aeruginosa* cell and the carrier is a *Pseudomonas* (eg, *P fluorescens*) cell. This is demonstrated in the Examples.
- 30

- Preferably, the carrier cells are of a strain or species that is not pathogenic to an organism (eg, a plant, animal or human) that comprises the target cells. The carrier cells may be of a strain or species that is symbiotic or probiotic to an organism (eg, a plant, animal or human) that comprises the target cells,
- 35

eg, probiotic or symbiotic in the gut of the organism.

In an example, the carrier cell comprises a Chitinase class I exoenzyme and/or the carrier cell genome encodes a Chitinase class I exoenzyme. Optionally, the carrier cell in this example is a *Pseudomonas*,
 5 eg, *P fluorescens*, cell.

In an example, the carrier cell comprises a *pepI* gene. Optionally, the carrier cell in this example is a *Pseudomonas*, eg, *P fluorescens*, cell.

10 In an example, the carrier cell is a motile bacterial cell. Optionally, the carrier cell in this example is a *Pseudomonas*, eg, *P fluorescens*, cell.

For example, each target cell is a lag phase cell, exponential phase cell or a stationary phase cell. For example, each carrier cell is a lag phase cell, exponential phase cell or a stationary phase cell.

15 Preferably, the target cell is a *Pseudomonas* (optionally a *P fluorescens* or *P aeruginosa*) cell, *Erwinia* (optionally *E carotovora*), *Xanthomonas*, *Agrobacterium*, *Burkholderi*, *Clavibacterium*, *Enterobacteria*, *Pantoea*, *Pectobacterium* (eg, *P atrosepticum*), *Rhizobium*, *Streptomyces* (eg, *S scabies*), *Xylella* (eg, *X fastidiosa*), *Candidatus* (eg, *C liberibacter*), *Phytoplasma*, *Ralstonia* (eg, *R solanacearum*), or *Dickeya* (eg, *D dadantii*) cell.
 20

Each target cell (eg, the plurality of target cells) may be a cell of a genus or species disclosed in Table 1 or 2. Each target cell (eg, the plurality of target cells) may be comprised by a plant or a plant environment (such as soil) and selected from a genus or species disclosed in Table 1.

25 The method may be carried out *in vitro* or *ex vivo*.

The target cell may be comprised by

- (a) a plant microbiome (eg, a microbiome of any plant part disclosed herein),
- 30 (b) an animal or human microbiome (eg, a microbiome of any human or animal organ or tissue or part disclosed herein); or
- (c) a soil, manure, food or beverage microbiome.

For example, the cell is comprised by a plant leaf, stem, root, seed, bulb, flower or fruit microbiome.
 35

Optionally, a microbiome herein is a gut, lung, kidney, urethral, bladder, blood, vaginal, eye, ear, nose, penile, bowel, liver, heart, tongue, hair or skin microbiome.

For example, the target cell is a cell of a species found in soil.

5

The method may be carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed.

10

The method may reduce the number of target cells of said plurality at least 10^5 , 10^6 or 10^7 -fold, eg, between 10^5 and 10^7 -fold, or between 10^5 and 10^8 -fold or between 10^5 and 10^9 -fold. The skilled person will be familiar with determining fold-killing or reduction in cells, eg, using a cell sample that is representative of a microbiome or cell population. For example, the extent of killing or reduction is

15

determined using a cell sample, eg, a sample obtained from a subject to which the carrier cells of the invention have been administered, or an environmental sample (eg, aqueous, water or soil sample) obtained from an environment (eg, a water source, waterway or field) that has been contacted with the carrier cells of the invention. For example, the method reduces the number of target cells of said plurality at least 10^5 , 10^6 or 10^7 -fold and optionally the plurality comprises at least 100,000;

20

1,000,000; or 10,000,000 target cells respectively. Optionally, the plurality of target cells is comprised by a cell population, wherein at least 5, 6 or 7 log₁₀ of cells of the population are killed by the method, and optionally the plurality comprises at least 100,000; 1,000,000; or 10,000,000 target cells respectively.

25

Optionally, the method kills at least 99%, 99.9%, 99.99%, 99.999%, 99.9999% or 99.99999% cells of said plurality of target cells.

In an example, the method is carried out on a population (or said plurality) of said target cells and the method kills all (or essentially all) of the cells of said population (or said plurality). In an

30

example, the method is carried out on a population (or said plurality) of said target cells and the method kills 100% (or about 100%) of the cells of said population (or plurality).

Preferably, at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% of the target cells are killed. This is surprisingly reproducibly demonstrated in the Examples (using conjugative delivery of components of

35

a CRISPR/Cas antibacterial system to target cells).

In an Aspect:-

The method is a method of increasing the biomass of a plant or part thereof, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the plant comprises said target cells (optionally on leaves and/or stems thereof or comprised by the apoplast of the plant), whereby target cells are killed and said biomass is increased.

- 10 Optionally, the target cells are *Pseudomonas* (eg, *P. syringae*) cells, eg, wherein the cells are comprised by a crop plant, such as a tomato plant.

- For example, leaf, fruit, ear, seed, grain, head, pod, stem, trunk, tuber and/or root biomass is increased. For example, leaf or fruit dry biomass, leaf or fruit wet biomass or number of flowers is increased. For example, average biomass or number is increased over a plurality of plants on which the method of the invention has been practised.

- An increase in biomass (eg, average biomass or number) may be an increase by at least 5, 10, 15, 20, 25, 30, 40, or 50% compared to the biomass of plant(s) that have not been exposed to the carrier bacteria, but which comprise the target bacteria. Increases in plant biomass may be determined by measuring the weight of harvested material (eg, fruit, grain, cane, leaves, tubers, nuts or seeds) per area harvested and comparing the measurement of harvested material from plants that have been treated per the invention versus the same area of harvested material from plants of the same species and strain grown that have not been treated per the invention, where all plants are grown under the same conditions, eg, in the same field. In some systems units of volume, such as bushels, are used instead of units of weight.

In an Aspect:-

The method is a method of promoting germination of a plant seed, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the seed comprises said target cells, whereby target cells are killed and germination is promoted.

35

Promoting germination may be decreasing the time to onset of germination and/or decreasing the duration of germination. Promoting germination may be increasing the percentage (eg, by at least 5, 10, 15 or 20%) of germination of seeds comprised by a plurality of seeds that are exposed to the carrier cells in the method.

5

Each seed may comprise target cells on the seed surface.

An increase in germination (eg, average germination) in a plurality of seeds exposed to the carrier cells in the method may be obtained, which is an increase by at least 5, 10, 15, 20, 25, 30, 40, or 50% compared to the germination of seeds that have not been exposed to the carrier cells, but which seeds comprise the target bacteria.

The method may be useful for treating pre-emergent seedlings have pathogens present which stop successful germination. Thus, an Aspect provides:-

15 The method is a method of promoting growth of a plant seedling, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the seedling comprises said target cells, whereby target cells are killed

20 and seedling growth is promoted.

Each seedling may comprise target cells on leaves and/or stems of the seedling.

An increase in growth (eg, average growth) in a plurality of seedlings exposed to the carrier cells in the method may be obtained, which is an increase by at least 5, 10, 15, 20, 25, 30, 40, or 50% compared to the growth of seedlings that have not been exposed to the carrier cells, but which seedlings comprise the target bacteria.

An Aspect:-

30 The method is a method of increasing leaf chlorophyll (eg, chlorophyll a and/or b) production in a plant, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the plant comprises said target cells

35 (optionally on leaves and/or stems thereof, or comprised by the apoplast of the plant), whereby target cells are killed and chlorophyll is increased in the plant. Chlorophyll measurement may be measured,

for example, by spectrophotometry, high performance liquid chromatography (HPLC) or fluorometry.

5 The method is a method of increasing the amount of chlorophyll (eg, chlorophyll a and/or b) in a plant, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed, wherein the plant comprises said target cells (optionally on leaves and/or stems thereof, or comprised by the apoplast of the plant), whereby target
10 cells are killed and chlorophyll is increased in the plant.

An Aspect:-

The method is a method of reducing a biofilm comprised by a subject or comprised on a surface, wherein the biofilm comprises target cells, wherein the method is carried out using a first cell
15 population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, thereby killing the target cells in the biofilm or reducing the growth or proliferation of target cells, optionally wherein the method is carried out ex vivo or in vitro.

20 The subject may be a human or animal, optionally wherein the surface is a lung surface.

The subject may be a plant, optionally wherein the biofilm is comprised by a leaf, trunk, root or stem of the plant.

25 The surface may be comprised by a domestic or industrial apparatus or container, eg, a fermentation vessel.

There is further provided:-

A carrier bacterial cell for use in a method of killing a bacterial target cell according to the invention, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent
30 that is toxic in the target cell, wherein the carrier cell is capable of conjugating to the target cell wherein the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell is killed.

35 The carrier cell may be any carrier cell or carrier cell disclosed herein. The target cell may be any carrier cell or target cell disclosed herein.

There is provided:-

A pharmaceutical composition comprising a plurality of carrier cells of the invention for administration to a human or animal subject for killing a plurality of bacterial target cells comprised by the subject, wherein each target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump whereby each target cell is an antibiotic resistant cell, wherein plasmids encoding the antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and an antibiotic resistant infection of bacterial target cells is treated or prevented in the subject.

10

Preferably, at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% of the target cells are killed. This is surprisingly reproducibly demonstrated in the Examples (using conjugative delivery of components of a CRISPR/Cas antibacterial system to target cells).

15 The plurality of target cells may comprise at least 10^7 , 10^8 , 10^9 , 10^{10} , 10^{11} or 10^{12} target cells. For example, the plurality of target cells is comprised by a gut, blood, lung, oral cavity, liver, kidney, bladder, urethra or skin microbiota of the subject.

There is provided:-

20 A method of treating or preventing a disease or condition in a plant, the method comprising contacting the plant (eg, one or more stems and/or one or more leaves of the plant, or the plant apoplast) with a composition comprising a plurality of carrier cells of the invention, wherein the plant comprises target bacterial cells that mediate the disease or condition, wherein each target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein plasmids encoding the
25 antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and the disease or condition is treated or prevented.

Use of a plurality of carrier cells of the invention in the manufacture of a composition for
30 administration to a plant or environment (eg, soil), for killing bacterial target cells comprised by the plant or environment, wherein the target cells comprise at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein the target cells are contacted with the carrier cells and the plasmids comprising the anti-microbial agent are transferred into the target cells, wherein the agent is expressed in the target cells and the target cells are killed.

35

Use of a carrier cell of the invention in the manufacture of a composition, for killing a bacterial target cell *ex vivo* or wherein the target cell is not comprised by a human or animal (eg, the target cell is comprised by a plant or soil), wherein the target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein the target cell is contacted with the carrier cell and the carrier cell conjugates to the target cell, whereby the plasmid is introduced into the target cell, wherein the antibacterial agent is expressed in the target cell and the target cell is killed.

Optionally, the use comprises using a plurality of said carrier cells to kill a plurality of said target cells, wherein the target cells are comprised by a plant or plant environment (eg, soil) and the killing

10

a) increases (or is for increasing) the biomass of the plant or part thereof (eg, leaf, fruit, ear, seed, grain, head, pod, stem, trunk, tuber and/or root biomass is increased);

15

b) promotes (or is for promoting) germination of one or more seeds of the plant;

c) increases (or is for increasing) the amount of leaf chlorophyll of the plant; and/or

20

d) reduces (or is for reducing) a biofilm comprised by the plant, wherein the biofilm comprises target cells (eg, *Pseudomonas* cells).

Optionally, the target cell or plurality of target cells is in an environment, eg, soil, or in an environment for growing plants.

Example Target Cells

For example, each target cell is a gram-positive bacterial cell (eg, a *Staphylococcus* (such as *S aureus*, eg, methicillin-resistant *Staphylococcus aureus* (MRSA)), *Streptococcus pneumoniae*, *Clostridium difficile*, *Enterococcus* spp. or *Listeria monocytogenes* cell). For example, each target cell is a gram-negative bacterial cell (eg, a *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Stenotrophomonas maltophilia*, *Campylobacter jejuni*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Vibrio cholerae* or *Salmonella* spp. Cell) For example, each target cell is a cell of a genus or species disclosed in Table 1 herein, Table 2 herein. Reference is made to Journal of Plant Pathology (2010), 92 (3), 551-592 *Edizioni ETS Pisa, 2010* 551, LETTER TO THE EDITOR, "COMPREHENSIVE LIST OF NAMES OF PLANT PATHOGENIC BACTERIA, 1980-2007", C.T. Bull et al, the disclosure of which is incorporated herein by reference to provide examples of bacterial genera, species and strains of importance to plants and which may be genera, species and strains of target cells of the invention. Examples are disclosed in Table 1 herein.

For example, each target cell is resistant to a fluoroquinolone, β -lactam (eg, methicillin), tetracycline or linezolid antibiotic. For example, each target cell is resistant to vancomycin, eg, wherein the cell is a vancomycin-resistant *Enterococcus* cell.

5

For example, each target cell is an *Azotobacter*, *Burkholderia*, *Cupriavidus*, *Enterococcus*, *Lysobacter*, *Paucimonas*, *Paraburkholderia*, *Ralstonia*, *Stenotrophomonas*, *Variovorax*, *Xanthomonas* or *Pseudomonas* cell.

10 For example, each target cell is an *E coli* cell, eg, wherein the efflux pump protein is encoded by *TolC* or an orthologue or homologue of such a pump protein. For example, each target cell is *Klebsiella* cell (such as *K pneumoniae* cell), eg, wherein the efflux pump protein is selected from KexC, KexD, KexE, KexF, KexEF, AcrA, AcrB, AcrAB, OqxA, OqxB, OqxAB, EefA, EefB, EefC and EefABC or an orthologue or homologue of such a pump protein.

15

For example, each target cell is an *Azotobacter*, *Burkholderia*, *Cupriavidus*, *Lysobacter*, *Paraburkholderia*, *Ralstonia*, *Variovorax*, *Xanthomonas* or *Pseudomonas* cell.

For example, each target cell is a cell of a *Pseudomonas* species, optionally wherein the species is
20 selected from *Pseudomonas aeruginosa*, *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*, *Pseudomonas coronafaciens*, *Pseudomonas otitidis*, *Pseudomonas putida*, *Pseudomonas salegens*, *Pseudomonas savastanoi*, *Pseudomonas syringae* and *Pseudomonas viridiflava*.

25 For example, each target cell is a cell of a species selected from *Azotobacter chroococcum*, *Azotobacter salinestris*, *Burkholderia ambifaria*, *Burkholderia cenocepacia*, *Burkholderia lata*, *Burkholderia pyrrocinia*, *Cupriavidus basilensis*, *Cupriavidus necator*, *Cupriavidus taiwanensis*, *Lysobacter gummosus*, *Paraburkholderia sprentiae*, *Paraburkholderia terricola*, *Ralstonia pseudosolanacearum*, *Ralstonia solanacearum*, *Variovorax paradoxus*, *Xanthomonas arboricola*,
30 *Xanthomonas axonopodis*, *Xanthomonas campestris*, *Xanthomonas citri*, *Xanthomonas euvesicatoria* and *Xanthomonas perforans*.

For example, each target cell is a *Stenotrophomonas*, *Enterococcus*, *Paucimonas* or *Pseudomonas* cell.

35

For example, each target cell is a cell of a *Pseudomonas* species, optionally wherein the species is selected from *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*, *Pseudomonas coronafaciens*, *Pseudomonas putida*, *Pseudomonas savastanoi*, *Pseudomonas syringae* and
 5 *Pseudomonas viridiflava*.

For example, each target cell is a cell of a species selected from *Stenotrophomonas rhizophila*, *Enterococcus faecalis*, *Paucimonas lemoignei*, *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*,
 10 *Pseudomonas coronafaciens*, *Pseudomonas putida*, *Pseudomonas savastanoi*, *Pseudomonas syringae* and *Pseudomonas viridiflava*.

Optionally, the efflux pump comprises a protein

- (a) encoded by *Pseudomonas syringae* PSPTO_0820 or PSPTO_4977 gene or an orthologue or
 15 homologue thereof; or
- (b) produced by a strain disclosed herein.

Optionally, the genome of the target cell comprises (i) a *P syringae* PSPTO_0820 gene or an orthologue or homologue thereof; and (ii) a *P syringae* PSPTO_4977 gene or an orthologue or
 20 homologue thereof.

Optionally, the efflux pump is a MexAB-OprM efflux pump, eg, *P. syringae* MexAB-OprM efflux pump. Optionally, the efflux pump protein is a protein of such a pump.

25 Optionally, the efflux pump is an AdeABC efflux pump, eg, *A. baumannii* AdeABC efflux pump. Optionally, the efflux pump protein is a protein of such a pump.

Optionally, the efflux pump protein is encoded by *Pseudomonas syringae* gene PSPTO_0820, PSPTO_4977, PSPTO_02375, PSPTO_1308, PSPTO_2592, PSPTO_2755, PSPTO_3100,
 30 PSPTO_3302, PSPTO_430 or PSPTO_5191, or an orthologue or homologue thereof. See Table 7 for the role of the products of such genes in *P syringae*. The orthologue or homologue may be from a different genus or species (ie not *Pseudomonas* or *P syringae*).

Optionally, the efflux pump protein is a *Pseudomonas syringae* AcrB, D or F family protein or a
 35 homologue or orthologue thereof. Optionally, the efflux pump protein is a *Pseudomonas syringae* cation efflux protein or a homologue or orthologue thereof. Optionally, the efflux pump protein is a

Pseudomonas syringae isothiocyanate protein or a homologue or orthologue thereof. Optionally, the efflux pump protein is a *Pseudomonas syringae* TpsC transporter protein or a homologue or orthologue thereof. Optionally, the efflux pump protein is a *Pseudomonas syringae* SaxG protein or a homologue or orthologue thereof. Optionally, the efflux pump protein is a *Pseudomonas aeruginosa* MexB, D or F protein or a homologue or orthologue thereof. Optionally, the efflux pump is a *Pseudomonas aeruginosa* MexAB-OprM, MexCD-OprJ, MexEF-OprN or MexXY pump or a homologue or orthologue thereof. Optionally, the efflux pump protein is a *Pseudomonas aeruginosa* MexAB-OprM, MexCD-OprJ, MexEF-OprN or MexXY pump protein or a homologue or orthologue thereof. The orthologue or homologue may be from a different genus or species (ie not *Pseudomonas* or *P. syringae*).

Optionally, the efflux pump protein is a protein of a Mex efflux pump. The Mex protein may be a protein that is a surface exposed protein on the target bacteria. In some embodiments, the Mex protein is selected from the group consisting of OprM, MexA, MexB, MexX, and MexY.

Optionally, the efflux pump protein is a bacterial TolC protein (eg, a *Pseudomonas* or *E. coli* TolC protein) or a homologue or orthologue thereof.

In an example, each target cell is comprised by a plant microbiome. In an example, each target cell is comprised by an environment microbiome, eg, a water or waterway (eg, river, pond, lake or sea) microbiome. In an example, each target cell is comprised by a soil microbiome. In an example, each target cell is comprised by an animal (ie, non-human animal) microbiome. In an example, each target cell is comprised by a human microbiome (eg, a lung, kidney, GI tract, gut, blood, oral, nasal or liver microbiome).

PSPTO_0820, Orthologues & Homologues

A *PSPTO_0820* gene orthologue or homologue may be gene comprised any of the following strains.

Example *Pseudomonas* Strains

For example, the target cell is a cell of a strain selected from *Pseudomonas aeruginosa* strain: IOMTU 133, *Pseudomonas aeruginosa* DSM 50071, *Pseudomonas aeruginosa* genome assembly NCTC10332, *Pseudomonas aeruginosa* isolate B10W, *Pseudomonas aeruginosa* isolate PA14Or, *Pseudomonas aeruginosa* NCGM2.S1, *Pseudomonas aeruginosa* PAK, *Pseudomonas aeruginosa* strain 243931, *Pseudomonas aeruginosa* strain 24Pae112, *Pseudomonas aeruginosa* strain 268, *Pseudomonas aeruginosa* strain 60503, *Pseudomonas aeruginosa* strain AR_0095, *Pseudomonas aeruginosa* strain AR_0353, *Pseudomonas aeruginosa* strain AR_0354, *Pseudomonas aeruginosa* strain AR_455, *Pseudomonas aeruginosa* strain BAMCPA07-48, *Pseudomonas aeruginosa* strain CCUG 51971,

- Pseudomonas aeruginosa* strain E90, *Pseudomonas aeruginosa* strain FDAARGOS_571, *Pseudomonas aeruginosa* strain GIMC5002:PAT-169, *Pseudomonas aeruginosa* strain H26023, *Pseudomonas aeruginosa* strain L10, *Pseudomonas aeruginosa* strain M1608, *Pseudomonas aeruginosa* strain M37351, *Pseudomonas aeruginosa* strain MRSN12280, *Pseudomonas aeruginosa* strain NCTC13715, *Pseudomonas aeruginosa* strain Pa58, *Pseudomonas aeruginosa* strain PABL048, *Pseudomonas aeruginosa* strain PAK, *Pseudomonas aeruginosa* strain PASGNDM345, *Pseudomonas aeruginosa* strain PASGNDM699, *Pseudomonas aeruginosa* strain PA-VAP-3, *Pseudomonas aeruginosa* strain PB368, *Pseudomonas aeruginosa* strain PB369, *Pseudomonas aeruginosa* strain S0490, *Pseudomonas aeruginosa* strain ST773, *Pseudomonas aeruginosa* strain T2436, *Pseudomonas aeruginosa* strain W60856, *Pseudomonas aeruginosa* strain WPB099, *Pseudomonas aeruginosa* strain WPB100, *Pseudomonas aeruginosa* strain WPB101, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* VRFPA04, *Pseudomonas amygdali* pv. *lachrymans* str. M301315, *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas avellanae* strain R2leaf, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas coronafaciens* pv. *oryzae* str. 1_6, *Pseudomonas coronafaciens* strain X-1, *Pseudomonas otitidis* MrB4, *Pseudomonas salegens* strain CECT 8338, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas savastanoi* pv. *savastanoi* NCPPB 3335, *Pseudomonas* sp. KBS0707, *Pseudomonas* sp. LPH1, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* group genomsp. 3 isolate CFBP6411, *Pseudomonas syringae* isolate CFBP3840, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *actinidiae* ICMP 18884, *Pseudomonas syringae* pv. *actinidiae* ICMP 9853, *Pseudomonas syringae* pv. *actinidiae* str. Shaanxi_M228, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 12.29, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 14.08, *Pseudomonas syringae* pv. *actinidiae* strain MAFF212063, *Pseudomonas syringae* pv. *actinidiae* strain NZ-45, *Pseudomonas syringae* pv. *actinidiae* strain NZ-47, *Pseudomonas syringae* pv. *actinidiae* strain P155, *Pseudomonas syringae* pv. *avii* isolate CFBP3846, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *tomato* str. DC3000, *Pseudomonas syringae* pv. *tomato* strain B13-200, *Pseudomonas syringae* pv. *tomato* strain delta IV/IX, *Pseudomonas syringae* pv. *tomato* strain delta VI, *Pseudomonas syringae* pv. *tomato* strain delta X, *Pseudomonas syringae* strain CFBP 2116 and *Pseudomonas syringae* strain Ps25, which strains have NCBI Accession Numbers respectively of AP017302.1, CP012001.1, LN831024.1, CP017969.1, LT608330.1, AP012280.1, CP020659.1, CP041772.1, CP029605.1, CP032761.1, CP041774.1, CP027538.1, CP027172.1, CP027171.1, CP030328.1, CP015377.1, CP043328.1, CP044006.1, CP033833.1, CP043549.1, CP033685.1, CP019338.1, CP008862.2, CP008863.1, CP028162.1, LR134330.1, CP021775.1, CP039293.1, LR657304.1, CP020703.1, CP020704.1, CP028330.1, CP025050.1, CP025049.1, CP011369.1,

CP041945.1, CP039988.1, CP008864.2, CP031878.1, CP031877.1, CP031876.1, CP034244.1, CP000438.1, CP008739.2, CP031225.1, CP020351.1, CP026558.1, CP042804.1, CP026562.1, CP046441.1, CP046035.1, CP050260.1, AP022642.1, LT629787.1, CP000058.1, CP008742.1, CP041754.1, CP017290.1, CP007014.1, LT963408.1, LT963409.1, CP012179.1, CP011972.2, 5 CP018202.1, CP032631.1, CP019730.1, CP019732.1, CP024712.1, CP017007.1, CP017009.1, CP032871.1, LT963402.1, LT963391.1, CP047260.1, AE016853.1, CP019871.1, CP047072.1, CP047071.1, CP047073.1, LT985192.1 and CP034558.1, or an orthologue or homologue of such a pump. Optionally, such RND efflux protein is encoded by gene *P. syringae* PSPTO_0820 or an orthologue or homologue thereof.

10

Example Non-*Pseudomonas* Strains

For example, the target cell is a cell of a strain selected from *Azotobacter chroococcum* NCIMB 8003, *Azotobacter chroococcum* strain B3, *Azotobacter salinestris* strain KACC 13899, *Burkholderia ambifaria* MC40-6, *Burkholderia cenocepacia* AU 1054 chromosome 1, *Burkholderia cenocepacia* 15 HI2424 chromosome 3, *Burkholderia cenocepacia* MC0-3, *Burkholderia cenocepacia* strain CR318 chromosome 3, *Burkholderia cenocepacia* strain FDAARGOS_720, *Burkholderia lata* strain A05, *Burkholderia pyrrocinia* strain mHSR5, *Cupriavidus basilensis* strain 4G11, *Cupriavidus necator* N-1 plasmid pBB1, *Cupriavidus taiwanensis* STM 3679, *Lysobacter gummosus* strain 3.2.11, *Paraburkholderia sprentiae* WSM5005, *Paraburkholderia terricola* strain mHS1, *Ralstonia* 20 *pseudosolanacearum* strain CRMrs218, *Ralstonia solanacearum* strain UA-1591, *Variovorax paradoxus* S110, *Variovorax* sp. PBL-H6, *Xanthomonas arboricola* pv. *juglandis* strain Xaj 417, *Xanthomonas arboricola* pv. *pruni* strain 15-088, *Xanthomonas arboricola* strain 17, *Xanthomonas axonopodis* pv. *dieffenbachiae* LMG 695, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO18C8, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO98C12, *Xanthomonas campestris* pv. *campestris* 25 MAFF302021, *Xanthomonas citri* pv. *glycines* strain 2098, *Xanthomonas euvesicatoria* strain LMG930, *Xanthomonas perforans* strain LH3 and *Xanthomonas* sp. ISO98C4, which strains have NCBI Accession Numbers respectively of CP010415.1, CP011835.1, CP045302.1, CP001027.1, CP000378.1, CP000460.1, CP000960.1, CP017240.1, CP050980.1, CP024945.1, CP024903.1, CP010537.1, CP002879.1, LT984803.1, CP011131.1, CP017561.1, CP024941.1, CP021764.1, 30 CP034195.1, CP001636.1, LR594659.1, CP012251.1, CP044334.1, CP011256.1, CP014347.1, CP012063.1, CP012057.1, AP019684.1, CP041965.1, CP018467.1, CP018475.1 and CP012060.1.

For example, the target cell comprises a RND efflux pump or RND efflux pump protein of a strain selected from

35 (a) *Pseudomonas aeruginosa* strain: IOMTU 133, *Pseudomonas aeruginosa* DSM 50071, *Pseudomonas aeruginosa* genome assembly NCTC10332, *Pseudomonas aeruginosa* isolate B10W,

- Pseudomonas aeruginosa* isolate PA14Or, *Pseudomonas aeruginosa* NCGM2.S1, *Pseudomonas aeruginosa* PAK, *Pseudomonas aeruginosa* strain 243931, *Pseudomonas aeruginosa* strain 24Pae112, *Pseudomonas aeruginosa* strain 268, *Pseudomonas aeruginosa* strain 60503, *Pseudomonas aeruginosa* strain AR_0095, *Pseudomonas aeruginosa* strain AR_0353, *Pseudomonas aeruginosa* strain AR_0354,
- 5 *Pseudomonas aeruginosa* strain AR_455, *Pseudomonas aeruginosa* strain BAMCPA07-48, *Pseudomonas aeruginosa* strain CCUG 51971, *Pseudomonas aeruginosa* strain E90, *Pseudomonas aeruginosa* strain FDAARGOS_571, *Pseudomonas aeruginosa* strain GIMC5002:PAT-169, *Pseudomonas aeruginosa* strain H26023, *Pseudomonas aeruginosa* strain L10, *Pseudomonas aeruginosa* strain M1608, *Pseudomonas aeruginosa* strain M37351, *Pseudomonas aeruginosa* strain
- 10 MRSN12280, *Pseudomonas aeruginosa* strain NCTC13715, *Pseudomonas aeruginosa* strain Pa58, *Pseudomonas aeruginosa* strain PABL048, *Pseudomonas aeruginosa* strain PAK, *Pseudomonas aeruginosa* strain PASGNDM345, *Pseudomonas aeruginosa* strain PASGNDM699, *Pseudomonas aeruginosa* strain PA-VAP-3, *Pseudomonas aeruginosa* strain PB368, *Pseudomonas aeruginosa* strain PB369, *Pseudomonas aeruginosa* strain S04 90, *Pseudomonas aeruginosa* strain ST773, *Pseudomonas aeruginosa* strain T2436, *Pseudomonas aeruginosa* strain W60856, *Pseudomonas aeruginosa* strain WPB099, *Pseudomonas aeruginosa* strain WPB100, *Pseudomonas aeruginosa* strain WPB101, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* VRFPA04, *Pseudomonas amygdali* pv. *lachrymans* str. M301315, *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244,
- 20 *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas avellanae* strain R2leaf, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas coronafaciens* pv. *oryzae* str. 1_6, *Pseudomonas coronafaciens* strain X-1, *Pseudomonas otitidis* MrB4, *Pseudomonas salegens* strain CECT 8338, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas savastanoi* pv. *savastanoi* NCPPB 3335, *Pseudomonas* sp. KBS0707, *Pseudomonas* sp. LPH1, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* group genomsp. 3 isolate CFBP6411, *Pseudomonas syringae* isolate CFBP3840, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *actinidiae* ICMP 18884, *Pseudomonas syringae* pv. *actinidiae* ICMP 9853, *Pseudomonas syringae* pv. *actinidiae* str. Shaanxi_M228, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 12.29, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 14.08, *Pseudomonas syringae* pv. *actinidiae* strain MAFF212063, *Pseudomonas syringae* pv. *actinidiae* strain NZ-45, *Pseudomonas syringae* pv. *actinidiae* strain NZ-47, *Pseudomonas syringae* pv. *actinidiae* strain P155, *Pseudomonas syringae* pv. *avii* isolate CFBP3846, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *tomato* str. DC3000, *Pseudomonas syringae* pv. *tomato* strain B13-200, *Pseudomonas syringae* pv. *tomato* strain delta
- 35 IV/IX, *Pseudomonas syringae* pv. *tomato* strain delta VI, *Pseudomonas syringae* pv. *tomato* strain delta X, *Pseudomonas syringae* strain CFBP 2116 and *Pseudomonas syringae* strain Ps25, which

- strains have NCBI Accession Numbers respectively of AP017302.1, CP012001.1, LN831024.1, CP017969.1, LT608330.1, AP012280.1, CP020659.1, CP041772.1, CP029605.1, CP032761.1, CP041774.1, CP027538.1, CP027172.1, CP027171.1, CP030328.1, CP015377.1, CP043328.1, CP044006.1, CP033833.1, CP043549.1, CP033685.1, CP019338.1, CP008862.2, CP008863.1, CP028162.1, LR134330.1, CP021775.1, CP039293.1, LR657304.1, CP020703.1, CP020704.1, CP028330.1, CP025050.1, CP025049.1, CP011369.1, CP041945.1, CP039988.1, CP008864.2, CP031878.1, CP031877.1, CP031876.1, CP034244.1, CP000438.1, CP008739.2, CP031225.1, CP020351.1, CP026558.1, CP042804.1, CP026562.1, CP046441.1, CP046035.1, CP050260.1, AP022642.1, LT629787.1, CP000058.1, CP008742.1, CP041754.1, CP017290.1, CP007014.1, LT963408.1, LT963409.1, CP012179.1, CP011972.2, CP018202.1, CP032631.1, CP019730.1, CP019732.1, CP024712.1, CP017007.1, CP017009.1, CP032871.1, LT963402.1, LT963391.1, CP047260.1, AE016853.1, CP019871.1, CP047072.1, CP047071.1, CP047073.1, LT985192.1 and CP034558.1, or an orthologue or homologue of such a pump; or
- (b) *Azotobacter chroococcum* NCIMB 8003, *Azotobacter chroococcum* strain B3, *Azotobacter salinestris* strain KACC 13899, *Burkholderia ambifaria* MC40-6, *Burkholderia cenocepacia* AU 1054 chromosome 1, *Burkholderia cenocepacia* HI2424 chromosome 3, *Burkholderia cenocepacia* MC0-3, *Burkholderia cenocepacia* strain CR318 chromosome 3, *Burkholderia cenocepacia* strain FDAARGOS_720, *Burkholderia lata* strain A05, *Burkholderia pyrrocinia* strain mHSR5, *Cupriavidus basilensis* strain 4G11, *Cupriavidus necator* N-1 plasmid pBB1, *Cupriavidus taiwanensis* STM 3679, *Lysobacter gummosus* strain 3.2.11, *Paraburkholderia sprentiae* WSM5005, *Paraburkholderia terricola* strain mHS1, *Ralstonia pseudosolanacearum* strain CRMRS218, *Ralstonia solanacearum* strain UA-1591, *Variovorax paradoxus* S110, *Variovorax* sp. PBL-H6, *Xanthomonas arboricola* pv. *juglandis* strain Xaj 417, *Xanthomonas arboricola* pv. *pruni* strain 15-088, *Xanthomonas arboricola* strain 17, *Xanthomonas axonopodis* pv. *dieffenbachiae* LMG 695, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO18C8, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO98C12, *Xanthomonas campestris* pv. *campestris* MAFF302021, *Xanthomonas citri* pv. *glycines* strain 2098, *Xanthomonas euvesicatoria* strain LMG930, *Xanthomonas perforans* strain LH3 and *Xanthomonas* sp. ISO98C4, which strains have NCBI Accession Numbers respectively of CP010415.1, CP011835.1, CP045302.1, CP001027.1, CP000378.1, CP000460.1, CP000960.1, CP017240.1, CP050980.1, CP024945.1, CP024903.1, CP010537.1, CP002879.1, LT984803.1, CP011131.1, CP017561.1, CP024941.1, CP021764.1, CP034195.1, CP001636.1, LR594659.1, CP012251.1, CP044334.1, CP011256.1, CP014347.1, CP012063.1, CP012057.1, AP019684.1, CP041965.1, CP018467.1, CP018475.1 and CP012060.1, or an orthologue or homologue of such a pump. Optionally, such RND efflux protein is encoded by gene *P. syringae* *PSPTO_0820* or an orthologue or homologue thereof.
- For example, the target cell comprises an RND efflux pump protein encoded by gene *P. syringae* *PSPTO_0820* or an orthologue or homologue thereof.

For example, when the target cell comprises an RND efflux pump protein encoded by gene *P syringae* *PSPTO_0820* or an orthologue or homologue thereof. The target cell is an *Azotobacter*, *Burkholderia*, *Cupriavidus*, *Lysobacter*, *Paraburkholderia*, *Ralstonia*, *Variovorax*, *Xanthomonas* or *Pseudomonas* cell. For example, the target cell is a cell of a *Pseudomonas* species, optionally wherein the species is selected from *Pseudomonas aeruginosa*, *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*, *Pseudomonas coronafaciens*, *Pseudomonas otitidis*, *Pseudomonas putida*, *Pseudomonas salegens*, *Pseudomonas savastanoi*, *Pseudomonas syringae* and *Pseudomonas viridiflava*. For example, the target cell is a cell of a species selected from *Azotobacter chroococcum*, *Azotobacter salinestris*, *Burkholderia ambifaria*, *Burkholderia cenocepacia*, *Burkholderia lata*, *Burkholderia pyrrocinia*, *Cupriavidus basilensis*, *Cupriavidus necator*, *Cupriavidus taiwanensis*, *Lysobacter gummosus*, *Paraburkholderia sprentiae*, *Paraburkholderia terricola*, *Ralstonia pseudosolanacearum*, *Ralstonia solanacearum*, *Variovorax paradoxus*, *Xanthomonas arboricola*, *Xanthomonas axonopodis*, *Xanthomonas campestris*, *Xanthomonas citri*, *Xanthomonas euvesicatoria* and *Xanthomonas perforans*.

PSPTO_4977, Orthologues & Homologues

A *PSPTO_4977* gene orthologue or homologue may be gene comprised any of the following strains.

Example Non-*Pseudomonas* Strains

For example, the target cell is a cell of a strain selected from *Stenotrophomonas rhizophila* strain GA1, *Enterococcus faecalis* strain V583 and *Paucimonas lemoignei* strain NCTC10937, which strains have NCBI Accession Numbers respectively CP031729.1, CP022312.1 and LS483371.1.

Example *Pseudomonas* Strains

For example, the target cell is a cell of a strain selected from *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas asturiensis* strain CC1524, *Pseudomonas avellanae* strain R2, *Pseudomonas cerasi* isolate PL963, *Pseudomonas chlororaphis* strain PCL1606, *Pseudomonas chlororaphis* subsp. *aurantiaca* strain JD37, *Pseudomonas chlororaphis* subsp. *aureofaciens* strain ChPhzTR36, *Pseudomonas chlororaphis* subsp. *chlororaphis* strain DSM 50083, *Pseudomonas chlororaphis* subsp. *piscium* strain DSM 21509, *Pseudomonas cichorii* JBC1, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas putida* GB-1 chromosome, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas* sp. 09C 129, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *lapsea* strain ATCC 10859, *Pseudomonas syringae* pv.

maculicola str. ES4326, *Pseudomonas syringae* pv. pisi str. PP1, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* UMAF0158 and *Pseudomonas viridiflava* strain CFBP 1590, which strains have NCBI Accession Numbers respectively of CP020351.1, CP026558.1, CP042804.1, CP047265.1, CP026562.1, LT963395.1, CP011110.1, CP009290.1, CP027721.1, CP027712.1, CP027707.1, CP007039.1, CP046441.1, CP000926.1, CP000058.1, CP025261.1, CP007014.1, CP012179.1, LT963391.1, CP013183.1, CP047260.1, CP034078.1, CP005969.1, AE016853.1, CP005970.1 and LT855380.1.

For example, the target cell comprises a RND efflux pump or RND efflux pump protein of a strain selected from

(a) *Stenotrophomonas rhizophila* strain GA1, *Enterococcus faecalis* strain V583 and *Paucimonas lemoignei* strain NCTC10937, which strains have NCBI Accession Numbers respectively CP031729.1, CP022312.1 and LS483371.1, or an orthologue or homologue of such a pump; or

(b) *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas asturiensis* strain CC1524, *Pseudomonas avellanae* strain R2, *Pseudomonas cerasi* isolate PL963, *Pseudomonas chlororaphis* strain PCL1606, *Pseudomonas chlororaphis* subsp. *aurantiaca* strain JD37, *Pseudomonas chlororaphis* subsp. *aureofaciens* strain ChPhzTR36, *Pseudomonas chlororaphis* subsp. *chlororaphis* strain DSM 50083, *Pseudomonas chlororaphis* subsp. *piscium* strain DSM 21509, *Pseudomonas cichorii* JBC1, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas putida* GB-1 chromosome, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas* sp. 09C 129, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *lapse* strain ATCC 10859, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *pisi* str. PP1, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* UMAF0158 and *Pseudomonas viridiflava* strain CFBP 1590, which strains have NCBI Accession Numbers respectively of CP020351.1, CP026558.1, CP042804.1, CP047265.1, CP026562.1, LT963395.1, CP011110.1, CP009290.1, CP027721.1, CP027712.1, CP027707.1, CP007039.1, CP046441.1, CP000926.1, CP000058.1, CP025261.1, CP007014.1, CP012179.1, LT963391.1, CP013183.1, CP047260.1, CP034078.1, CP005969.1, AE016853.1, CP005970.1 and LT855380.1, or an orthologue or homologue of such a pump.

For example, the target cell comprises an RND efflux pump protein encoded by gene *P syringae* *PSPTO_4977* or an orthologue or homologue thereof.

For example, when the target cell comprises an RND efflux pump protein encoded by gene *P syringae* *PSPTO_4977* or an orthologue or homologue thereof: The target cell is a *Stenotrophomonas*,

Enterococcus, *Paucimonas* or *Pseudomonas* cell. For example, the target cell is a cell of a *Pseudomonas* species, optionally wherein the species is selected from *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*, *Pseudomonas coronafaciens*, *Pseudomonas putida*, *Pseudomonas savastanoi*,
 5 *Pseudomonas syringae* and *Pseudomonas viridiflava*. For example, the target cell is a cell of a species selected from *Stenotrophomonas rhizophila*, *Enterococcus faecalis*, *Paucimonas lemoignei*, *Pseudomonas amygdali*, *Pseudomonas asturiensis*, *Pseudomonas avellanae*, *Pseudomonas cerasi*, *Pseudomonas chlororaphis*, *Pseudomonas cichorii*, *Pseudomonas coronafaciens*, *Pseudomonas putida*, *Pseudomonas savastanoi*, *Pseudomonas syringae* and *Pseudomonas viridiflava*.

10

Example Carrier Cells

For example, each carrier cell is a gram-positive bacterial cell. For example, each carrier cell is a gram-negative bacterial cell. For example, the carrier cell is a cell of a genus or species disclosed in Table 1 of WO2017211753 (the disclosure of this table and each genus and species individually being
 15 incorporated herein for disclosure of cell genus or species that may be used in the present invention).

20

For example, the carrier cell is a cell of phylum *Proteobacteria*, class *Gammaproteobacteria*, order *Pseudomonadales* or family *Pseudomonadaceae*. In a preferred example, the carrier is a *Pseudomonas* (eg, *P. fluorescens*) cell.

25

For example, the carrier is an *E. coli* cell (eg, *E. coli*, K12, Nissle or S17 cell).

For example, the carrier is a gram positive cell, eg, a *Bacillus* (such as *Bacillus subtilis*) or *Clostridiales* (such as *Clostridium butyricum*) cell.

30

In an example, the subject is a shellfish. The shellfish may be selected from shrimp, crayfish, crab, lobster, clam, scallop, oyster, prawn and mussel.

The subject may be any subject disclosed herein. The subject may be an animal, such as a livestock animal, eg, a bird (such as a poultry bird; or a chicken or a turkey) or swine,

In an alternative, the subject is a plant, eg, and the target bacteria are plant pathogen bacteria. In an example, the target bacteria are *Pseudomonas*, eg, *P. syringae* or *P. aeruginosa*.

In an alternative, the carrier and target cells are archaeal cells. For example the target cells are methanobacterium cells. For example the target cells are methanogen cells. For example, the target cells comprise one or more species of cell selected from:

- *Methanobacterium bryantii*
- 5 • *Methanobacterium formicum*
- *Methanobrevibacter arboriphilicus*
- *Methanobrevibacter gottschalkii*
- *Methanobrevibacter ruminantium*
- *Methanobrevibacter smithii*
- 10 • *Methanococcus chunghsingensis*
- *Methanococcus burtonii*
- *Methanococcus aeolicus*
- *Methanococcus deltae*
- *Methanococcus jannaschii*
- 15 • *Methanococcus maripaludis*
- *Methanococcus vannielii*
- *Methanocorpusculum labreanum*
- *Methanoculleus bourgensis* (*Methanogenium olentangyi* & *Methanogenium bourgense*)
- *Methanoculleus marisnigri*
- 20 • *Methanoflorens stordalenmirensis*[34]
- *Methanofollis liminatans*
- *Methanogenium cariaci*
- *Methanogenium frigidum*
- *Methanogenium organophilum*
- 25 • *Methanogenium wolfei*
- *Methanomicrobium mobile*
- *Methanopyrus kandleri*
- *Methanoregula boonei*
- *Methanosaeta concilii*
- 30 • *Methanosaeta thermophila*
- *Methanosarcina acetivorans*
- *Methanosarcina barkeri*
- *Methanosarcina mazei*
- *Methanosphaera stadtmanae*
- 35 • *Methanospirillum hungatei*
- *Methanothermobacter defluvii* (*Methanobacterium defluvii*)

- *Methanothermobacter thermautotrophicus* (*Methanobacterium thermoautotrophicum*)
- *Methanothermobacter thermoflexus* (*Methanobacterium thermoflexum*)
- *Methanothermobacter wolfei* (*Methanobacterium wolfei*)
- *Methanothrix soehngenii*

5

Optionally, the target cells are not pathogenic to the subject, for example when the method is a non-medical method. In an example, the method is a cosmetic method.

10 For example, the target cells are methane-producing cells, and optionally the subject is a livestock animal, preferably a ruminant, or a cow (eg, a beef or dairy cattle). By reducing methane-producing cells in such animal, the invention may in one embodiment enhance the weight of the animal (eg, enhance the yield of meat from the animal) and/or enhance the yield of milk or another product of the animal, such as fur or fat.

15 In an example, the target cells are selected from *E. coli*, *Salmonella* and *Campylobacter* cells. In an example, the target cells are *E. coli*, *Salmonella* or *Campylobacter* cells. In an example, each animal is a chicken (eg, a broiler or hen-layer) and the target cells are *Salmonella* or *Campylobacter* cells. In an example, each animal is a cow (eg, a beef or dairy cow) and the target cells are methanogen cells.

20 In an example, the target cells are selected from *Mycoplasma* (eg, *Mycoplasma mycoides* (eg, *Mycoplasma mycoides* subsp. *Mycoides*), *Mycoplasma leachii* or *Mycoplasma bovis*), *Brucella abortus*, *Listeria monocytogenes*, *Clostridium* (eg, *Clostridium chauvoei* or *Clostridium septicum*), *Leptospira* (eg, *L. canicola*, *L. icterohaemorrhagiae*, *L. grippotyphosa*, *L. hardjo* or *L. Pomona*), *Mannheimia haemolytica*, *Trueperella pyogenes*, *Mycobacterium bovis*, *Campylobacter* spp. (eg, *Campylobacter jejuni* or *Campylobacter coli*), *Bacillus anthracis*, *E. coli* (eg, *E. coli* O157:H7) or *Pasteurella multocida* (eg, *Pasteurella multocida* B:2, E:2, A:1 or A:3). In the example, optionally the subject or animal is a livestock animal, such as a cow, sheep, goat or chicken (preferably a cow).

30 Optionally, eg, wherein the subject is an animal (eg, a livestock animal or a wild animal), the target cells are zoonotic bacterial cells, such as cells of a species selected from *Bacillus anthracis*, *Mycobacterium bovis* (eg, wherein the animal is a cow), *Campylobacter* spp (eg, wherein the animal is a poultry animal), *Mycobacterium marinum* (eg, wherein the animal is a fish), Shiga toxin-producing *E. coli* (eg, wherein the animal is a ruminant), *Listeria* spp (eg, wherein the animal is a cow or sheep), *Chlamydia abortus* (eg, wherein the animal is a sheep), *Coxiella burnetii* (eg, wherein the animal is a cow, sheep or goat), *Salmonella* spp (eg, wherein the animal is a poultry animal),

35

Streptococcus suis (eg, wherein the animal is a pig) and Corynebacterium (eg, C ulcerans) (eg, wherein the animal is a cow).

5 In an example, a plurality of carrier cells as described herein (eg, carrier cells of any configuration, aspect, example or embodiment described herein) is administered to the subject, wherein the carrier cells comprise the plasmid DNA encoding the agent.

10 In an example, each animal is a chicken (eg, a broiler or hen-layer) and the target cells are *Salmonella* or *Campylobacter* cells. In an example, each animal is a cow (eg, a beef or dairy cow) and the target cells are methanogen cells.

Optionally, the target cells are *Salmonella* cells. In an example, the target cells comprise *S enterica* and/or *S typhimurium* cells; optionally wherein the *S enterica* is *S enterica* subspecies *enterica*.
 15 Optionally, the method kills a plurality of different *S enterica* subspecies *enterica* serovars; optionally wherein each serovar is selected from the group consisting of Typhimurium, Enteritidis, Virchow, Montevideo, Heidelberg, Hadar, Binza, Bredeney, Infantis, Kentucky, Seftenberg, Mbandaka, Anatum, Agona and Dublin. Optionally, the method kills *S enterica* subspecies *enterica* serovars Typhimurium, Infantis and Enteritidis. Optionally, the method kills *S enterica* subspecies *enterica* serovars Typhimurium and Enteritidis. Optionally, the method kills *S enterica* subspecies *enterica* serovars Typhimurium and Infantis. Optionally, the method kills *S enterica* subspecies *enterica* serovars Enteritidis and Infantis. The most prevalent serovars in chicken are *Salmonella Enteritidis*, *Salmonella Infantis* and *Salmonella Typhimurium*. In general, similar serovars of *Salmonella* are found in infected humans and chicken (*S. Enteritidis* and *S. Typhimurium*). By killing *Salmonella* in livestock animals, the invention is useful for reducing the pool of zoonotic bacteria that are available
 20 for transmission to humans (such as by eating the livestock or products made therefrom, such as meat or dairy products for human consumption).
 25

Advantageously, the carrier cells are *Enterobacteriaceae* cells, optionally *E coli* cells. Optionally, the method kills *S enterica* subspecies *enterica* serovars Typhimurium and Enteritidis serovars.
 30

Optionally the method reduces target cells in the gastrointestinal tract of the animal; optionally the method reduces target cells in the jejunum, ileum, colon, liver, spleen or caecum of the animal; optionally wherein the animal is a bird and the method reduces target cells in the caecum of the bird. This may be important to reduce spread of zoonotic or other detrimental target strains in the faeces of
 35 the subjects, such as livestock animals. Thus, in an example the method is carried out on a group of

subjects (eg, a herd or flock, such as a herd of swine or a flock of birds), wherein spread of cells of the target species is reduced in the group.

Thus, in an example the method is carried out on a group (optionally a flock or herd) of animals,
5 wherein some or all of the animals comprise target cells (eg, *Salmonella* cells), wherein spread of cells of the target species is reduced in the group; or wherein spread is reduced from the group to a second group of animals.

Optionally, the plasmid comprises a RP4 origin of transfer (oriT). The plasmid may be any type of
10 plasmid disclosed herein.

The agent may be any antibacterial agent disclosed herein, preferably a guided nuclease that is programmed to cut one or more target sequences in target cells. A suitable nuclease may be a TALEN, meganuclease, zinc finger nuclease or Cas nuclease. For example, the agent comprises one
15 or more components (eg, a Cas nuclease and/or a guide RNA or a crRNA) of a CRISPR/Cas system that is operable in a target cell to cut a protospacer sequence comprised by the target cell, optionally wherein the target cells comprise first and second strains of a bacterial species and each strain comprises the protospacer sequence, wherein cells of the strains are killed. For example, the system is operable to cut at least 3 different protospacer sequences comprised by the cell genome. Optionally,
20 each or some of said protospacer sequences is comprised by a pathogenicity island that is comprised by the cell. Optionally, the agent is operable to cut a plurality of different protospacer sequences comprised by the target cell genome. Optionally, the agent comprises one or more components of a CRISPR/Cas system that is operable in a target cell to cut at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different protospacer sequences comprised by the target cell genome (eg, comprised by the target cell
25 chromosome).

In an embodiment, the agent

(a) comprises a guided nuclease that is capable of recognising and modifying a target nucleic acid sequence, wherein the target sequence is comprised by an endogenous chromosome or
30 episome of the target cells but is not comprised by the carrier cells, wherein the nuclease modifies the chromosome or episome to kill the target cells or inhibit the growth or proliferation of the target cells; and/or

(b) encodes a guide RNA or crRNA of a CRISPR/Cas system that operates with a Cas nuclease in the target cells to cut a protospacer sequence comprised by the target cells.

35

Optionally, each target cell is a *Salmonella* cell and each carrier cell is an *Enterobacteriaceae* cell.

Optionally, the target cell are cells of a species or strain that is pathogenic to the subject and the method treats or reduces a symptom of an infection by pathogenic target cells.

- Any administration of cells to a subject herein may be by oral administration. Any administration of
 5 cells to a subject herein may preferably be by administration to the GI tract. Any administration of cells to a subject herein may be by systemic, intranasal or inhaled administration.

There is also provided:

- A non-medical method of killing zoonotic bacterial target cells in an animal, the method comprising
 10 administering to the animal a plurality of the carrier cells, wherein said plasmids are transferred from carrier cells into target cells for expression therein to produce the antibacterial agent, thereby killing target cells in the subject or reducing the growth or proliferation of target cells, optionally wherein the target cells are *Salmonella* cells and/or the carrier cells are *Enterobacteriaceae* cells.
- 15 The animal may be any animal disclosed herein, eg, a livestock animal, domesticated animal or wild animal (eg, a bat or bird)).

Optionally, any method herein reduces *Salmonella* in the gastrointestinal tract of the subject.

- Optionally, the target cells comprise different *Salmonella* spp. types that are killed.
 20

There is provided the following definitions:-

- Homologue:** A gene, nucleotide or protein sequence related to a second gene, nucleotide or protein sequence by descent from a common ancestral DNA or protein sequence. The term, homologue, may apply to the relationship between genes separated by the event of or to the relationship between genes
 25 separated by the event of genetic duplication.

Orthologue: Orthologues are genes, nucleotide or protein sequences in different species that evolved from a common ancestral gene, nucleotide or protein sequence by speciation. Normally, orthologues retain the same function in the course of evolution.

- 30 Optionally any *Salmonella* herein is *Salmonella enterica* subsp. *enterica* serovar Typhimurium str. LT2.

- Optionally, each plasmid encodes a plurality of guide RNAs or crRNAs of a CRISPR/Cas system wherein the guide RNAs or crRNAs are operable with Cas nuclease in the target cell to recognise a
 35 plurality of protospacer sequences comprised by the target cell genome, optionally wherein the target cell is a *Salmonella* cell and the protospacer sequences comprise one or more nucleotide sequences of

genes selected from *invB*, *sicP* and *sseE*. For example, the protospacer sequences comprise nucleotide sequences of genes *invB*, *sicP* and *sseE*. In an example, the plasmid also encodes a Cas, eg, a Cas9, Cas3, Cpf1, Cas12, Cas13, CasX or CasY. In an embodiment, the Cas is a Type I, II, III, IV, V or VI Cas, preferably a Type I or II Cas. In an example, the DNA also encodes a Cas3 and
 5 cognate Cascade proteins (eg, CasA, B, C, D and E). Optionally, the Cas (and Cascade of present) are *E coli* Cas (and Cascade).

The plasmid may comprise one or more CRISPR spacers, wherein each spacer consists of 20-40, 25-35, or 30-35 consecutive nucleotides of a gene comprised by the genome of the target cell; eg,
 10 (a) a gene selected from *avrA*, *sptP*, *sicP*, *sipA*, *sipD*, *sipC*, *sipB*, *sicA*, *invB*, *ssaE*, *sseA*, *sseB*, *sscA*, *sseC*, *sseD*, *sseE*, *sscB*, *sseF*, *sseG*, *mgtC*, *cigR*, *pipA*, *pipB*, *pipC*, *sopB* and *pipD* of *Salmonella* or a homologue or orthologue thereof;
 (b) a gene comprised by a pathogenicity island that is comprised by the target cell genome;
 (c) a secretion system (eg, a type III protein secretion system) gene comprised by the target cell
 15 genome.

Optionally, the plasmid comprises a RP4 origin of transfer (*oriT*) and/or a p15A origin of replication.

In an example, the plasmid is a conjugative phagemid.
 20

In an example, the plasmid encodes a Cas3 and optionally one or more Cascade proteins (eg, one or more of CasA, B, C, D and E). In an embodiment, the plasmid encodes a Cas3 and CasA, B, C, D and E. In an embodiment, the plasmid encodes an *E coli* Cas3 and CasA, B, C, D and E. Optionally, the guided nuclease (eg, Cas3) is a Type I-A, -B, -C, -D, -E, -F or -U Cas.
 25

In an example, the agent in any configuration, aspect, example, option or embodiment herein, the agent comprises one or more components of a CRISPR/Cas system that is operable in the target cell to cut a protospacer sequence comprised by the target cell.

30 In an example, the system is operable to cut at least 3 different protospacer sequences comprised by the target cell genome. In an embodiment, each or some of said protospacer sequences is comprised by a pathogenicity island that is comprised by the target cell.

In an example, the plasmid
 35 (a) encodes a guided nuclease that is capable of recognising and modifying a target cell nucleic acid sequence, wherein the target sequence is comprised by an endogenous

chromosome or episome of the target cell(s) but is not comprised by the carrier cell(s), wherein the nuclease modifies the chromosome or episome to kill the target cell(s) or inhibit the growth or proliferation of the target cell(s); and/or

- 5 (b) encodes a guide RNA or crRNA of a CRISPR/Cas system that operates with a Cas nuclease in the target cell to cut a protospacer sequence comprised by the target cell.

Optionally, the plasmid comprises a constitutive promoter for expression of the guide RNAs or crRNAs. Optionally, the plasmid comprises a constitutive promoter for expression of a Cas nuclease that is operable in a target cell with the guide RNAs or crRNAs to modify (eg, cut) protospacer
10 sequences of the target cell genome.

Optionally, the Cas, Cascade proteins, gRNAs and crRNAs are E. coli K12 (MG1655) Cas, Cascade proteins, gRNAs and crRNAs respectively. Optionally, the plasmid is devoid of nucleotide sequences encoding Cas1 and Cas2 proteins.

15 In embodiments, the growth or proliferation of target cells is reduced (eg, by at least 40, 50, 60, 70, 80, or 90% compared to growth in the absence of the agent). The invention finds application, for example, in controlling or killing target bacteria that are pathogenic to humans, animals or plants. The invention finds application, for example, in controlling or killing zoonotic target bacteria
20 comprised by an animal (eg, a livestock animal). For example, the carrier cells may be comprised by a medicament for treating or preventing a disease or condition in a human or animal; a growth promoting agent for administration to animals for promoting growth thereof; killing zoonotic bacteria in the animals; for administration to livestock as a pesticide; a pesticide to be applied to plants; or a plant fertilizer.

25 An advantage may be that the carrier cells may be used as producer cells in which DNA encoding the antibacterial agent can be replicated.

Example Plasmids

30 A method of delivery of any agent, such as a CRISPR-Cas system (or a component thereof) can be by bacterial conjugation, a natural process whereby a donor bacterium (carrier bacterium) transfers plasmid DNA from itself to a recipient bacterium (target bacterium). Donor bacteria elaborate a surface structure, the pilus which can be considered to be like a syringe or drinking straw through which the DNA is delivered. The donor pilus binds to the surface of a receptive recipient and this
35 event triggers the process of DNA transfer. Plasmids are suitable for this conjugative process, where the plasmid comprises DNA encoding the agent of the invention.

DNA transfer by conjugation may only take place with a 'susceptible recipient' but does not generally occur with a recipient carrying a similar type of plasmid. Because conjugation is via pilus bridge, it is possible for that bridge to attach itself not to a recipient but to the donor bacterium. This could result in a futile cycle of transfer of the plasmid DNA to itself. Plasmids thus naturally encode incompatibility factors. One is a surface arrayed protein that prevents the pilus binding to bacterium displaying that surface protein such as itself or any other bacterium carrying the same plasmid. Additionally, plasmids naturally encode another incompatibility system that closely regulates the copy number of the plasmid inside a bacterium. Thus, should a conjugation event manage to evade surface exclusion and start to transfer DNA by conjugation, the recipient will prevent that plasmid establishing as it already maintains the current copy number and will not accept and maintain a further unwanted additional copy.

In an example of the invention, the plasmid is a member of a plasmid incompatibility group, wherein the target cell does not comprise a plasmid of said group. Optionally, the plasmid of the invention is a member of the incompatibility group P (ie, the plasmid is an *incP* plasmid). *Salmonella* very rarely carry *incP* plasmids, so this *incP* plasmid is useful where the target cell is a *Salmonella* cell. For example within the *Enterobacteriaceae* the following is a non-exclusive list of potential plasmids that could use for delivery: *IncFI*, *IncFII*, *IncFIII*, *IncFIV*, *IncFV*, *IncM*, *Inc9*, *IncIO*, *Incl*, *IncA*, *IncB*, *IncC*, *IncH*, *IncIa*, *IncIIc*, *IncI2*, *IncIy*, *IncJ*, *IncL*, *IncN*, *Inc2e*, *IncO*, *IncP*, *IncS*, *IncT* and/or *IncW*. Thus, optionally, the target cell is an *Enterobacteriaceae* cell and the DNA of the invention is comprised by a plasmid, wherein the plasmid is selected from an *IncFI*, *IncFII*, *IncFIII*, *IncFIV*, *IncFV*, *IncM*, *Inc9*, *IncIO*, *Incl*, *IncA*, *IncB*, *IncC*, *IncH*, *IncIa*, *IncIIc*, *IncI2*, *IncIy*, *IncJ*, *IncL*, *IncN*, *Inc2e*, *IncO*, *IncP*, *IncS*, *IncT* and *IncW* plasmid.

In an example, the carrier cell of the invention comprises two or more plasmids, each plasmid comprising a DNA that encodes an antibacterial agent, wherein a first of said plasmids is a member of a first incompatibility group, wherein the target cell does not comprise a plasmid of said first group, and wherein a second of said plasmids is a member of a second incompatibility group, wherein the target cell does not comprise a plasmid of said second group. For example, a carrier cell may comprise an *incP* plasmid encoding an anti-target cell CRISPR-Cas system or a component thereof (eg, encoding a first crRNA or guide RNA that targets a first protospacer sequence of the target cell genome) and wherein the carrier cell further comprises an *incFI* plasmid encoding an anti-target cell CRISPR-Cas system or a component thereof (eg, encoding a second crRNA or guide RNA that targets a second protospacer sequence of the target cell genome), the protospacers comprising different nucleotide sequences. For example, the protospacers are comprised by different genes of the target

cell genome. For example, the protospacers are comprised by one or more pathogenicity islands of the target cell genome. Optionally, the target cell is an *Enterobacteriaceae* cell. Optionally, the carrier cell comprises a group of plasmids comprising 2, 3, 4, 5, 6 or more different types of plasmid, wherein each plasmid is capable of being conjugatively transferred into a target cell, wherein the

5 plasmids encode different agents or different components of an antibacterial agent. For example, the plasmids encode different crRNAs or gRNAs that target different protospacers comprised by the target cell genome. For example, the group of plasmids comprises up to n different types of plasmid, wherein the plasmids are members of up to n different incompatibility groups, eg, groups selected from *IncFI*, *IncFII*, *IncFIII*, *IncFIV*, *IncFV*, *IncM*, *Inc9*, *IncIO*, *IncI*, *IncA*, *IncB*, *IncC*, *IncH*, *IncIa*,

10 *IncIIc*, *IncI2*, *IncIy*, *IncJ*, *IncL*, *IncN*, *Inc2e*, *IncO*, *IncP*, *IncS*, *IncT* and *IncW*. For example, $n=2$, 3, 4, 5, 6, 7, 8, 9 or 10.

For example, the carrier cell comprises (i) a first plasmid that encodes a first type of CRISPR/Cas system that targets a first protospacer comprised by the target cell genome, or encodes a component of

15 said system; and (ii) a second plasmid that encodes a second type of CRISPR/Cas system that targets a second protospacer comprised by the target cell genome, or encodes a component of said system, wherein the first and second types are different. For example, the first type is a Type I system, and the second type is a Type II system (eg, the first plasmid encodes a Cas3, Cascade and a crRNA or guide RNA that is operable with the Cas3 and Cascade in the target cell to modify the first

20 protospacer; and the second plasmid encodes a Cas9 and a crRNA or guide RNA that is operable with the Cas9 in the target cell to modify the second protospacer). In an alternative, the Cas3 and Cascade are encoded by an endogenous target cell gene, wherein the first plasmid encodes the crRNA or guide RNA that is operable with the endogenous Cas3 and Cascade in the target cell to modify the first protospacer. In an alternative, the Cas9 is encoded by an endogenous target cell gene, wherein the

25 second plasmid encodes the crRNA or guide RNA that is operable with the endogenous Cas9 in the target cell to modify the second protospacer. Optionally, the Cas3 and Cascade are encoded by endogenous genes of the target cell and the Cas9 is encoded by the second plasmid.

Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first

30 plasmid encoding a Type I CRISPR/Cas system (or component thereof, eg, a Cas3 or a crRNA or a gRNA) and a second plasmid encoding a Type III CRISPR/Cas system (or a component thereof).

Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type I CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type IV CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II

35 system, the invention alternatively provides in an embodiment a first plasmid encoding a Type I CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type V CRISPR/Cas

system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type I CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type VI CRISPR/Cas system (or a component thereof).

- 5 Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type II CRISPR/Cas system (or component thereof, eg, a Cas9 or a crRNA or a gRNA) and a second plasmid encoding a Type III CRISPR/Cas system (or a component thereof).
 Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type II CRISPR/Cas system (or component thereof) and a second plasmid
 10 encoding a Type IV CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type II CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type V CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type II CRISPR/Cas system (or component
 15 thereof) and a second plasmid encoding a Type VI CRISPR/Cas system (or a component thereof).

- Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type V CRISPR/Cas system (or component thereof, eg, a Cas12a or a crRNA) and a second plasmid encoding a Type III CRISPR/Cas system (or a component thereof). Instead of a
 20 Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type V CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type IV CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type V CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type V CRISPR/Cas system (or a
 25 component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment a first plasmid encoding a Type V CRISPR/Cas system (or component thereof) and a second plasmid encoding a Type VI CRISPR/Cas system (or a component thereof).

- Instead of a Type I and Type II system, the invention alternatively provides in an embodiment first
 30 and second plasmids, each encoding a Type I CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment first and second plasmids, each encoding a Type II CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment first and second plasmids, each encoding a Type III CRISPR/Cas system (or a component thereof). Instead of a Type
 35 I and Type II system, the invention alternatively provides in an embodiment first and second plasmids, each encoding a Type IV CRISPR/Cas system (or a component thereof). Instead of a

Type I and Type II system, the invention alternatively provides in an embodiment first and second plasmids, each encoding a Type V CRISPR/Cas system (or a component thereof). Instead of a Type I and Type II system, the invention alternatively provides in an embodiment first and second plasmids, each encoding a Type VI CRISPR/Cas system (or a component thereof).

5

Optionally, the plasmids are members of different incompatibility groups, eg. groups selected from *IncFI*, *IncFII*, *IncFIII*, *IncFIV*, *IncFV*, *IncM*, *Inc9*, *IncIO*, *Incl*, *IncA*, *IncB*, *IncC*, *IncH*, *Incla*, *Incllc*, *IncI2*, *IncIy*, *IncJ*, *IncL*, *IncN*, *Inc2e*, *IncO*, *IncP*, *IncS*, *IncT* and *IncW*. In an example here, the target cell is an *Enterobacteriaceae* cell.

10

Advantageously, the carrier cells are for treating or preventing a target cell infection in a human or an animal subject (eg, a chicken, cow, pig, fish or shellfish). Advantageously, the carrier cells are of a species that is probiotic to said subject or is probiotic to humans or animals (eg, chickens). For example, the carrier cells are probiotic *E coli* cell. For example, the carrier cells are probiotic *Bacillus* cell. In an example, the carrier cells are of a species that is pathogenic to said subject, or is pathogenic to humans or animals (eg, chickens). Advantageously, each plasmid encodes one or more guide RNAs or one or more crRNAs that are capable of hybridizing in the target cell to respective target nucleic acid sequence(s), wherein the target sequence(s) are comprised by an endogenous chromosome and/or endogenous episome of the target cell. For example, each plasmid encodes 2, 3, 4, 5, 6, 7, 7, 9, or 10 (or more than 10) different gRNAs or different crRNAs that hybridise to a respective target sequence, wherein the target sequences are different from each other. For example, 3 different gRNAs or crRNAs are encoded by each plasmid. For example, 2 different gRNAs or crRNAs are encoded by each plasmid. For example, 3 different gRNAs or crRNAs are encoded by each plasmid. For example, 4 different gRNAs or crRNAs are encoded by each plasmid. For example, 5 different gRNAs or crRNAs are encoded by each plasmid. For example, 6 different gRNAs or crRNAs are encoded by each plasmid. For example, 7 different gRNAs or crRNAs are encoded by each plasmid. For example, 8 different gRNAs or crRNAs are encoded by each plasmid. For example, 9 different gRNAs or crRNAs are encoded by each plasmid. For example, 10 different gRNAs or crRNAs are encoded by each plasmid. For example, 11 different gRNAs or crRNAs are encoded by each plasmid. For example, 12 different gRNAs or crRNAs are encoded by each plasmid. For example, 13 different gRNAs or crRNAs are encoded by each plasmid. In an example, the target cells are *Salmonella* cells (eg, wherein the subject is a chicken). In an example, the target cells are *E coli* cells. In an example, the target cells are *Campylobacter* cells (eg, wherein the subject is a chicken). In an example, the target cells are *Edwardsiella* cells (eg, wherein the subject is a fish or shellfish, eg, a catfish or a shrimp or prawn). In an example, the target cells are *E coli* cells.

35

Optionally, each plasmid comprises an expressible *tra1* and/or *tra2* module or a homologue thereof.
Any episome herein may be a plasmid.

- 5 Optionally, each plasmid comprises an expressible operon of a *tra1* and/or *tra2* module or a homologue thereof.

Optionally, each plasmid is comprised by a RK2 or R6K plasmid.

- 10 Optionally, each plasmid comprises an *oriV* of a RK2 or R6K plasmid, or a homologue thereof.

Optionally, each plasmid comprises an *oriT* of a RK2 or R6K plasmid, or a homologue thereof.

- 15 Optionally, the agent comprises one or more components of a CRISPR/Cas system that is operable in the target cell to cut a protospacer sequence comprised by the target cell, eg, wherein the protospacer sequence is comprised by the cell chromosome.

In an embodiment, the cutting herein kills the target cell. In an alternative, the cutting inhibits the growth or proliferation of the target cell.

20

Optionally, the agent encodes a guide RNA or crRNA of a CRISPR/Cas system that is operable with a Cas nuclease in the target cell to cut a protospacer sequence comprised by the target cell, eg, wherein the protospacer sequence is comprised by the cell chromosome.

- 25 In an example, the target cell is a *Salmonella* cell and the protospacer is comprised by a *pipA*, *pipB*, *pipC*, *hilA*, *sicP*, *mart* or *sopB* gene. In an example, the protospacer is comprised by a gene that is a homologue or orthologue of a *Salmonella* *sicP*, *sseF*, *pipA*, *pipB*, *pipC*, *hilA*, *sicP*, *mart* or *sopB* gene.

- 30 Optionally, each plasmid comprises a gene that encodes a product, wherein the product is essential for survival or proliferation of the carrier cell when in an environment that is devoid of the product, wherein the carrier cell chromosome does not comprise an expressible gene encoding the product and optionally the plasmid is the only episomal DNA comprised by the carrier cell that encodes the product. For example, the gene is selected from an *aroA*, *argH*, *hisD*, *leuB*, *lysA*, *metB*, *proC*, *thrC*, *pheA*, *tyrA*, *trpC* and *pflA* gene; or wherein the gene is an anti-toxin gene and optionally the first DNA
35 encodes a cognate toxin.

For example, the carrier cell is an *E coli* (eg, Nissle, F18 or S17 *E coli* strain), *Bacillus* (eg, *B subtilis*), *Enterococcus* or *Lactobacillus* cell.

5 Optionally, the carrier cell is a cell of a human, chicken pig, sheep, cow, fish (eg, catfish or salmon) or shellfish (eg, shrimp or lobster) commensal bacterial strain (eg, a commensal *E coli* strain).

Optionally, each carrier cell is for administration to a microbiota of a human or animal subject for medical use.

10 For example, the medical use is for treating or preventing a disease disclosed herein. For example, the medical use is for treating or preventing a condition disclosed herein.

Optionally, the medical use is for the treatment or prevention of a disease or condition mediated by said target cells.

15 Optionally, the carrier cell(s) is(are) for administration to an animal for enhancing growth or weight of the animal.

In alternative, the administration is to a human for enhancing the growth or weight of the human.

20 Optionally, the enhancing is not a medical therapy. Optionally, the enhancing is a medical therapy.

Optionally, the use comprises the administration of a plurality of carrier cells to a microbiota (eg, a gut microbiota) of the subject, wherein the microbiota comprises target cells and first DNA is transferred into target cells for expression therein to produce the antibacterial agent, thereby killing target cells in the subject or reducing the growth or proliferation of target cells.

For example a plant herein in any configuration or embodiment of the invention is selected from a tomato plant, a potato plant, a wheat plant, a corn plant, a maize plant, an apple tree, a bean-producing plant, a pea plant, a beetroot plant, a stone fruit plant, a barley plant, a hop plant and a grass. For example, the plant is a tree, eg, palm, a horse chestnut tree, a pine tree, an oak tree or a hardwood tree. For example the plant is a plant that produces fruit selected from strawberries, raspberries, blackberries, redcurrants, kiwi fruit, bananas, apples, apricots, avocados, cherries, oranges, clementines, satsumas, grapefruits, plus, dates, figs, limes, lemons, melons, mangos, pears, olives or grapes. Optionally, the plant is a dicotyledon. Optionally, the plant is a flowering plant. Optionally, the plant is a monocotyledon.

In any configuration, embodiment or example herein, the target bacteria are *P. syringae* bacteria (eg, comprised by a plant). *Pseudomonas syringae* pv. *syringae* is a common plant-associated bacterium that causes diseases of both monocot and dicot plants worldwide. In an example the target bacteria are *P. syringae* bacteria of a pathovar selected from *P. s. pv. aceris*, *P. s. pv. aptata*, *P.*

5 *s. pv. atrofaciens*, *P. s. pv. dysoxylis*, *P. s. pv. japonica*, *P. s. pv. lapsa*, *P. s. pv. panici*, *P. s. pv. papulans*, *P. s. pv. pisi*, *P. s. pv. syringae* and *P. s. pv. morsprunorum*.

- *P. s. pv. aceris* attacks maple *Acer* species.
- *P. s. pv. actinidiae* attacks kiwifruit *Actinidia deliciosa*.
- 10 • *P. s. pv. aesculi* attacks horse chestnut *Aesculus hippocastanum*, causing bleeding canker.
- *P. s. pv. aptata* attacks beets *Beta vulgaris*.
- *P. s. pv. atrofaciens* attacks wheat *Triticum aestivum*.
- *P. s. pv. dysoxylis* attacks the kohekohe tree *Dysoxylum spectabile*.
- *P. s. pv. japonica* attacks barley *Hordeum vulgare*.
- 15 • *P. s. pv. lapsa* attacks wheat *Triticum aestivum*.
- *P. s. pv. panici* attacks *Panicum* grass species.
- *P. s. pv. papulans* attacks crabapple *Malus sylvestris* species.
- *P. s. pv. phaseolicola* causes halo blight of beans.
- *P. s. pv. pisi* attacks peas *Pisum sativum*.
- 20 • *P. s. pv. syringae* attacks *Syringa*, *Prunus*, and *Phaseolus* species.
- *P. s. pv. glycinea* attacks soybean, causing bacterial blight of soybean.

In an example, the target bacteria are *P. syringae* selected from a serovar recited in a bullet point in the immediately preceding paragraph and the bacteria are comprised by a plant also mentioned in that

25 bullet point.

In an example, the weight (ie, biomass) is dry weight. For example, the method is for increasing dry weight (eg, within 1 or 2 weeks of said administration). Optionally, the increase is an increase of at least 5, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20% compared to a control plant of the same species

30 or strain to which the administration of carrier cells has not taken place, wherein all plants are kept under the same environmental conditions. For example, such an increase is within 1, 2, 3, 4, 5, 6, or 8 weeks following the first administration of the carrier cells. In an example, the method is for increasing the dry weight of a leaf and/or fruit of the plant, such as a tomato plant.

35 In an example, the weight is wet weight. For example, the method is for increasing wet weight (eg, within 1 or 2 weeks of said administration). Optionally, the increase is an increase of at least 5, 10,

11, 12, 13, 14, 15, 16, 17, 18, 19 or 20% compared to a control plant of the same species or strain to which the administration of carrier cells has not taken place, wherein all plants are kept under the same environmental conditions. For example, such an increase is within 1, 2, 3, 4, 5, 6, or 8 weeks following the first administration of the carrier cells. In an example, the method is for increasing the
 5 dry weight of a leaf and/or fruit of the plant, such as a tomato plant.

For example, the microbiota is comprised by a leaf, trunk, root or stem of the plant.

The target bacteria (or target cell) may be comprised by a microbiota of a plant. In an example, the
 10 microbiota is comprised by a leaf. In an example, the microbiota is comprised by a xylem. In an example, the microbiota is comprised by a phloem. In an example, the microbiota is comprised by a root. In an example, the microbiota is comprised by a tuber. In an example, the microbiota is comprised by a bulb. In an example, the microbiota is comprised by a seed. In an example, the microbiota is comprised by an exocarp, epicarp, mesocarp or endocarp. In an example, the microbiota
 15 is comprised by a fruit, eg, a simple fruits; aggregate fruits; or multiple fruits. In an example, the microbiota is comprised by a seed or embryo, eg, by a seed coat; a seed leaf; cotyledons; or a radicle. In an example, the microbiota is comprised by a flower, eg, comprised by a peduncle; sepal; petals; stamen; filament; anther or pistil. In an example, the microbiota is comprised by a root; eg, a tap root system, or a fibrous root system. In an example, the microbiota is comprised by a leaf or leaves, eg,
 20 comprised by a leaf blade, petiole or stipule. In an example, the microbiota is comprised by a stem, eg, comprised by bark, epidermis, phloem, cambium, xylem or pith.

In an example “reducing a biofilm” comprises reducing the coverage area of the biofilm. In an example “reducing a biofilm” comprises reducing the proliferation of the biofilm. In an example
 25 “reducing a biofilm” comprises reducing the durability of the biofilm. In an example “reducing a biofilm” comprises reducing the spread of the biofilm (eg, in or on the subject, eg, spread to the environment containing the subject). The subject may be a human or animal.

For example, the biofilm is comprised by a lung of the subject, eg, wherein the target cells are
 30 *Pseudomonas* (eg, *P. aeruginosa*) cells. This may be useful wherein the subject is a human suffering from a lung disease or condition, such as pneumonia or cystic fibrosis.

For example, the biofilm is comprised by an animal or human organ disclosed herein. For example, the biofilm is comprised by a microbiota of a human or animal disclosed herein.

35 Optionally, said surface is a surface *ex vivo*, such as a surface comprised by a domestic or industrial apparatus or container.

Optionally, the target cells are comprised by a biofilm, eg, a biofilm as disclosed herein.

Optionally, the target bacteria are *Salmonella*, *Pseudomonas*, *Escherichia*, *Klebsiella*, *Campylobacter*,
 5 *Helicobacter*, *Acinetobacter*, *Enterobacteriaceae*, *Clostridium*, *Staphylococcus* or *Streptococcus*
 bacteria. For example, the target bacteria are *Salmonella enterica* bacteria. For example, the target
 bacteria are selected from the group consisting of *Salmonella enterica* subsp. *enterica*, serovars
 Typhimurium, Enteritidis, Virchow, Montevideo, Hadar and Binza.

- 10 Optionally, the target bacteria are *E. coli* bacteria. For example, the target bacteria are
 enterohemorrhagic *E. coli* (EHEC), *E. coli* Serotype O157:H7 or Shiga-toxin producing *E. coli*
 (STEC)). In an example, the target bacteria are selected from
- Shiga toxin-producing *E. coli* (STEC) (STEC may also be referred to as Verocytotoxin-
 producing *E. coli* (VTEC);
 - 15 • Enterohemorrhagic *E. coli* (EHEC) (this pathotype is the one most commonly heard about in
 the news in association with foodborne outbreaks);
 - Enterotoxigenic *E. coli* (ETEC);
 - Enteropathogenic *E. coli* (EPEC);
 - Enteroaggregative *E. coli* (EAEC);
 - 20 • Enteroinvasive *E. coli* (EIEC); and
 - Diffusely adherent *E. coli* (DAEC).

Enterohemorrhagic *Escherichia coli* (EHEC) serotype O157:H7 is a human pathogen responsible for
 outbreaks of bloody diarrhoea and haemolytic uremic syndrome (HUS) worldwide. Conventional
 25 antimicrobials trigger an SOS response in EHEC that promotes the release of the potent Shiga toxin
 that is responsible for much of the morbidity and mortality associated with EHEC infection. Cattle are
 a natural reservoir of EHEC, and approximately 75% of EHEC outbreaks are linked to the
 consumption of contaminated bovine-derived products. EHEC causes disease in humans but is
 asymptomatic in adult ruminants. Characteristics of *E. coli* serotype O157:H7 (EHEC) infection
 30 includes abdominal cramps and bloody diarrhoea, as well as the life-threatening complication
 haemolytic uremic syndrome (HUS). Currently there is a need for a treatment for EHEC infections
 (Goldwater and Bettelheim, 2012). The use of conventional antibiotics exacerbates Shiga toxin-
 mediated cytotoxicity. In an epidemiology study conducted by the Centers for Disease Control and
 Prevention, patients treated with antibiotics for EHEC enteritis had a higher risk of developing HUS
 35 (Slutsker et al., 1998). Additional studies support the contraindication of antibiotics in EHEC
 infection; children on antibiotic therapy for hemorrhagic colitis associated with EHEC had an

increased chance of developing HUS (Wong et al., 2000; Zimmerhackl, 2000; Safdar et al., 2002; Tarr et al., 2005). Conventional antibiotics promote Shiga toxin production by enhancing the replication and expression of *stx* genes that are encoded within a chromosomally integrated lambdoid prophage genome. The approach of some configurations of present invention rely on nuclease cutting. *Stx* induction also promotes phage-mediated lysis of the EHEC cell envelope, allowing for the release and dissemination of Shiga toxin into the environment (Karch et al., 1999; Matsushiro et al., 1999; Wagner et al., 2002). Thus, advantageously, these configurations of the invention provide alternative means for treating EHEC in human and animal subjects. This is exemplified below with surprising results on the speed and duration of anti-EHEC action produced by nuclease action (as opposed to conventional antibiotic action).

In an example, the subject (eg, a human or animal) is suffering from or at risk of haemolytic uremic syndrome (HUS), eg, the subject is suffering from an E coli infection, such as an EHEC *E coli* infection.

15

There is provided:-

A pharmaceutical composition, livestock growth promoting composition, soil improver, herbicide, plant fertilizer, food or food ingredient sterilizing composition, dental composition, personal hygiene composition or disinfectant composition (eg, for domestic or industrial use) comprising a plurality of the carrier cells.

20

Herein, a carrier cell is, eg, a probiotic cell for administration to a human or animal subject. For example, the carrier cell is commensal in a microbiome (eg, gut or blood microbiome) of a human or animal subject, wherein the carrier is for administration to the subject. In an example, a carrier cell is a bacterial cell (and optionally the target cell is a bacterial cell). In an example, a carrier cell is an archaeal cell (and optionally the target cell is an archaeal cell)

25

Optionally, the carrier cell is a gram-positive bacterial cell and the target cell is a gram-positive bacterial cell.

30

Optionally, the carrier cell is a gram-positive bacterial cell and the target cell is a gram-negative bacterial cell.

Optionally, the carrier cell is a gram-negative bacterial cell and the target cell is a gram-positive bacterial cell.

35

Optionally, the carrier cell is a gram-negative bacterial cell and the target cell is a gram-negative bacterial cell.

5 Optionally, the carrier cell is a *Bacillus* bacterial cell and the target cell is a gram-positive bacterial cell.

Optionally, the carrier cell is a *Bacillus* bacterial cell and the target cell is a gram-negative bacterial cell.

10 Optionally, the carrier cell is a *Bacillus* bacterial cell and the target cell is a *Salmonella* bacterial cell.

Optionally, the carrier cell is a *Bacillus* bacterial cell and the target cell is an *E coli* bacterial cell.

15 Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is a *Pseudomonas* bacterial cell.

Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is a gram-positive bacterial cell.

20 Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is a gram-negative bacterial cell.

Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is a *Salmonella* bacterial cell.

25 Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is an *E coli* bacterial cell.

Optionally, the carrier cell is an *E coli* bacterial cell and the target cell is a *Pseudomonas* bacterial cell.

30 A *Bacillus* cell herein is optionally a *B subtilis* cell.

Optionally, the carrier cell is a probiotic or commensal *E coli* bacterial cell for administration to a human or animal subject. Optionally, the carrier cell is a probiotic or commensal *Bacillus* bacterial cell for administration to a human or animal subject.

35

Herein, optionally the plasmid is a closed circular DNA.

In an embodiment, the plasmid DNA is dsDNA. In an embodiment, the plasmid DNA is ssDNA.

Optionally, the target cell is a *Salmonella* cell (eg, wherein the carrier cell is an *E coli* cell), eg, a
 5 *Salmonella enterica* subsp. *enterica*, eg, a *Salmonella enterica* subsp. *enterica* serovar Typhimurium, Enteritidis, Virchow, Montevideo, Hadar or Binza.

For example, the target bacteria are selected from the group consisting of *S enterica*; *S typhimurium*;
P aeruginosa; *E coli*; *K pneumoniae*; *C jejuni*; *H pylori*; *A baumannii*; *C difficile*; *S aureus*; *S*
 10 *pyogenes* or *S thermophilus*.

In an example, the target cell is a cell of a species that causes nosocomial infection in humans.

Optionally, the target cell is comprised by an animal (eg, poultry animal (such as chicken), swine,
 15 cow, fish (eg, catfish or salmon) or shellfish (eg, prawn or lobster)) microbiome. Optionally, the microbiome is a gut microbiome. For example, the target cell is a *Salmonella* cell comprised by a chicken gut biofilm. For example, the target cell is a *Salmonella* cell comprised by a chicken gut biofilm sample *ex vivo*.

20 In an embodiment, each plasmid comprises a bacterial oriV and/or an oriT. In an embodiment, each plasmid comprises and oriV and/or an oriT.

In an embodiment, the plasmid comprises an oriV and does not encode any replication protein (eg, *pir* or *trfA*) that is operable with the oriV to initiate replication of the plasmid.
 25

In an example, the invention relates to a composition comprising a plurality of carrier cells of the invention. Optionally, all of the carrier cells comprise identical said plasmids. Optionally, the plurality comprises a first sub-population of carrier cells (first cells) and a second sub-population of carrier cells (second cells) wherein the first cells comprise identical first said plasmids and the
 30 second cells comprise identical second said plasmids (which are different from the first plasmids of the first cells). For example, the first plasmids encode a first guide RNA or crRNA and the second plasmids encode a second guide RNA or crRNA, wherein the first guide RNA/crRNA is capable of hybridizing to a first protospacer sequence in first target cells; and the second guide RNA/crRNA is capable of hybridizing to a second protospacer sequence in second target cells, wherein the
 35 protospacers are different. Optionally, the first target cells are different from the second target cells. Optionally, the first target cells are of the same species or strain as the second target cells.

Alternatively, the first target cells are of species or strain that is different from the species or strain of the second target cells (in this way a cocktail of carrier cells is provided, eg. for administration to a human or animal or plant, to target and kill a plurality of target cells of different species or strains).

- 5 Optionally, the composition is comprised by a liquid (eg, an aqueous liquid or in water), the composition comprising the carrier cells at an amount of from 1×10^3 to 1×10^{10} (eg, from 1×10^4 to 1×10^{10} ; from 1×10^4 to 1×10^9 ; from 1×10^4 to 1×10^8 ; from 1×10^4 to 1×10^7 ; from 1×10^3 to 1×10^{10} ; from 1×10^3 to 1×10^9 ; from 1×10^3 to 1×10^8 ; from 1×10^3 to 1×10^7 ; from 1×10^5 to 1×10^{10} ; from 1×10^5 to 1×10^9 ; from 1×10^5 to 1×10^8 ; from 1×10^5 to 1×10^7 ; from 1×10^6 to 1×10^{10} ; from 1×10^6 to 1×10^9 ; from 1×10^6 to 1×10^8 ; or from 1×10^6 to 1×10^7) cfu/ml. For example, the liquid is a beverage, such for human or animal consumption. For example, the beverage is a livestock beverage, eg, a poultry beverage (ie, a beverage for consumption by poultry, such as chicken).

- 15 In an example, the composition is a dietary (eg, dietary supplement) composition for consumption by humans or animals. In an example, the composition is a slimming composition for consumption by humans or animals. In an example, the composition is a growth promotion composition for consumption by humans or animals. In an example, the composition is a body building composition for consumption by humans. In an example, the composition is a probiotic composition for consumption by humans or animals. In an example, the composition is a biocidal composition for consumption by humans or animals. In an example, the composition is a pesticidal composition for consumption by humans or animals. In an example, the composition is a zoonosis control composition for consumption by animals.

- 25 In an example, the composition comprises vitamins in addition to the carrier cells. In an example, the composition comprises vitamin A, B (eg, B12), C, D, E and/or K in addition to the carrier cells. In an example, the composition comprises lipids in addition to the carrier cells. In an example, the composition comprises carbohydrates in addition to the carrier cells. In an example, the composition comprises proteins and/or amino acids in addition to the carrier cells. In an example, the composition comprises minerals in addition to the carrier cells. In an example, the composition comprises metal ions (eg, Mg^{2+} , Cu^{2+} and/or Zn^{2+}) in addition to the carrier cells. In an example, the composition comprises sodium ions, potassium ions, magnesium ions, calcium ions, manganese ions, iron ions, cobalt ions, copper ions, zinc ions and/or molybdenum ions.

- 30 In an example, the composition is a plant fertilizer composition. In an example, the composition is a herbicide. In an example, the composition is a pesticide composition for application to plants.

35

In any embodiment or example, where appropriate: The plants are, for example, crop plants. The plants are, for example, wheat. The plants are, for example, corn. The plants are, for example, maize. The plants are, for example, fruiting plants. The plants are, for example, vegetable plants. The plants are, for example, tomato plants. The plants are, for example, potato plants. The plants are, for
 5 example, grass plants. The plants are, for example, flowering plants. The plants are, for example, trees. The plants are, for example, shrubs.

In an example, the composition is for environmental application, wherein the environment is an outdoors environment (eg, application to a field or waterway or reservoir).
 10

In an example, the composition is comprised by a food or food ingredient (eg, for human or animal consumption). In an example, the composition is comprised by a beverage or beverage ingredient (eg, for human or animal consumption).

15 In an example the target cell(s) are human biofilm cells, eg, wherein the biofilm is a gut, skin, lung, eye, nose, ear, gastrointestinal tract (GI tract), stomach, hair, kidney, urethra, bronchiole, oral cavity, mouth, liver, heart, anus, rectum, bladder, bowel, intestine, penis, vagina or scrotum biofilm. In an example the target cell(s) are animal biofilm cells, eg, wherein the biofilm is a gut, skin, lung, eye, nose, ear, gastrointestinal tract (GI tract), caecum, jejunum, ileum, colon, stomach, hair, feather,
 20 scales, kidney, urethra, bronchiole, oral cavity, mouth, liver, spleen, heart, anus, rectum, bladder, bowel, intestine, penis, vagina or scrotum biofilm. For example, the biofilm is a bird (eg, chicken) caecum biofilm. For example, the biofilm is a bird (eg, chicken) gastrointestinal tract (GI tract), caecum, jejunum, ileum, colon or stomach biofilm.

25 In an example, any method herein is *ex vivo*. In an example, a method herein is *in vivo*. In an example, a method herein is *in vitro*. In an example, a method herein is carried out in an environment, eg, in a domestic (such as in a house), industrial (such as in a factory) or agricultural environment (such as in a field). In an example, a method herein is carried out in or on a container; or on a surface.

30 In an example each plasmid comprises one or more components of a CRISPR/Cas system operable to perform protospacer cutting in the target cell (eg, wherein the protospacer comprises 10-20, 10-30, 10-40, 10-100, 12-15 or 12-20 consecutive nucleotides that are capable of hybridizing in the target cell with a crRNA or gRNA encoded by the NSI). For example, the system is a Type I, II, III, IV or V CRISPR/Cas system.

35

In an example, the or each plasmid encodes a Cas9 (and optionally a second, different, Cas, such as a Cas3, Cas9, Cpf1, Cas13a, Cas13b or Cas10); and/or a Cas3 (and optionally a second, different, Cas, such as a Cas3, Cas9, Cpf1, Cas13a, Cas13b or Cas10). In an example, the or each plasmid encodes a Cas selected from a Cas3, Cas9, Cpf1, Cas13a, Cas13b and Cas10. Additionally or alternatively, the
5 plasmid encodes a guide RNA or crRNA or tracrRNA. For example, the guide RNA or crRNA or tracrRNA is cognate to (ie, operable with in the target cell) the first Cas.

In an example, a Cas herein is a Cas9. In an example, a Cas herein is a Cas3. The Cas may be identical to a Cas encoded by the target bacteria.

10

In an embodiment, each plasmid is a shuttle vector.

Optionally, the target cell is devoid of a functional endogenous CRISPR/Cas system before transfer therein of the plasmid, eg, wherein the plasmid comprises a component of an exogenous CRISPR/Cas
15 system that is functional in the target cell and toxic to the target cell. An embodiment provides an antibacterial composition comprising a plurality of carrier cells of the invention, wherein each target cell is optionally according to this paragraph, for administration to a human or animal subject for medical use.

20 In an example, the composition of the invention is a herbicide, pesticide, insecticide, plant fertilizer or cleaning agent.

Optionally, target bacteria herein are comprised by a microbiome of the subject, eg, a gut microbiome. Alternatively, the microbiome is a skin, scalp, hair, eye, ear, oral, throat, lung, blood, rectal, anal,
25 vaginal, scrotal, penile, nasal or tongue microbiome.

In an example the subject (eg, human or animal) is further administered a medicament simultaneously or sequentially with the carrier cell administration. In an example, the medicament is an antibiotic, antibody, immune checkpoint inhibitor (eg, an anti-PD-1, anti-PD-L1 or anti-CTLA4 antibody),
30 adoptive cell therapy (eg, CAR-T therapy) or a vaccine.

In an embodiment, the plasmid encodes a guided nuclease, such as a Cas nuclease, TALEN, zinc finger nuclease or meganuclease. Thus, the toxic agent may comprise a guided nuclease, such as a Cas nuclease, TALEN, zinc finger nuclease or meganuclease. Optionally, the plasmid encodes a
35 restriction nuclease that is capable of cutting the chromosome of the target cell.

Optionally, the composition is a pharmaceutical composition for use in medicine practised on a human or animal subject.

5 In an example, the animal is a livestock or companion pet animal (eg, a cow, pig, goat, sheep, horse, dog, cat or rabbit). In an example, the animal is an insect (an insect at any stage of its lifecycle, eg, egg, larva or pupa). In an example, the animal is a protozoan. In an example, the animal is a cephalopod.

10 Optionally, the composition is a herbicide, pesticide, food or beverage processing agent, food or beverage additive, petrochemical or fuel processing agent, water purifying agent, cosmetic additive, detergent additive or environmental (eg, soil) additive or cleaning agent.

15 For example the carrier bacteria are *Lactobacillus* (eg, *L reuteri* or *L lactis*), *E coli*, *Bacillus* or *Streptococcus* (eg, *S thermophilus*) bacteria. Usefully, the carrier can provide protection for the plasmid from the surrounding environment. The use of a carrier may be useful for oral administration or other routes where the carrier can provide protection for the plasmid from the acid stomach or other harsh environments in the subject. Furthermore, the carrier can be formulated into a beverage, for example, a probiotic drink, eg, an adapted Yakult (trademark), Actimel (trademark), Kevita (trademark), Activia (trademark), Jarrow (trademark) or similar drink for human consumption.

20 Optionally, the carrier cell(s) or composition are for administration to a human or animal subject for medical use, comprising killing target bacteria using the agent or expression product of the plasmid, wherein the target bacteria mediate as disease or condition in the subject. In an example, when the subject is a human, the subject is not an embryo. In an example, the carrier cells are probiotic in the subject.

30 Optionally, the environment is a microbiome of soil; a plant, part of a part (e.g., a leaf, fruit, vegetable or flower) or plant product (e.g., pulp); water; a waterway; a fluid; a foodstuff or ingredient thereof; a beverage or ingredient thereof; a medical device; a cosmetic; a detergent; blood; a bodily fluid; a medical apparatus; an industrial apparatus; an oil rig; a petrochemical processing, storage or transport apparatus; a vehicle or a container.

35 Optionally, the environment is an *ex vivo* bodily fluid (e.g., urine, blood, blood product, sweat, tears, sputum or spit), bodily solid (e.g., faeces) or tissue of a human or animal subject that has been administered the composition.

Optionally, the environment is an *in vivo* bodily fluid (e.g., urine, blood, blood product, sweat, tears, sputum or spit), bodily solid (e.g., faeces) or tissue of a human or animal subject that has been administered the composition.

- 5 In an embodiment, the plasmid is a phagemid or cloning vector (eg, a shuttle vector, eg, a pUC vector).

Optionally, the antibacterial agent comprises one or more components of a CRISPR/Cas system, eg, a DNA sequence encoding one or more components of Type I Cascade (eg, CasA).

10

Optionally, the agent comprises a DNA sequence encoding guided nuclease, such as a Cas nuclease, TALEN, zinc finger nuclease or meganuclease.

- 15 In an example, the carrier cell(s) or composition are comprised by a medical container, eg, a syringe, vial, IV bag, inhaler, eye dropper or nebulizer. In an example, the carrier cell(s) or composition are comprised by a sterile container. In an example, the carrier cell(s) or composition are comprised by a medically-compatible container. In an example, the carrier cell(s) or composition are comprised by a fermentation vessel, eg, a metal, glass or plastic vessel. In an example, the carrier cell(s) or composition are comprised by an agricultural apparatus. In an example, the carrier cell(s) or composition are comprised by food production or processing apparatus. In an example, the carrier cell(s) or composition are comprised by a horticultural apparatus. In an example, the carrier cell(s) or composition are comprised by a farming apparatus. In an example, the carrier cell(s) or composition are comprised by petrochemicals recovery or processing apparatus. In an example, the carrier cell(s) or composition are comprised by a distillation apparatus. In an example, the carrier cell(s) or composition are comprised by cell culture vessel (eg, having a capacity of at least 50, 100, 1000, 10000 or 100000 litres). Additionally or alternatively, the target cell(s) are comprised by any of these apparatus etc.
- 20
- 25

- 30 In an example, the carrier cell(s) or composition are comprised by a medicament, e.g in combination with instructions or a packaging label with directions to administer the medicament by oral, IV, subcutaneous, intranasal, intraocular, vaginal, topical, rectal or inhaled administration to a human or animal subject. In an example, the carrier cell(s) or composition are comprised by an oral medicament formulation. In an example, the carrier cell(s) or composition are comprised by an intranasal or ocular medicament formulation. In an example, the carrier cell(s) or composition are comprised by a personal hygiene composition (eg, shampoo, soap or deodorant) or cosmetic formulation. In an example, the carrier cell(s) or composition are comprised by a detergent
- 35

formulation. In an example, the carrier cell(s) or composition are comprised by a cleaning formulation, eg, for cleaning a medical or industrial device or apparatus. In an example, the carrier cell(s) or composition are comprised by foodstuff, foodstuff ingredient or foodstuff processing agent. In an example, the carrier cell(s) or composition are comprised by beverage, beverage ingredient or beverage processing agent. In an example, the carrier cell(s) or composition are comprised by a medical bandage, fabric, plaster or swab. In an example, the carrier cell(s) or composition are comprised by a herbicide or pesticide. In an example, the carrier cell(s) or composition are comprised by an insecticide.

In an example, the CRISPR/Cas component(s) are component(s) of a Type I CRISPR/Cas system. In an example, the CRISPR/Cas component(s) are component(s) of a Type II CRISPR/Cas system. In an example, the CRISPR/Cas component(s) are component(s) of a Type III CRISPR/Cas system. In an example, the CRISPR/Cas component(s) are component(s) of a Type IV CRISPR/Cas system. In an example, the CRISPR/Cas component(s) are component(s) of a Type V CRISPR/Cas system. In an example, the CRISPR/Cas component(s) comprise a Cas9-encoding nucleotide sequence (eg, *S pyogenes* Cas9, *S aureus* Cas9 or *S thermophilus* Cas9). In an example, the CRISPR/Cas component(s) comprise a Cas3-encoding nucleotide sequence (eg, *E coli* Cas3, *C difficile* Cas3 or *Salmonella* Cas3). In an example, the CRISPR/Cas component(s) comprise a Cpf-encoding nucleotide sequence. In an example, the CRISPR/Cas component(s) comprise a CasX-encoding nucleotide sequence. In an example, the CRISPR/Cas component(s) comprise a CasY-encoding nucleotide sequence.

In an example, each carrier cell encodes a CRISPR/Cas component from a nucleotide sequence (NSI) comprising a promoter that is operable in the target bacteria.

Optionally, target bacteria are gram negative bacteria (eg, a spirilla or vibrio). Optionally, target bacteria are gram positive bacteria. Optionally, target bacteria are mycoplasma, chlamydiae, spirochete or mycobacterium bacteria. Optionally, target bacteria are *Streptococcus* (eg, *pyogenes* or *thermophilus*). Optionally, target bacteria are *Staphylococcus* (eg, *aureus*, eg, MRSA). Optionally, target bacteria are *E. coli* (eg, O157: H7), eg, wherein the Cas is encoded by the vector or an endogenous target cell Cas nuclease (eg, Cas3) activity is de-repressed. Optionally, target bacteria are *Pseudomonas* (eg, *syringae* or *aeruginosa*). Optionally, target bacteria are *Vibro* (eg, *cholerae* (eg, O139) or *vulnificus*). Optionally, target bacteria are *Neisseria* (eg, *gonorrhoeae* or *meningitidis*). Optionally, target bacteria are *Bordetella* (eg, *pertussis*). Optionally, target bacteria are *Haemophilus* (eg, *influenzae*). Optionally, target bacteria are *Shigella* (eg, *dysenteriae*). Optionally, target bacteria are *Brucella* (eg, *abortus*). Optionally, target bacteria are *Francisella* host. Optionally, target bacteria

- are *Xanthomonas*. Optionally, target bacteria are *Agrobacterium*. Optionally, target bacteria are *Erwinia*. Optionally, target bacteria are *Legionella* (eg, *pneumophila*). Optionally, target bacteria are *Listeria* (eg, *monocytogenes*). Optionally, target bacteria are *Campylobacter* (eg, *jejuni*). Optionally, target bacteria are *Yersinia* (eg, *pestis*). Optionally, target bacteria are *Borelia* (eg, *burgdorferi*).
- 5 Optionally, target bacteria are *Helicobacter* (eg, *pylori*). Optionally, target bacteria are *Clostridium* (eg, *dificile* or *botulinum*). Optionally, target bacteria are *Ehrlichia* (eg, *chaffeensis*). Optionally, target bacteria are *Salmonella* (eg, *typhi* or *enterica*, eg, serotype typhimurium, eg, DT 104). Optionally, target bacteria are *Chlamydia* (eg, *pneumoniae*). Optionally, target bacteria are *Parachlamydia* host. Optionally, target bacteria are *Corynebacterium* (eg, *amycolatum*). Optionally,
- 10 target bacteria are *Klebsiella* (eg, *pneumoniae*). Optionally, target bacteria are *Enterococcus* (eg, *faecalis* or *faecim*, eg, linezolid-resistant). Optionally, target bacteria are *Acinetobacter* (eg, *baumannii*, eg, multiple drug resistant).

Further examples of target cells are as follows:-

- 15 1. Optionally the target bacteria are *Staphylococcus aureus* cells, eg, resistant to an antibiotic selected from methicillin, vancomycin, linezolid, daptomycin, quinupristin, dalfopristin and teicoplanin.
2. Optionally the target bacteria are *Pseudomonas aeruginosa* cells, eg, resistant to an antibiotic selected from cephalosporins (eg, ceftazidime), carbapenems (eg, imipenem or
- 20 meropenem), fluoroquinolones, aminoglycosides (eg, gentamicin or tobramycin) and colistin.
3. Optionally the target bacteria are *Klebsiella* (eg, *pneumoniae*) cells, eg, resistant to carbapenem.
4. Optionally the target bacteria are *Streptococcus* (eg, *thermophilus*, *pneumoniae* or *pyogenes*) cells, eg, resistant to an antibiotic selected from erythromycin, clindamycin, beta-lactam, macrolide,
- 25 amoxicillin, azithromycin and penicillin.
5. Optionally the target bacteria are *Salmonella* (eg, serotype Typhi) cells, eg, resistant to an antibiotic selected from ceftriaxone, azithromycin and ciprofloxacin.
6. Optionally the target bacteria are *Shigella* cells, eg, resistant to an antibiotic selected from ciprofloxacin and azithromycin.
- 30 7. Optionally the target bacteria are *Mycobacterium tuberculosis* cells, eg, resistant to an antibiotic selected from Resistance to isoniazid (INH), rifampicin (RMP), fluoroquinolone, amikacin, kanamycin and capreomycin and azithromycin.
8. Optionally the target bacteria are *Enterococcus* cells, eg, resistant to vancomycin.
9. Optionally the target bacteria are *Enterobacteriaceae* cells, eg, resistant to an antibiotic
- 35 selected from a cephalosporin and carbapenem.

10. Optionally the target bacteria are *E. coli* cells, eg, resistant to an antibiotic selected from trimethoprim, itrofurantoin, cefalexin and amoxicillin.
11. Optionally the target bacteria are *Clostridium* (eg, *dificile*) cells, eg, resistant to an antibiotic selected from fluoroquinolone antibiotic and carbapenem.
- 5 12. Optionally the target bacteria are *Neisseria gonorrhoea* cells, eg, resistant to an antibiotic selected from cefixime (eg, an oral cephalosporin), ceftriaxone (an injectable cephalosporin), azithromycin and tetracycline.
13. Optionally the target bacteria are *Acinetobacter baumannii* cells, eg, resistant to an antibiotic selected from beta-lactam, meropenem and a carbapenem.
- 10 14. Optionally the target bacteria are *Campylobacter* (eg, *jejuni*) cells, eg, resistant to an antibiotic selected from ciprofloxacin and azithromycin.
15. Optionally, the target cell(s) produce Beta (β)-lactamase (eg, ESBL-producing *E. coli* or ESBL-producing *Klebsiella*).
16. Optionally, the target cell(s) are bacterial cells that are resistant to an antibiotic recited in any
- 15 one of examples 1 to 14.

In an example, the target cell(s) is a cell of a species selected from *Shigella*, *E coli*, *Salmonella*, *Serratia*, *Klebsiella*, *Yersinia*, *Pseudomonas* and *Enterobacter*.

- Optionally, the composition comprises carrier cells that are each or in combination capable of
- 20 conjugative transfer of first DNAs into target cells of species selected from two or more of *Shigella*, *E coli*, *Salmonella*, *Serratia*, *Klebsiella*, *Yersinia*, *Pseudomonas* and *Enterobacter*.

- In an example, the reduction in growth or proliferation of target cells is at least 50, 60, 70, 80, 90 or 95%. Optionally, the composition or carrier cell(s) are administered simultaneously or sequentially
- 25 with an an antibiotic that is toxic to the target cells. For example, the antibiotic can be any antibiotic disclosed herein.

- Optionally, the expression of the agent is under the control of an inducible promoter that is operable in the target cell. Optionally, the expression of the agent is under the control of a constitutive
- 30 promoter that is operable in the target cell.

In embodiments, the plasmid contains a screenable or selectable marker gene. For example, the selectable marker gene is an antibiotic resistance gene.

- 35 The carrier bacteria can be bacteria of a species or genus as follows. For example, the species is found in warm-blooded animals (eg, livestock vertebrates). For example, the species is found in

- humans. For example, the species is found in plants. Preferably, non-pathogenic bacteria that colonize the non-sterile parts of the human or animal body (e.g., skin, digestive tract, urogenital region, mouth, nasal passages, throat and upper airway, ears and eyes) are utilized as carrier cells, and in an example the methodology of the invention is used to combat a target cell bacterial infection of
- 5 such a part of the body of a human or animal. In another embodiment, the infection is systemic infection. Examples of particularly preferred carrier bacterial species include, but are not limited to: non-pathogenic strains of *Escherichia coli* (*E. coli* F18, S17 and *E. coli* strain Nissle), various species of *Lactobacillus* (such as *L. casei*, *L. plantarum*, *L. paracasei*, *L. acidophilus*, *L. fermentum*, *L. zeae* and *L. gasseri*), or other nonpathogenic or probiotic skin- or GI colonizing bacteria such as
- 10 *Lactococcus*, *Bifidobacteria*, *Eubacteria*, and bacterial mini-cells, which are anucleoid cells destined to die but still capable of transferring plasmids (see; e.g., Adler et al., Proc. Natl. Acad. Sci. USA 57: 321-326, 1970; Frazer and Curtiss III, Current Topics in Microbiology and Immunology 69: 1-84, 1975; U.S. Patent No. 4,968,619 to Curtiss III). In some embodiments, the target recipient cells are pathogenic bacteria comprised by a human, animal or plant, eg, on the skin or in the digestive tract,
- 15 urogenital region, mouth, nasal passage, throat and upper airway, eye(s) and ear(s). Of particular interest for targeting and eradication are pathogenic strains of *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus pneumoniae* and other species, *Enterobacter spp.*, *Enterococcus spp.* and *Mycobacterium tuberculosis*.
- 20 The present invention finds use with a wide array of settings or environments, eg, in therapeutic, agricultural, or other settings, including, but not limited to, those described in U.S. patents 6,271,359, 6,261,842, 6,221,582, 6,153,381, 6,106,854, and 5,627,275. Others are also discussed herein, and still others will be readily apparent to those of skill in the art.
- 25 A single carrier bacterial strain might harbor more than one type of such plasmid (eg, differing in the antibacterial agent that they encode). Further, in another example two or more different carrier bacterial strains, each containing one or more such plasmids, may be combined for a multi-target effect, ie, for killing two or more different target species or strains, or for killing the cells of the same species or strain of target cell.
- 30 The present invention finds utility for treatment of humans and in a variety of veterinary, agronomic, horticultural and food processing applications. For human and veterinary use, and depending on the cell population or tissue targeted for protection, the following modes of administration of the carrier bacteria of the invention are contemplated: topical, oral, nasal, ocular, aural, pulmonary (e.g., via an
- 35 inhaler), ophthalmic, rectal, urogenital, subcutaneous, intraperitoneal and intravenous. The bacteria may be supplied as a pharmaceutical composition, in a delivery vehicle suitable for the mode of

administration selected for the patient being treated. The term "patient" or "subject" as used here may refer to humans or animals (animals being particularly useful as models for clinical efficacy of a particular donor strain, for example, or being farmed or livestock animals). Commercially-relevant animals are chicken, turkey, duck, catfish, salmon, cod, herring, lobster, shrimp, prawns, cows, sheep, goats, pigs, goats, geese or rabbits.

For example, to deliver the carrier bacteria to the gastrointestinal tract or to the nasal passages, the preferred mode of administration may be by oral ingestion or nasal aerosol, or by feeding (alone or incorporated into the subject's feed or food and/or beverage, such as drinking water). In this regard, the carrier cells may be comprised by a food of livestock (or farmed or companion animal), eg, the carrier bacteria are comprised by a feed additive for livestock. Alternatively, the additive is a beverage (eg, water) additive for livestock. It should be noted that probiotic bacteria, such as *Lactobacillus acidophilus*, are sold as gel capsules containing a lyophilized mixture of bacterial cells and a solid support such as mannitol. When the gel capsule is ingested with liquid, the lyophilized cells are re-hydrated and become viable, colonogenic bacteria. Thus, in a similar fashion, carrier bacterial cells of the present invention can be supplied as a powdered, lyophilized preparation in a gel capsule, or in bulk, eg, for sprinkling onto food or beverages. The re-hydrated, viable bacterial cells will then populate and/or colonize sites throughout the upper and/or lower gastrointestinal system, and thereafter come into contact with the target bacteria.

For topical applications, the carrier bacteria may be formulated as an ointment or cream to be spread on the affected skin surface. Ointment or cream formulations are also suitable for rectal or vaginal delivery, along with other standard formulations, such as suppositories. The appropriate formulations for topical, vaginal or rectal administration are well known to medicinal chemists.

The present invention will be of particular utility for topical or mucosal administrations to treat a variety of bacterial infections or bacterially related undesirable conditions. Some representative examples of these uses include treatment of (1) conjunctivitis, caused by *Haemophilus sp.*, and corneal ulcers, caused by *Pseudomonas aeruginosa*; (2) otitis externa, caused by *Pseudomonas aeruginosa*; (3) chronic sinusitis, caused by many Gram-positive cocci and Gram-negative rods, or for general decontamination of bronchii; (4) cystic fibrosis, associated with *Pseudomonas aeruginosa*; (5) enteritis, caused by *Helicobacter pylori* (eg, to treat or prevent gastric ulcers), *Escherichia coli*, *Salmonella typhimurium*, *Campylobacter* or *Shigella sp.*; (6) open wounds, such as surgical or non-surgical, eg, as a prophylactic measure; (7) burns to eliminate *Pseudomonas aeruginosa* or other Gram-negative pathogens; (8) acne, eg, caused by *Propionobacter acnes*; (9) nose or skin infection, eg, caused by methicillin resistant *Staphylococcus aureus* (MRSA); (10) body odor, eg, caused by Gram-positive anaerobic bacteria (i.e., use of carrier cells in deodorants); (11) bacterial vaginosis, eg,

associated with *Gardnerella vaginalis* or other anaerobes; and (12) gingivitis and/or tooth decay caused by various organisms.

5 In one example, the target cells are *E coli* cells and the disease or condition to be treated or prevented in a human is a uterine tract infection or a ventilator associated infection, eg, pneumonia, sepsis, septicaemia or HUS.

10 In other embodiments, the carrier cells of the present invention find application in the treatment of surfaces for the removal or attenuation of unwanted target bacteria, for example use in a method of treating such a surface or an environment comprising target bacteria, wherein the method comprises contacting the surface or environment with carrier bacteria of the invention, allowing conjugative transfer of the first DNA of the invention from the carrier to the target bacteria, and allowing the antibacterial agent to kill target cells. For example, surfaces that may be used in invasive treatments such as surgery, catheterization and the like may be treated to prevent infection of a subject by
15 bacterial contaminants on the surface. It is contemplated that the methods and compositions of the present invention may be used to treat numerous surfaces, objects, materials and the like (e.g., medical or first aid equipment, nursery and kitchen equipment and surfaces) to control bacterial contamination thereon.

20 Pharmaceutical preparations or other compositions comprising the carrier bacteria may be formulated in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form, as used herein, refers to a physically discrete unit of the pharmaceutical preparation appropriate for the patient or plant or environment or surface undergoing treatment. Each dosage should contain a quantity of the carrier bacteria calculated to produce the desired antibacterial effect in association with the selected
25 carrier. Procedures for determining the appropriate dosage unit are well known to those skilled in the art. Dosage units may be proportionately increased or decreased based on the weight of a patient, plant, surface or environment. Appropriate concentrations for achieving eradication of pathogenic target cells (eg, comprised by a tissue of the patient) may be determined by dosage concentration curve calculations, as known in the art.

30 Other uses for the carrier bacteria of the invention are also contemplated. These include a variety agricultural, horticultural, environmental and food processing applications. For example, in agriculture and horticulture, various plant pathogenic bacteria may be targeted in order to minimize plant disease. One example of a plant pathogen suitable for targeting is *Erwinia* (eg, *E amylovora*, the
35 causal agent of fire blight). Similar strategies may be utilized to reduce or prevent wilting of cut flowers. For veterinary or animal farming, the carrier cells of the invention may be incorporated into

animal feed (chicken, swine, poultry, goat, sheep, fish, shellfish or cattle feed) to reduce bio-burden or to eliminate certain pathogenic organisms (e.g., *Salmonella*, such as in chicken, turkey or other poultry). In other embodiments, the invention may be applied on meat or other foods to eliminate unwanted or pathogenic bacteria (e.g., *E. coli* O157:H7 on meat, or *Proteus* spp., one cause of "fishy odour" on seafood).

Environmental utilities comprise, for example, engineering carrier bacteria, eg, *Bacillus thurengiensis* and one of its conjugative plasmids, to deliver and conditionally express an insecticidal agent in addition to or instead of an antibacterial agent (e.g., for the control of mosquitos that disseminate malaria or West Nile virus). In such applications, as well as in the agricultural and horticultural or other applications described above, formulation of the carrier bacteria as solutions, aerosols, or gel capsules are contemplated.

As used herein, the term "carrier cell" may include dividing and/or non-dividing bacterial cells (minicells and maxicells), or conditionally non-functional cells.

In an example the plasmid is an engineered RK2 plasmid (ie, a RK2 plasmid that has been modified by recombinant DNA technology or a progeny of such a modified plasmid). Plasmid RK2 is a promiscuous plasmid that can replicate in 29 (and probably many more) gram-negative species (Guiney and Lanka, 1989, p 27-54. In C. M. Thomas (ed) Promiscuous plasmids in gram-negative bacteria. London, Ltd London United Kingdom.). Plasmid RK2 is a 60-kb self-transmissible plasmid with a complete nucleotide sequence known (Pansegrau et al., 1994, J. Mol. Biol. 239, 623-663). A minimal replicon derived from this large plasmid has been obtained that is devoid of all its genes except for a *trfA* gene, that encodes plasmid's Rep protein called TrfA, and an origin of vegetative replication *oriV*. For a review of RK2 replication and its control by TrfA protein, see Helinski et al., 1996 (In *Escherichia coli* and *Salmonella* Cellular and Molecular Biology, Vol. 2 (ed. F. Neidhardt, et al., 2295-2324, ASM Press, Washington D.C.).

In an example the plasmid is an engineered R6K plasmid (ie, a R6K plasmid that has been modified by recombinant DNA technology or a progeny of such a modified plasmid).

The present invention is optionally for an industrial or domestic use, or is used in a method for such use. For example, it is for or used in agriculture, oil or petroleum industry, food or drink industry, clothing industry, packaging industry, electronics industry, computer industry, environmental industry, chemical industry, aerospace industry, automotive industry, biotechnology industry, medical industry, healthcare industry, dentistry industry, energy industry, consumer products industry, pharmaceutical industry, mining industry, cleaning industry, forestry industry, fishing industry, leisure

industry, recycling industry, cosmetics industry, plastics industry, pulp or paper industry, textile industry, clothing industry, leather or suede or animal hide industry, tobacco industry or steel industry.

- 5 The present invention is optionally for use in an industry or the environment is an industrial environment, wherein the industry is an industry of a field selected from the group consisting of the medical and healthcare; pharmaceutical; human food; animal food; plant fertilizers; beverage; dairy; meat processing; agriculture; livestock farming; poultry farming; fish and shellfish farming; veterinary; oil; gas; petrochemical; water treatment; sewage treatment; packaging; electronics and
- 10 computer; personal healthcare and toiletries; cosmetics; dental; non-medical dental; ophthalmic; non-medical ophthalmic; mineral mining and processing; metals mining and processing; quarrying; aviation; automotive; rail; shipping; space; environmental; soil treatment; pulp and paper; clothing manufacture; dyes; printing; adhesives; air treatment; solvents; biodefence; vitamin supplements; cold storage; fibre retting and production; biotechnology; chemical; industrial cleaning products; domestic
- 15 cleaning products; soaps and detergents; consumer products; forestry; fishing; leisure; recycling; plastics; hide, leather and suede; waste management; funeral and undertaking; fuel; building; energy; steel; and tobacco industry fields.

- In an example, the plasmid comprises a CRISPR array that targets target bacteria, wherein the array
- 20 comprises one, or two or more different spacers (eg, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50 or more spacers) for targeting the genome of target bacteria.

- In an example, the target bacteria are comprised by an environment as follows. In an example, the environment is a microbiome of a human, eg, the oral cavity microbiome or gut microbiome or the
- 25 bloodstream. In an example, the environment is not an environment in or on a human. In an example, the environment is not an environment in or on a non-human animal. In an embodiment, the environment is an air environment. In an embodiment, the environment is an agricultural environment. In an embodiment, the environment is an oil or petroleum recovery environment, eg, an oil or petroleum field or well. In an example, the environment is an environment in or on a foodstuff
- 30 or beverage for human or non-human animal consumption. In an example, the environment is a maritime environment, eg, in seawater or on a boat (eg, in ship or boat ballast water).

- In an example, the environment is a human or animal microbiome (eg, gut, vaginal, scalp, armpit, skin or oral cavity microbiome). In an example, the target bacteria are comprised by a human or
- 35 animal microbiome (eg, gut, vaginal, scalp, armpit, skin or oral cavity microbiome).

In an example, the carrier bacteria or composition of the invention are administered intranasally, topically or orally to a human or non-human animal, or is for such administration. The skilled person aiming to treat a microbiome of the human or animal will be able to determine the best route of administration, depending upon the microbiome of interest. For example, when the microbiome is a gut microbiome, administration can be intranasally or orally. When the microbiome is a scalp or armpit microbiome, administration can be topically. When the microbiome is in the mouth or throat, the administration can be orally.

In an example, the environment is harboured by a beverage or water (eg, a waterway or drinking water for human consumption) or soil. The water is optionally in a heating, cooling or industrial system, or in a drinking water storage container.

In an example, the carrier and/or target bacteria are *Firmicutes* selected from *Anaerotruncus*, *Acetanaerobacterium*, *Acetitomaculum*, *Acetivibrio*, *Anaerococcus*, *Anaerofilum*, *Anaerosinus*, *Anaerostipes*, *Anaerovorax*, *Butyrivibrio*, *Clostridium*, *Capracoccus*, *Dehalobacter*, *Dialister*, *Dorea*, *Enterococcus*, *Ethanoligenens*, *Faecalibacterium*, *Fusobacterium*, *Gracilibacter*, *Guggenheimella*, *Hespellia*, *Lachnobacterium*, *Lachnospira*, *Lactobacillus*, *Leuconostoc*, *Megamonas*, *Moryella*, *Mitsuokella*, *Oribacterium*, *Oxobacter*, *Papillibacter*, *Propionispira*, *Pseudobutyrvibrio*, *Pseudoramibacter*, *Roseburia*, *Ruminococcus*, *Sarcina*, *Seinonella*, *Shuttleworthia*, *Sporobacter*, *Sporobacterium*, *Streptococcus*, *Subdoligranulum*, *Syntrophococcus*, *Thermobacillus*, *Turibacter* and *Weissella*.

In an example, the carrier bacteria, composition, use or method is for reducing pathogenic infections or for re-balancing gut or oral biofilm eg, for treating or preventing obesity or disease in a human or animal; or for treating or preventing a GI condition (such as Crohn's disease, IBD or colitis). For example, the DNA, carrier bacteria, composition, use or method is for knocking-down *Salmonella*, *Campylobacter*, *Erwinia*, *Xanthomonas*, *Edwardsiella*, *Pseudomonas*, *Klebsiella*, *Pectobacterium*, *Clostridium difficile* or *E coli* bacteria in a gut biofilm of a human or animal or a plant, preferably in a human or animal.

In an example, the animal is a chicken, eg, and the target bacteria are *Salmonella* or *Campylobacter*. In an example, the animal is a fish (eg, catfish or salmon) or shellfish (eg, prawn or lobster), eg, and the target bacteria are *Edwardsiella*. In an example, the plant is a potato plant and, eg, the target bacteria are *Pectobacterium*. In an example, the plant is a cabbage plant and, eg, the target bacteria are *Xanthomonas* (eg, *X campestris*). In an example, the plant is a marijuana plant and, eg, the target bacteria are *Pseudomonas* (eg, *P cannabina* or *P amygdali*), *Agrobacterium* (eg, *A tumefaciens*) or

Xanthomonas (eg, *X campestris*). In an example, the plant is a hemp plant and, eg, the target bacteria are *Pseudomonas* (eg, *P cannabina* or *P amygdali*), *Agrobacterium* (eg, *A tumefaciens*) or Xanthomonas (eg, *X campestris*).

- 5 In an example, the disease or condition is a cancer, inflammatory or autoimmune disease or condition, eg, obesity, diabetes IBD, a GI tract condition or an oral cavity condition.

Optionally, the environment is comprised by, or the target bacteria are comprised by, a gut biofilm, skin biofilm, oral cavity biofilm, throat biofilm, hair biofilm, armpit biofilm, vaginal biofilm, rectal
 10 biofilm, anal biofilm, ocular biofilm, nasal biofilm, tongue biofilm, lung biofilm, liver biofilm, kidney biofilm, genital biofilm, penile biofilm, scrotal biofilm, mammary gland biofilm, ear biofilm, urethra biofilm, labial biofilm, organ biofilm or dental biofilm. Optionally, the environment is comprised by, or the target bacteria are comprised by, a plant (eg, a tobacco, crop plant, fruit plant, vegetable plant or tobacco, eg on the surface of a plant or contained in a plant) or by an environment (eg, soil or water
 15 or a waterway or aqueous liquid).

In an example, the carrier cell(s) or composition is for treating a disease or condition in an animal or human, wherein the disease or condition. In an example, the disease or condition is caused by or mediated by an infection of target cells comprised by the subject or patient. In an example, the
 20 disease or condition is associated with an infection of target cells comprised by the subject or patient. In an example, a symptom of the disease or condition is an infection of target cells comprised by the subject or patient.

- Optionally, the disease or condition of a human or animal subject is selected from
- 25 (a) A neurodegenerative disease or condition;
 - (b) A brain disease or condition;
 - (c) A CNS disease or condition;
 - (d) Memory loss or impairment;
 - (e) A heart or cardiovascular disease or condition, eg, heart attack, stroke or atrial
 30 fibrillation;
 - (f) A liver disease or condition;
 - (g) A kidney disease or condition, eg, chronic kidney disease (CKD);
 - (h) A pancreas disease or condition;
 - (i) A lung disease or condition, eg, cystic fibrosis or COPD;
 - 35 (j) A gastrointestinal disease or condition;
 - (k) A throat or oral cavity disease or condition;

- (l) An ocular disease or condition;
- (m) A genital disease or condition, eg, a vaginal, labial, penile or scrotal disease or condition;
- (n) A sexually-transmissible disease or condition, eg, gonorrhea, HIV infection, syphilis or Chlamydia infection;
- (o) An ear disease or condition;
- (p) A skin disease or condition;
- (q) A heart disease or condition;
- (r) A nasal disease or condition
- (s) A haematological disease or condition, eg, anaemia, eg, anaemia of chronic disease or cancer;
- (t) A viral infection;
- (u) A pathogenic bacterial infection;
- (v) A cancer;
- (w) An autoimmune disease or condition, eg, SLE;
- (x) An inflammatory disease or condition, eg, rheumatoid arthritis, psoriasis, eczema, asthma, ulcerative colitis, colitis, Crohn's disease or IBD;
- (y) Autism;
- (z) ADHD;
- (aa) Bipolar disorder;
- (bb) ALS [Amyotrophic Lateral Sclerosis];
- (cc) Osteoarthritis;
- (dd) A congenital or development defect or condition;
- (ee) Miscarriage;
- (ff) A blood clotting condition;
- (gg) Bronchitis;
- (hh) Dry or wet AMD;
- (ii) Neovascularisation (eg, of a tumour or in the eye);
- (jj) Common cold;
- (kk) Epilepsy;
- (ll) Fibrosis, eg, liver or lung fibrosis;
- (mm) A fungal disease or condition, eg, thrush;
- (nn) A metabolic disease or condition, eg, obesity, anorexia, diabetes, Type I or Type II diabetes.
- (oo) Ulcer(s), eg, gastric ulceration or skin ulceration;
- (pp) Dry skin;

- (qq) Sjogren's syndrome;
- (rr) Cytokine storm;
- (ss) Deafness, hearing loss or impairment;
- (tt) Slow or fast metabolism (ie, slower or faster than average for the weight, sex and age
- 5 of the subject);
- (uu) Conception disorder, eg, infertility or low fertility;
- (vv) Jaundice;
- (ww) Skin rash;
- (xx) Kawasaki Disease;
- 10 (yy) Lyme Disease;
- (zz) An allergy, eg, a nut, grass, pollen, dust mite, cat or dog fur or dander allergy;
- (aaa) Malaria, typhoid fever, tuberculosis or cholera;
- (bbb) Depression;
- (ccc) Mental retardation;
- 15 (ddd) Microcephaly;
- (eee) Malnutrition;
- (fff) Conjunctivitis;
- (ggg) Pneumonia;
- (hhh) Pulmonary embolism;
- 20 (iii) Pulmonary hypertension;
- (jjj) A bone disorder;
- (kkk) Sepsis or septic shock;
- (lll) Sinusitis;
- (mmm) Stress (eg, occupational stress);
- 25 (nnn) Thalassaemia, anaemia, von Willebrand Disease, or haemophilia;
- (ooo) Shingles or cold sore;
- (ppp) Menstruation;
- (qqq) Low sperm count.

30 NEURODEGENERATIVE OR CNS DISEASES OR CONDITIONS FOR TREATMENT OR PREVENTION BY THE INVENTION

In an example, the neurodegenerative or CNS disease or condition is selected from the group consisting of Alzheimer disease, geropsychosis, Down syndrome, Parkinson's disease, Creutzfeldt-jakob disease, diabetic neuropathy, Parkinson syndrome, Huntington's disease, Machado-Joseph

35 disease, amyotrophic lateral sclerosis, diabetic neuropathy, and Creutzfeldt Creutzfeldt- Jakob

disease. For example, the disease is Alzheimer disease. For example, the disease is Parkinson syndrome.

In an example, wherein the method of the invention is practised on a human or animal subject for treating a CNS or neurodegenerative disease or condition, the method causes downregulation of Treg cells in the subject, thereby promoting entry of systemic monocyte-derived macrophages and/or Treg cells across the choroid plexus into the brain of the subject, whereby the disease or condition (eg, Alzheimer's disease) is treated, prevented or progression thereof is reduced. In an embodiment the method causes an increase of IFN-gamma in the CNS system (eg, in the brain and/or CSF) of the subject. In an example, the method restores nerve fibre and/or reduces the progression of nerve fibre damage. In an example, the method restores nerve myelin and/or reduces the progression of nerve myelin damage. In an example, the method of the invention treats or prevents a disease or condition disclosed in WO2015136541 and/or the method can be used with any method disclosed in WO2015136541 (the disclosure of this document is incorporated by reference herein in its entirety, eg, for providing disclosure of such methods, diseases, conditions and potential therapeutic agents that can be administered to the subject for effecting treatment and/or prevention of CNS and neurodegenerative diseases and conditions, eg, agents such as immune checkpoint inhibitors, eg, anti-PD-1, anti-PD-L1, anti-TIM3 or other antibodies disclosed therein).

20 CANCERS FOR TREATMENT OR PREVENTION BY THE METHOD

Cancers that may be treated include tumours that are not vascularized, or not substantially vascularized, as well as vascularized tumours. The cancers may comprise non-solid tumours (such as haematological tumours, for example, leukaemias and lymphomas) or may comprise solid tumours. Types of cancers to be treated with the invention include, but are not limited to, carcinoma, blastoma, and sarcoma, and certain leukaemia or lymphoid malignancies, benign and malignant tumours, and malignancies e.g., sarcomas, carcinomas, and melanomas. Adult tumours/cancers and paediatric tumours/cancers are also included.

Haematologic cancers are cancers of the blood or bone marrow. Examples of haematological (or haematogenous) cancers include leukaemias, including acute leukaemias (such as acute lymphocytic leukaemia, acute myelocytic leukaemia, acute myelogenous leukaemia and myeloblasts, promyelocytic, myelomonocytic, monocytic and erythroleukaemia), chronic leukaemias (such as chronic myelocytic (granulocytic) leukaemia, chronic myelogenous leukaemia, and chronic lymphocytic leukaemia), polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's lymphoma (indolent and high grade forms), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, myelodysplastic syndrome, hairy cell leukaemia and myelodysplasia.

Solid tumours are abnormal masses of tissue that usually do not contain cysts or liquid areas. Solid tumours can be benign or malignant. Different types of solid tumours are named for the type of cells that form them (such as sarcomas, carcinomas, and lymphomas). Examples of solid tumours, such as

5 sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, and other sarcomas, synovioma, mesothelioma, Ewing's tumour, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary

10 thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumour, cervical cancer, testicular tumour, seminoma, bladder carcinoma, melanoma, and CNS tumours (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma,

15 germinoma, medulloblastoma, Schwannoma craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, retinoblastoma and brain metastases).

AUTOIMMUNE DISEASES FOR TREATMENT OR PREVENTION BY THE METHOD

- 20 1. Acute Disseminated Encephalomyelitis (ADEM)
2. Acute necrotizing hemorrhagic leukoencephalitis
3. Addison's disease
4. Agammaglobulinemia
5. Alopecia areata
- 25 6. Amyloidosis
7. Ankylosing spondylitis
8. Anti-GBM/Anti-TBM nephritis
9. Antiphospholipid syndrome (APS)
10. Autoimmune angioedema
- 30 11. Autoimmune aplastic anemia
12. Autoimmune dysautonomia
13. Autoimmune hepatitis
14. Autoimmune hyperlipidemia
15. Autoimmune immunodeficiency
- 35 16. Autoimmune inner ear disease (AIED)
17. Autoimmune myocarditis

18. Autoimmune oophoritis
19. Autoimmune pancreatitis
20. Autoimmune retinopathy
21. Autoimmune thrombocytopenic purpura (ATP)
- 5 22. Autoimmune thyroid disease
23. Autoimmune urticaria
24. Axonal & neuronal neuropathies
25. Balo disease
26. Behcet's disease
- 10 27. Bullous pemphigoid
28. Cardiomyopathy
29. Castleman disease
30. Celiac disease
31. Chagas disease
- 15 32. Chronic fatigue syndrome
33. Chronic inflammatory demyelinating polyneuropathy (CIDP)
34. Chronic recurrent multifocal osteomyelitis (CRMO)
35. Churg-Strauss syndrome
36. Cicatricial pemphigoid/benign mucosal pemphigoid
- 20 37. Crohn's disease
38. Cogan's syndrome
39. Cold agglutinin disease
40. Congenital heart block
41. Coxsackie myocarditis
- 25 42. CREST disease
43. Essential mixed cryoglobulinemia
44. Demyelinating neuropathies
45. Dermatitis herpetiformis
46. Dermatomyositis
- 30 47. Devic's disease (neuromyelitis optica)
48. Discoid lupus
49. Dressler's syndrome
50. Endometriosis
51. Eosinophilic esophagitis
- 35 52. Eosinophilic fasciitis
53. Erythema nodosum

- 54. Experimental allergic encephalomyelitis
- 55. Evans syndrome
- 56. Fibromyalgia
- 57. Fibrosing alveolitis
- 5 58. Giant cell arteritis (temporal arteritis)
- 59. Giant cell myocarditis
- 60. Glomerulonephritis
- 61. Goodpasture's syndrome
- 62. Granulomatosis with Polyangiitis (GPA) (formerly called Wegener's Granulomatosis)
- 10 63. Graves' disease
- 64. Guillain-Barre syndrome
- 65. Hashimoto's encephalitis
- 66. Hashimoto's thyroiditis
- 67. Hemolytic anemia
- 15 68. Henoch-Schonlein purpura
- 69. Herpes gestationis
- 70. Hypogammaglobulinemia
- 71. Idiopathic thrombocytopenic purpura (ITP)
- 72. IgA nephropathy
- 20 73. IgG4-related sclerosing disease
- 74. Immunoregulatory lipoproteins
- 75. Inclusion body myositis
- 76. Interstitial cystitis
- 77. Juvenile arthritis
- 25 78. Juvenile diabetes (Type 1 diabetes)
- 79. Juvenile myositis
- 80. Kawasaki syndrome
- 81. Lambert-Eaton syndrome
- 82. Leukocytoclastic vasculitis
- 30 83. Lichen planus
- 84. Lichen sclerosus
- 85. Ligneous conjunctivitis
- 86. Linear IgA disease (LAD)
- 87. Lupus (SLE)
- 35 88. Lyme disease, chronic
- 89. Meniere's disease

90. Microscopic polyangiitis
91. Mixed connective tissue disease (MCTD)
92. Mooren's ulcer
93. Mucha-Habermann disease
- 5 94. Multiple sclerosis
95. Myasthenia gravis
96. Myositis
97. Narcolepsy
98. Neuromyelitis optica (Devic's)
- 10 99. Neutropenia
100. Ocular cicatricial pemphigoid
101. Optic neuritis
102. Palindromic rheumatism
103. PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with
- 15 Streptococcus)
104. Paraneoplastic cerebellar degeneration
105. Paroxysmal nocturnal hemoglobinuria (PNH)
106. Parry Romberg syndrome
107. Parsonnage-Turner syndrome
- 20 108. Pars planitis (peripheral uveitis)
109. Pemphigus
110. Peripheral neuropathy
111. Perivenous encephalomyelitis
112. Pernicious anemia
- 25 113. POEMS syndrome
114. Polyarteritis nodosa
115. Type I, II, & III autoimmune polyglandular syndromes
116. Polymyalgia rheumatica
117. Polymyositis
- 30 118. Postmyocardial infarction syndrome
119. Postpericardiotomy syndrome
120. Progesterone dermatitis
121. Primary biliary cirrhosis
122. Primary sclerosing cholangitis
- 35 123. Psoriasis
124. Psoriatic arthritis

125. Idiopathic pulmonary fibrosis
126. Pyoderma gangrenosum
127. Pure red cell aplasia
128. Raynauds phenomenon
- 5 129. Reactive Arthritis
130. Reflex sympathetic dystrophy
131. Reiter's syndrome
132. Relapsing polychondritis
133. Restless legs syndrome
- 10 134. Retroperitoneal fibrosis
135. Rheumatic fever
136. Rheumatoid arthritis
137. Sarcoidosis
138. Schmidt syndrome
- 15 139. Scleritis
140. Scleroderma
141. Sjogren's syndrome
142. Sperm & testicular autoimmunity
143. Stiff person syndrome
- 20 144. Subacute bacterial endocarditis (SBE)
145. Susac's syndrome
146. Sympathetic ophthalmia
147. Takayasu's arteritis
148. Temporal arteritis/Giant cell arteritis
- 25 149. Thrombocytopenic purpura (TTP)
150. Tolosa-Hunt syndrome
151. Transverse myelitis
152. Type 1 diabetes
153. Ulcerative colitis
- 30 154. Undifferentiated connective tissue disease (UCTD)
155. Uveitis
156. Vasculitis
157. Vesiculobullous dermatosis
158. Vitiligo
- 35 159. Wegener's granulomatosis (now termed Granulomatosis with Polyangiitis (GPA)).

INFLAMMATORY DISEASES FOR TREATMENT OR PREVENTION BY THE METHOD

1. Alzheimer
2. ankylosing spondylitis
3. arthritis (osteoarthritis, rheumatoid arthritis (RA), psoriatic arthritis)
- 5 4. asthma
5. atherosclerosis
6. Crohn's disease
7. colitis
8. dermatitis
- 10 9. diverticulitis
10. fibromyalgia
11. hepatitis
12. irritable bowel syndrome (IBS)
13. systemic lupus erythematosus (SLE)
- 15 14. nephritis
15. Parkinson's disease
16. ulcerative colitis.

For example, the composition comprising carrier cells is an animal feed and/or beverage (eg, mixed in drinking water). When supplied in a beverage, the system, component or agent may be comprised by carrier bacteria, wherein the carrier bacteria are comprised in the beverage at an amount of from 1×10^3 to 1×10^{10} (eg, from 1×10^4 to 1×10^{10} ; from 1×10^4 to 1×10^9 ; from 1×10^4 to 1×10^8 ; from 1×10^4 to 1×10^7 ; from 1×10^3 to 1×10^{10} ; from 1×10^3 to 1×10^9 ; from 1×10^3 to 1×10^8 ; from 1×10^3 to 1×10^7 ; from 1×10^5 to 1×10^{10} ; from 1×10^5 to 1×10^9 ; from 1×10^5 to 1×10^8 ; from 1×10^5 to 1×10^7 ; from 1×10^6 to 1×10^{10} ; from 1×10^6 to 1×10^9 ; from 1×10^6 to 1×10^8 ; or from 1×10^6 to 1×10^7) cfu/ml. When supplied in a beverage, the system, component or agent may be comprised by carrier bacteria, wherein the carrier bacteria are comprised in the beverage at an amount of at least 1×10^8 cfu/ml, eg, wherein the animal is a poultry bird, such as a chicken.

Optionally, the guided nuclease is any guided nuclease disclosed herein, eg, a Cas, TALEN, meganuclease or a zinc finger nuclease. In an example, the component is a crRNA or guide RNA that is operable in target cells with a cognate Cas nuclease. The Cas nuclease can be any Cas nuclease disclosed herein. The Cas nuclease may be an endogenous Cas of the target cells or may be encoded by an exogenous nucleic acid that is administered to the animal.

35

It will be understood that particular embodiments described herein are shown by way of illustration and not as limitations of the invention. The principal features of this invention can be employed in various embodiments without departing from the scope of the invention. Those skilled in the art will recognize, or be able to ascertain using no more than routine study, numerous equivalents to the specific procedures described herein. Such equivalents are considered to be within the scope of this invention and are covered by the claims. All publications and patent applications mentioned in the specification are indicative of the level of skill of those skilled in the art to which this invention pertains. All publications and patent applications and all US equivalent patent applications and patents are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. The use of the word "a" or "an" when used in conjunction with the term "comprising" in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more," "at least one," and "one or more than one." The use of the term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and "and/or." Throughout this application, the term "about" is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

As used in this specification and claim(s), the words "comprising" (and any form of comprising, such as "comprise" and "comprises"), "having" (and any form of having, such as "have" and "has"), "including" (and any form of including, such as "includes" and "include") or "containing" (and any form of containing, such as "contains" and "contain") are inclusive or open-ended and do not exclude additional, unrecited elements or method steps

The term "or combinations thereof" or similar as used herein refers to all permutations and combinations of the listed items preceding the term. For example, "A, B, C, or combinations thereof" is intended to include at least one of: A, B, C, AB, AC, BC, or ABC, and if order is important in a particular context, also BA, CA, CB, CBA, BCA, ACB, BAC, or CAB. Continuing with this example, expressly included are combinations that contain repeats of one or more item or term, such as BB, AAA, MB, BBC, AAABCCCC, CBBAAA, CABABB, and so forth. The skilled artisan will understand that typically there is no limit on the number of items or terms in any combination, unless otherwise apparent from the context.

Any part of this disclosure may be read in combination with any other part of the disclosure, unless otherwise apparent from the context.

All of the compositions and/or methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

10 EXAMPLES

Pseudomonas syringae pv. tomato str. DC3000, used in the Examples, has the complete genome sequence of which has GenBank accession number AE016853.1, the entire sequence of which is incorporated herein by reference.

15 *P. fluorescens* strain 896 (*pfu* 896), used in the Examples, has the complete genome sequence of GenBank accession number CABVIN000000000.1, the entire sequence of which is incorporated herein by reference. *P. fluorescens* strain 887 (*pfu* 887), used in the Examples, has the complete genome sequence of GenBank accession number CABVIQ000000000.1, the entire sequence of which is incorporated herein by reference.

Example 1: Effective Delivery, Killing & Maintenance of Antibacterial Agent Using Conjugation to Bacteria with RND-Efflux Pumps

25 **Aim of the study**

This study was performed to evaluate the efficacy of a conjugation-delivered anti-*P. syringae* antibacterial CRISPR/Cas agent, when used as a protective product to selectively target and kill *P. syringae* pv. tomato, DC3000 strain (*Pto* DC3000) in the cv. Moneymaker variety of tomato plants. Herein, we refer to the agent as a CRISPR Guided Biotic™ (GB™). The *Pto* DC3000 comprised genes encoding RND efflux pumps, including genes PSPTO_0820 and PSPTO_4977.

Background/Scope

35 *P. syringae* pv. tomato (*Pto*) is a pathogen of tomato plants. The disease caused by *Pto* is characterised by bacterial specks, which start to appear on the leaves of young transplants. If the disease is left unmanaged in the developing plants, it causes death of the plants. This has been reported as a major cause of concern in the United States¹ and more recently in Italy², where the yield of tomato crops has

been severely affected by the bacterial speck disease. We investigated CRISPR Guided Biotic™ (GB™) technology to target the pathogen on or in plants to protect or manage the disease and prevent the loss of yield.

- 5 Our GB™ technology against *Pto* DC3000, was based on the CRISPR/Cas system, carried on a conjugative plasmid vector. The active GB™ vector encoded a Cas nuclease and cognate crRNA, with crRNA spacers targeting two conserved and essential genes in the genome of *P. syringae* DC3000. Both genes are chromosomally located on the genome of *Pto* DC3000. A control GB™ vector contained all of the other components of the active GB™ vector but didn't encode the crRNA. For the delivery of
- 10 GB™ vectors to the target bacteria in plants, we selected a non-pathogenic bacterium which forms part of the normal microbiota of plants as well as being present in soil and water. Two strains were developed and compared for the delivery of GB™ vectors. To enable the conjugative transfer of GB™ vectors, the conjugative plasmid (p)RP4 was transformed into the delivery strains (ie, into the carrier cells). The pRP4 is a 60 kb plasmid, which is also incorporated in the genome of the *E. coli* S17^{3,4}. Finally, the
- 15 control and active GB™ vectors were transformed into the delivery strains.

Materials and Methods

- The Moneymaker tomato plants were sown and two weeks after sowing seedlings were transplanted into 9cm pots. The experiment was performed in a contaminant level 2 plant room. The plants were
- 20 allowed to grow for seven weeks, before the start of the experiment. The strains used in this study and their characteristics are as follows:-

Plant control GB™ 1	Delivery strain 1 containing conjugative pRP4 and GB™ control vector. The pRP4 encoded a tetracycline marker of selection and GB™ vector encoded a gentamicin marker for selection.
Plant active GB™ 1	Delivery strain 1 containing conjugative, pRP4 and GB™ active vector encoding crRNA targeting two conserved and essential genes. The pRP4 encoded a tetracycline marker of selection and GB™ vector encoded a gentamicin marker for selection.
Plant control GB™ 2	Delivery strain 2 containing conjugative pRP4 and GB™ control vector. The pRP4 encoded a tetracycline marker of selection and GB™ vector encoded a gentamicin marker for selection.
Plant active GB™ 2	Delivery strain 2 containing conjugative, pRP4 and GB™ active vector encoding crRNA targeting two conserved and essential genes. The pRP4 encoded a tetracycline marker of selection and GB™ vector encoded a gentamicin marker for selection.

Pto DC3000

P. syringae pv. *syringae* DC3000 wild type strain, with chromosomally encoded rifampicin marker for selection.

The GBTM control and active strains were inoculated in Lysogeny (L) media (Sigma-Aldrich, UK), containing 12.5 µg/mL tetracycline and 25 µg/mL of gentamicin. These cultures and *Pto* DC3000 in L media were allowed to grow shaking at 28 °C, overnight. After the overnight incubation, the cultures were centrifuged at 4000 xg for 15 minutes. After centrifugation, the supernatant was discarded. The pellet was gently suspended into 10mM MgCl₂ and centrifuged again as stated above. The pellet was washed three times by suspending in fresh 10mM MgCl₂ and centrifugation each time. Finally, the OD_{600nm} of each culture was measured using the spectrophotometer. The OD_{600nm} of each GBTM active and control strain was adjusted to 0.3 in 10mM MgCl₂ containing 0.04 % Silwet. The *Pto* DC3000 was adjusted to 0.1 in 10mM MgCl₂ containing 0.04 % SilwetTM. The following treatments were applied in this study.

Treatment combinations and the number of plants per treatment, used in this study:-

Treatment	Number of plants		
	Biological replicate 1	Biological replicate 2	Biological replicate 3
Plant control GB TM 1+ <i>Pto</i> DC3000	3	3	3
Plant active GB TM 1+ <i>Pto</i> DC3000	3	3	3
Plant control GB TM 2+ <i>Pto</i> DC3000	3	3	3
Plant active GB TM 2+ <i>Pto</i> DC3000	3	3	3
<i>Pto</i> DC3000- disease control	2	3	3
MgCl ₂ negative control	2	3	3

In the first experiment, for homogeneity of coverage of the plants the ‘dip inoculation method’ was used for the application of the respective GBTM treatment. For dip inoculation, the plant pot was carefully inverted and dipped in the treatment contained in a 1L beaker. The pathogen, *Pto* DC3000 control and 10mM MgCl₂ containing 0.04 % Silwet, as negative control was sprayed on the plants. For spray inoculation, plastic plant water spray bottles were used. The spray bottles had jet and mist control to ensure uniform spraying on plant. Both the GBTM treatment and *Pto* DC3000 were applied as single applications. For the remaining biological replicates, both the GBTM treatments and controls were

sprayed on the plants. The treatment was allowed to dry for 2-3 hours (hrs). After this time, *Pto* DC3000 was sprayed on all the plants, except for the plants in the negative control group in which the plants were only sprayed with 10mM MgCl₂ containing 0.04 % Silwet. The leaf disc samples were made and processed as follows: After the plants were dry, two leaf discs were collected from each of the three
 5 separate leaves per plant, by using a cork borer No. 2 (area = 0.125 cm²). The leaf discs were ground in 100 µL volume of 10mM MgCl₂. The leaf disc extracts were serially diluted in 10mM MgCl₂ and 10 µL spot of each dilution was plated in duplicate on the L media agar plates containing 50 µg/mL of rifampicin, which selects for *Pto* DC3000 and 25 µg/mL of Nystatin, which was used as an anti-fungal agent. The leaf disc extracts from each plant was obtained after 24, 48, 72 hrs and 7 days and were
 10 processed as described above. The plates were incubated at 28 °C, for 48 hrs. The bacterial colonies were counted and CFU/cm² was calculated⁵. Percentage (%) reduction in pathogen (*Pto* DC3000) load was calculated as: (CFU/cm² plant control GBTM - CFU/cm² plant active GBTM)/CFU/cm² plant control GBTM *100. The log reduction in pathogen (*Pto* DC3000) load was calculated as: log (CFU/cm² plant control GBTM) - log (CFU/cm² plant active GBTM).

15

Results and Discussion

The conjugative carrier bacteria with GBTM vector was applied on the tomato plants. These plants were then exposed to infection with *Pto* DC3000 by spray application on the plants, except for the first biological replicate in which dip inoculation method was used. Any surviving *Pto* DC3000 after
 20 treatment with the GBTM was enumerated and compared to the control groups.

The protection assays showed that *Pto* DC3000 applied as the positive control for disease on average achieved a 2.5 log increase in CFU/cm², 7 days post-infection (Figures 1 and 2). The treatment with active GBTM 1 showed an overall 1.7 log reduction in CFU/cm², compared with the control GBTM 1
 25 (Figure 1 and table 8). A similar trend in the CFU/cm² reduction of *Pto* DC3000 was observed for the active GBTM 2 with an overall 1.2 log reduction in the pathogen load on plants, compared with the control GBTM 2 (Figure 2 and Table 8).

Although, there was a variation in the log reduction values in the load of *Pto* DC3000, per timepoint
 30 between the active GBTM compared with the control GBTM (Figures 1 and 2), the active GBTM successfully reduced the pathogen load in all cases.

Conclusively, the reduction in the number of *Pto* DC3000 as a result of the application of active GBTM using conjugation showed the guided biotic is effective in killing on plants. Thus, surprisingly we were
 35 able to effectively achieve delivery of an antibacterial agent into the target cells using conjugation, despite the presence of RND efflux pumps. The delivered agent, furthermore, was advantageously

retained sufficiently to enable killing by measurable and meaningful amounts. This study also suggests that active conjugative GBTM survives on the plants for up to a week, acting as a bactericidal against *Pto* DC3000, keeping the bacterial burden down. In this respect, see Table 9: we calculated the percentage reduction in the bacterial load referred to as the % kill by active GB at day 1 post-treatment (beginning of the experiment) and also at day 7 (end of the experiment). The % kill at each time point (i.e. day 1 and day 7) was compared with the non-active (or control) GB. The difference in the % kill between day 7 and day 1 was calculated as the average difference in % kill for triplicate experiments, for each of the two delivery strains used (*Pfu* 896 and *Pfu* 887). As seen in Table 9, the killing effect was surprisingly durable and maintained or even increased at day 7.

The set of plants treated with *Pto* DC3000 only and the ones treated with the control GBTM and then exposed to *Pto* DC3000 developed characteristic bacterial specks, and signs of chlorosis and necrosis of the infected leaves were also visible, after 7 days of the treatment. Figures 3A and 3B are representative images of plants treated with the plant control GBTM 1 and then sprayed with *Pto* DC3000, showing successful infection by *Pto* DC3000. As a comparison, the plants treated with the plant active GBTM 1 showed infection control and healthier plants (Figure 3C). In this case, only localized symptoms of the disease were observed on some leaves (Figure 3D), which may represent the areas of the leaves where the plant active GBTM 1 did not come in contact with the active pathogen, *Pto* DC3000 or the plant active GBTM 1 did not survive or replicate in all foliar parts of the plant. Generally, plants treated according to the invention were healthier compared with the control.

Example 2: Bioinformatics Analysis to Determine Bacterial Species & Strains with Gene Orthologues & Homologues

In order to determine the homologues and orthologues for the *PSPTO_0477* and *PSPTO_0820*, the nucleotide sequences of these genes were used to perform the BLASTN search, using the NCBI online search tool (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>). The searches were performed against the databases available on 27.04.2020. The homologues to the genes *PSPTO_0477* and *PSPTO_0820* were found (Tables 3 to 6) by performing the BLASTN search against the NCBI's standard non-redundent nucleotide (nr/nt) collection database and the top 100 hits are reported. A BLASTN search against the standard non-redundent nucleotide (nr/nt) collection database excluding the *Pseudomonadales* provided the orthologues of *PSPTO_0477* and *PSPTO_0820* in the non-*Pseudomonas* species (Tables 4 and 6). For *PSPTO_0820*, this search achieved several best hits with the percentage (%) sequence identity in the range of 80-82 % of the length of the query sequence in the range of 97-98 %. The top best hit for each species is reported (Table 6).

Example 3 Determination of Desirable Carrier Strain Characteristics

Data mining of the genome sequence of a collection of *P. fluorescens* strains showed the presence or absence of genes or operons involved in the natural product pathways in these strains (Reference 6, Figure 2). We determined that motile *P. fluorescens* carrier strains used in our study performed well; non-motile strains were found to be poor performers. The gene encoding for PepI is present in the genome of only the motile strains used in our study and absent from the non-motile strains. PepI has a role in the RiPP (ribosomally synthesized and post-translationally modified peptides) pathway (Reference 7). PepI encodes for a 69 amino acid product which provides immunity against Pep5, a lantibiotic (an antimicrobial peptide) produced by gram positive *Staphylococcus epidermidis* (Reference 8). We also determined that another gene, the gene encoding for the chitinase class I exoenzyme, is present in most motile strains studied and is absent from the non-motile strains. This enzyme is produced by *Pseudomonas aeruginosa* and it breaks down the polymer chitin, which is present in the cell wall of algae and fungi into the extracellular environment (Reference 9). The presence of these two genes exclusively in the motile strains suggests the role of these genes in the improved performance in pathogen control, advantage in colonisation and thereby the yield gain in planta.

References

- ¹Jones JB, Mc Carter SM, and Gitaitis R. (1981). *Pseudomonas syringae* pv. *syringae* with a leaf spot disease of tomato transplants in southern Georgia. *Phytopathology*. **71**;1281-1285.
- ²Garibaldi A, Minuto A, Scortichini M and Gullino, M. (2007). First Report of Syringae Leaf Spot Caused by *Pseudomonas syringae* pv. *syringae* on Tomato in Italy. *Plant disease*. **91**;1518. doi: 10.1094/PDIS-91-11-1518B
- ³Pansegrau W, Lanka E, Barth PT, Figurski DH, Guiney DG, Haas D, Helinski DR, Schwab H, Stanisich VA, and Thomas CM. (1994). Complete nucleotide sequence of Birmingham IncP plasmids: compilation and comparative analysis. *J. Mol. Biol.* **239**;623–663.
- ⁴Strand TA, Lale R, Degnes KF, Lando M and Valla S. (2014). A new and improved host-independent plasmid system for RK2-based conjugal transfer. *PLoS One*. **9**(3):e90372. doi: 10.1371/journal.pone.0090372. PMID: 24595202; PMCID: PMC3940858.
- ⁵Jacob C, Panchal S and Melotto M. Surface Inoculation and Quantification of *Pseudomonas syringae* Population in the *Arabidopsis* Leaf Apoplast. (2017). *Bio Protoc*. **7**(5):e2167. doi: 10.21769/BioProtoc.2167. PMID: 28573169; PMCID: PMC5448416

⁶Stefanato FL, Trippel C, Uszkoreit S, Ferrafiat L, Grenga L, Dickens R, Kelly N, Kingdon ADH, Ambrosetti L, Findlay KC, Cheema J, Trick M, Chandra G, Tomalin G, Malone JG, Truman AW. (2019). Pan-genome analysis identifies intersecting roles for *Pseudomonas* specialized metabolites in potato pathogen inhibition. In review: bioRxiv 783258; doi: <https://doi.org/10.1101/783258>

5

⁷Hudson GA, and Mitchell DA. (2018). RiPP antibiotics: biosynthesis and engineering potential. *Curr Opin Microbiol.* **45**:61-69. doi:10.1016/j.mib.2018.02.010

⁸Reis M, Eschbach-Bludau M, Iglesias-Wind MI, Kupke T, Sahl HG. (1994). Producer immunity towards the lantibiotic Pep5: identification of the immunity gene *pepI* and localization and functional analysis of its gene product. *Appl Environ Microbiol.* **60**(8):2876-2883. doi:10.1128/AEM.60.8.2876-2883.1994

⁹Folders J, Algra J, Roelofs MS, van Loon LC, Tommassen J, Bitter W. (2001). Characterization of *Pseudomonas aeruginosa* chitinase, a gradually secreted protein. *J Bacteriol.* **183**(24):7044-7052. doi:10.1128/JB.183.24.7044-7052.2001

TABLE 1: Example Target Cell Genera, Species & Strains

20 These may be useful, for example, where the target cell is comprised by a plant (or any part of a plant disclosed herein), or an environment (eg, a plant environment, eg, soil).

<i>Acidovorax avenae</i> subsp. <i>cattleyae</i>	<i>Brenneria quercina</i>
<i>Acidovorax avenae</i> subsp.	<i>Brenneria rubrifaciens</i>
<i>Acidovorax konjaci</i>	<i>Brenneria salicis</i>
<i>Acidovorax valerianellae</i>	<i>Burkholderia</i>
<i>Agrobacterium</i>	<i>Burkholderia andropogonis</i>
<i>Agrobacterium larrymoorei</i>	<i>Burkholderia caryophylli</i>
<i>Agrobacterium radiobacter</i>	<i>Burkholderia cepacia</i>
<i>Agrobacterium rhizogenes</i>	<i>Burkholderia gladioli</i>
<i>Agrobacterium rubi</i>	<i>Burkholderia gladioli</i> pv. <i>agaricicola</i>
<i>Agrobacterium tumefaciens</i>	<i>Burkholderia gladioli</i> pv. <i>alliiicola</i>
<i>Agrobacterium vitis</i>	<i>Burkholderia gladioli</i> pv. <i>gladioli</i>
<i>Arthrobacter</i>	<i>Burkholderia glumae</i>
<i>Arthrobacter ilicis</i>	<i>Burkholderia</i>
<i>Bacillus</i>	
<i>Bacillus megaterium</i>	
<i>Bacillus megaterium</i> pv. <i>cerealis</i>	<i>Clavibacter</i>
<i>Bacillus pumilus</i>	<i>Clavibacter michiganensis</i>
<i>Brenneria</i>	<i>Clavibacter michiganensis</i> subsp.
<i>Brenneria alni</i>	<i>Clavibacter michiganensis</i> subsp.
<i>Brenneria nigrifluens</i>	<i>michiganensis</i>
	<i>Clavibacter michiganensis</i> subsp. <i>nebraskensis</i>

Clavibacter michiganensis subsp. *sepedonicus*
Clavibacter michiganensis subsp. *tessellarius*
Clavibacter rathayi
Clavibacter toxicus
Clavibacter tritici
Clavibacter xyli
Clavibacter xyli subsp. *cynodontis*
Clavibacter xyli subsp. *xyli*

Clostridium
Clostridium puniceum
Corynebacterium
Corynebacterium betae
Corynebacterium beticola
Corynebacterium fascians
Corynebacterium flaccumfaciens
Corynebacterium flaccumfaciens pv. *betae*
Corynebacterium flaccumfaciens pv. *flaccumfaciens*
Corynebacterium flaccumfaciens pv. *oortii*
Corynebacterium flaccumfaciens pv. *poinsettiae*
Corynebacterium flaccumfaciens subsp.
Corynebacterium flaccumfaciens subsp. *flaccumfaciens*
Corynebacterium flaccumfaciens subsp. *oortii*
Corynebacterium flaccumfaciens subsp. *poinsettiae*
Corynebacterium ilicis
Corynebacterium insidiosum
Corynebacterium iranikum
Corynebacterium michiganense
Corynebacterium michiganensis pv. *insidiosus*
Corynebacterium michiganensis pv. *iranikum*
Corynebacterium michiganense pv. *nebraskense*
Corynebacterium michiganense pv. *rathayi*
Corynebacterium michiganense pv. *sepedonicum*
Corynebacterium michiganense pv. *tritici*
Corynebacterium michiganense subsp. *insidiosum*
Corynebacterium michiganense subsp. *nebraskense*
Corynebacterium michiganense subsp. *sepedonicum*
Corynebacterium michiganense subsp. *tessellarius*
Corynebacterium oortii

Corynebacterium
Corynebacterium rathayi
Corynebacterium sepedonicum

Corynebacterium tritici
Curtobacterium
Curtobacterium flaccumfaciens

Curtobacterium flaccumfaciens pv.
Curtobacterium flaccumfaciens pv. *flaccumfaciens*
Curtobacterium flaccumfaciens pv. *ilicis*
Curtobacterium flaccumfaciens pv. *oortii*
Curtobacterium flaccumfaciens pv. *poinsettiae*

Dickeya
Dickeya chrysanthemi
Dickeya chrysanthemi pv. *chrysanthemi*
Dickeya chrysanthemi pv. *parthenii*
Dickeya dadantii
Dickeya dianthicola
Dickeya dieffenbachiae
Dickeya paradisiaca
Dickeya zeae

Enterobacter
Enterobacter agglomerans
Enterobacter cancerogenus
Enterobacter cloacae
Enterobacter cloacae subsp. *dissolvens*
Enterobacter nimipressuralis
Enterobacter pyrinus

Erwinia

Erwinia alni
Erwinia amylovora .
Erwinia amylovora pv. *pyri*
Erwinia ananatis corrig.
Erwinia ananatis pv. *ananatis*
Erwinia ananas pv. *uredovora*
Erwinia cacticida
Erwinia cancerogena
Erwinia carnegiana
Erwinia carotovora
Erwinia carotovora pv. *atroseptica*
Erwinia carotovora pv. *carotovora*
Erwinia carotovora subsp. *atroseptica*
Erwinia carotovora subsp. *carotovora*
Erwinia carotovora subsp. *betavascularum*
Erwinia carotovora subsp. *odorifera*
Erwinia carotovora subsp. *wasabiae*
Erwinia chrysanthemi
Erwinia chrysanthemi pv. *chrysanthemi*
Erwinia chrysanthemi pv.
Erwinia chrysanthemi pv. *dieffenbachiae*
Erwinia chrysanthemi pv. *paradisiaca*

Erwinia chrysanthemi pv. *parthenii*
Erwinia chrysanthemi pv. *zeae*
Erwinia cypripedii
Erwinia dissolvens
Erwinia herbicola
Erwinia herbicola f. sp.
Erwinia herbicola pv. *milletiae*
Erwinia mallotivora
Erwinia nigrifluens
Erwinia nimipressuralis
Erwinia papayae
Erwinia proteamaculans
Erwinia persicina
Enterobacter pyrinus
Erwinia psidii
Erwinia pyrifoliae
Erwinia rhapontici
Erwinia rubrifaciens
Erwinia salicis
Erwinia stewartii
Erwinia tracheiphila
Erwinia uredovora
Ewingella
Ewingella americana
Gluconobacter Asai
Gluconobacter oxydans
Herbaspirillum
Herbaspirillum rubrisubalbicans
Janthinobacterium
Janthinobacterium agaricidamnosum
Leifsonia
Leifsonia cynodontis
Leifsonia xyli
Leifsonia xyli subsp. *cynodontis*
Leifsonia xyli subsp. *xyli*

Nocardia

Nocardia vaccinii

Pantoea

Pantoea agglomerans
Pantoea agglomerans pv. *gypsophilae*
Pantoea agglomerans pv. *milletiae*
Pantoea ananatis
Pantoea ananatis pv. *ananatis*
Pantoea ananatis pv. *uredovora*
Pantoea stewartii
Pantoea stewartii subsp. *indologenes*
Pantoea stewartii subsp. *stewartii*
Pectobacterium
Pectobacterium
Pectobacterium

Pectobacterium cacticida corrig
Pectobacterium
Pectobacterium carotovorum

Pectobacterium carotovorum subsp. *atrosepticum*
Pectobacterium carotovorum subsp. *betavascularum*
Pectobacterium carotovorum subsp. *brasiliensis*
Pectobacterium carotovorum subsp. *carotovorum*
Pectobacterium carotovorum subsp. *odoriferum*
Pectobacterium carotovorum subsp. *wasabiae*
Pectobacterium chrysanthemi
Pectobacterium chrysanthemi pv.
chrysanthemi
Pectobacterium chrysanthemi pv. *dianthicola*
Pectobacterium chrysanthemi pv.
dieffenbachiae
Pectobacterium chrysanthemi pv. *parthenii*
Pectobacterium chrysanthemi pv. *zeae*
Pectobacterium cypripedii
Pectobacterium rhapontici
Pectobacterium wasabiae

Pseudomonas

Pseudomonas agarici
Pseudomonas amygdali
Pseudomonas andropogonis pv. *andropogonis*
Pseudomonas andropogonis pv. *sojae*
Pseudomonas andropogonis pv. *stizolobii*
Pseudomonas asplenii
Pseudomonas avellanae
Pseudomonas avenae
Pseudomonas avenae subsp. *avenae*
Pseudomonas avenae subsp. *citrulli*
Pseudomonas avenae subsp. *konjaci*
Pseudomonas beteli corrig.
Pseudomonas cannabina
Pseudomonas caricapapayae
Pseudomonas caryophylli
Pseudomonas cattleyae
Pseudomonas cepacia
Pseudomonas cichorii
Pseudomonas cissicola
Pseudomonas coronafaciens
Pseudomonas corrugata
Pseudomonas costantinii
Pseudomonas dodoneae
Pseudomonas ficuserectae
Pseudomonas flectens

Pseudomonas fuscovaginae
Pseudomonas gingeri
Pseudomonas gladioli
Pseudomonas gladioli pv. *agaricicola*
Pseudomonas gladioli pv. *alliicola*
Pseudomonas gladioli pv. *gladioli*
Pseudomonas glumae
Pseudomonas hibiscicola
Pseudomonas marginalis
Pseudomonas marginalis pv. *alfalfae*
Pseudomonas marginalis pv. *marginalis*
Pseudomonas marginalis pv. *pastinacae*
Pseudomonas mediterranea
Pseudomonas meliae
Pseudomonas palleroniana
Pseudomonas plantarii
Pseudomonas pomi
Pseudomonas pseudoalcaligenes subsp. *citrulli*
Pseudomonas pseudoalcaligenes subsp. *konjaci*
Pseudomonas rubrilineans
Pseudomonas rubrisubalbicans
Pseudomonas salomonii
Pseudomonas savastanoi
Pseudomonas savastanoi pv. *fraxini*
Pseudomonas savastanoi pv. *glycinea*
Pseudomonas savastanoi pv. *nerii*
Pseudomonas savastanoi pv. *phaseolicola*
Pseudomonas savastanoi pv. *retacarpa*
Pseudomonas savastanoi pv. *savastanoi*
Pseudomonas syringae
Pseudomonas syringae pv. *aceris*
Pseudomonas syringae pv. *actinidiae*
Pseudomonas syringae pv. *aesculi*
Pseudomonas syringae pv. *alisalensis*
Pseudomonas syringae pv. *antirrhini*
Pseudomonas syringae pv. *apii*
Pseudomonas syringae pv. *aptata*
Pseudomonas syringae pv.
Pseudomonas syringae pv. *atropurpurea*
Pseudomonas syringae pv. *avellanae*
Pseudomonas syringae pv. *avii*
Pseudomonas syringae pv. *berberidis*
Pseudomonas syringae pv. *broussoetiae*
Pseudomonas syringae pv. *castaneae*
Pseudomonas syringae pv. *cerasicola*
Pseudomonas syringae pv. *ciccaronei*
Pseudomonas syringae pv. *coriandricola*
Pseudomonas syringae pv. *coronafaciens*
Pseudomonas syringae pv. *coryli*
Pseudomonas syringae pv. *cunninghamiae*
Pseudomonas syringae pv. *daphniphylli*
Pseudomonas syringae pv. *delphinii*

Pseudomonas syringae pv. *dendropanacis*
Pseudomonas syringae pv. *dysoxyl*
Pseudomonas syringae pv. *eriobotryae*
Pseudomonas syringae pv. *garcae*
Pseudomonas syringae pv. *glycinea*
Pseudomonas syringae pv. *helianthi*
Pseudomonas syringae pv.
Pseudomonas syringae pv.
Pseudomonas syringae pv.
Pseudomonas syringae pv. *lapsa*
Pseudomonas syringae pv. *maculicola*
Pseudomonas syringae pv.
Pseudomonas syringae pv. *mori*
Pseudomonas syringae pv. *morsprunorum* .
Pseudomonas syringae pv. *myricae*
Pseudomonas syringae pv.
Pseudomonas syringae pv. *papulans*
Pseudomonas syringae pv. *passiflorae*
Pseudomonas syringae pv.
Pseudomonas syringae pv. *philadelphia*
Pseudomonas syringae pv. *photiniae*
Pseudomonas syringae pv. *pisi*
Pseudomonas syringae pv. *porri*
Pseudomonas syringae pv. *primulae*
Pseudomonas syringae pv. *raphiolepidis*
Pseudomonas syringae pv. *ribicola*
Pseudomonas syringae pv. *sesami*
Pseudomonas syringae pv. *solidagae*
Pseudomonas syringae pv. *spinaceae*
Pseudomonas syringae pv. *syringae*
Pseudomonas syringae pv. *tagetis*
Pseudomonas syringae pv. *theae*
Pseudomonas syringae pv. *tomato*
Pseudomonas syringae pv. *ulmi*
Pseudomonas syringae pv. *viburni*
Pseudomonas syringae pv.
Pseudomonas syzygii
Pseudomonas tolaasii
Pseudomonas tremae
Pseudomonas viridiflava

Ralstonia
Ralstonia solanacearum
Ralstonia syzygii
Rathayibacter
Rathayibacter iranica
Rathayibacter rathayi
Rathayibacter
Rathayibacter tritici
Rhizobacter
Rhizobacter dauci corrig.

Rhizobium
Rhizobium larrymoorei

Rhizobium radiobacter
Rhizobium rhizogenes
Rhizobium rubi
Rhizobium vitis

Rhodococcus
Rhodococcus fascians

Samsonia
Samsonia erythrinae

Serratia
Serratia marcescens
Serratia proteamaculans

Sphingomonas
Sphingomonas melonis Buonauro
Sphingomonas suberifaciens

Spiroplasma
Spiroplasma citri

Spiroplasma kunkelii
Spiroplasma phoeniceum

Streptomyces
Streptomyces acidiscabies
Streptomyces albidoflavus
Streptomyces candidus
Streptomyces caviscabies
Streptomyces collinus
Streptomyces europaeiscabiei
Streptomyces intermedius
Streptomyces ipomoeae
Streptomyces luridiscabiei
Streptomyces niveiscabiei
Streptomyces puniscabiei
Streptomyces reticuliscabiei
Streptomyces scabiei corrig.
Streptomyces setonii
Streptomyces steliiscabiei
Streptomyces turgidiscabies
Streptomyces wedmorensis

Xanthomonas
Xanthomonas albilineans
Xanthomonas alfalfae
Xanthomonas alfalfae subsp. *alfalfae*
Xanthomonas alfalfae subsp. *citrumelonis*
Xanthomonas arboricola
Xanthomonas axonopodis
Xanthomonas bromi
Xanthomonas campestris
Xanthomonas cassavae

Xanthomonas citri
Xanthomonas cucurbitae
Xanthomonas euvesicatoria
Xanthomonas fragariae
Xanthomonas fuscans
Xanthomonas fuscans
Xanthomonas gardneri
Xanthomonas hortorum
Xanthomonas hortorum
Xanthomonas hyacinthi
Xanthomonas oryzae
Xanthomonas populi
Xanthomonas sacchari
Xanthomonas theicola
Xanthomonas translucens
Xanthomonas vasicola

Xylella
Xylella fastidiosa
Xylophilus
Xylophilus ampelinus

‘*Candidatus*’ Plant Pathogenic Bacteria

‘*Candidatus* Liberibacter’
‘*Candidatus* Liberibacter asiaticus’
‘*Candidatus* Phlomobacter’
‘*Candidatus* Phlomobacter fragariae’
‘*Candidatus* Phytoplasma’

FFS0002-1 WO

TABLE 2: Further Example Bacteria

Optionally, the carrier cells are selected from this Table and/or the target cells are selected from this Table (eg, wherein the carrier and target cells are of a different species; or of the same species but are a different strain or the carrier cells are engineered but the target cells are wild-type or *vice versa*). For example the carrier cells are *E coli* cells and the target cells are *C difficile*, *E coli*, *Akkermansia*, *Enterobacteriaceae*, *Ruminococcus*, *Faecalibacterium*, *Firmicutes*, *Bacteroidetes*, *Salmonella*, *Klebsiella*, *Pseudomonas*, *Acinetobacter* or *Streptococcus* cells.

Abiotrophia	Acidocella	Actinomyces	Alkalilimnicola	Aquaspirillum
<i>Abiotrophia defectiva</i>	<i>Acidocella aminolytica</i>	<i>Actinomyces bovis</i>	<i>Alkalilimnicola ehrlichii</i>	<i>Aquaspirillum polymorphum</i>
Acaricomes	<i>Acidocella facilis</i>	<i>Actinomyces denticolens</i>		<i>Aquaspirillum</i>
<i>Acaricomes phytoseiuli</i>	Acidomonas	<i>Actinomyces europaeus</i>	Alkaliphilus	<i>putridiconchylum</i>
	<i>Acidomonas methanolica</i>	<i>Actinomyces georgiae</i>	<i>Alkaliphilus oremlandii</i>	<i>Aquaspirillum serpens</i>
Acetitomaculum		<i>Actinomyces gerencseriae</i>	<i>Alkaliphilus transvaalensis</i>	
<i>Acetitomaculum ruminis</i>	Acidothermus	<i>Actinomyces</i>	Allochromatium	Aquimarina
	<i>Acidothermus cellulolyticus</i>	<i>hordeovulneris</i>	<i>Allochromatium vinosum</i>	<i>Aquimarina latercula</i>
Acetivibrio		<i>Actinomyces howellii</i>		
<i>Acetivibrio cellulolyticus</i>	Acidovorax	<i>Actinomyces hyovaginalis</i>	Alloiococcus	Arcanobacterium
<i>Acetivibrio ethanolignens</i>	<i>Acidovorax anthurii</i>	<i>Actinomyces israelii</i>	<i>Alloiococcus otitis</i>	<i>Arcanobacterium</i>
<i>Acetivibrio multivorans</i>	<i>Acidovorax caeni</i>	<i>Actinomyces johnsonii</i>		<i>haemolyticum</i>
	<i>Acidovorax cattlewayae</i>	<i>Actinomyces meyeri</i>	Allokutzneria	<i>Arcanobacterium pyogenes</i>
Acetoanaerobium	<i>Acidovorax citrulli</i>	<i>Actinomyces naeslundii</i>	<i>Allokutzneria albata</i>	
<i>Acetoanaerobium noterae</i>	<i>Acidovorax defluvi</i>	<i>Actinomyces neuvi</i>		Archangium
	<i>Acidovorax delafeldii</i>	<i>Actinomyces odontolyticus</i>		<i>Archangium gephyra</i>
	<i>Acidovorax facilis</i>	<i>Actinomyces oris</i>		

FFS0002-1 WO

Acetobacter	<i>Acidovorax konjaci</i>	<i>Actinomyces radingae</i>	Arcobacter
<i>Acetobacter aceti</i>	<i>Acidovorax temperans</i>	<i>Actinomyces slackii</i>	<i>Arcobacter butzleri</i>
<i>Acetobacter cerevisiae</i>	<i>Acidovorax valerianellae</i>	<i>Actinomyces turicensis</i>	<i>Arcobacter cryaerophilus</i>
<i>Acetobacter cibinongensis</i>	Acinetobacter	<i>Actinomyces viscosus</i>	<i>Arcobacter halophilus</i>
<i>Acetobacter estunensis</i>	<i>Acinetobacter baumannii</i>	Actinoplanes	<i>Arcobacter nitrofigilis</i>
<i>Acetobacter fabarum</i>	<i>Acinetobacter baylyi</i>	<i>Actinoplanes auranticolor</i>	<i>Arcobacter skirrowii</i>
<i>Acetobacter ghanensis</i>	<i>Acinetobacter bouvetii</i>	<i>Actinoplanes brasiliensis</i>	Arhodomonas
<i>Acetobacter indonesiensis</i>	<i>Acinetobacter calcoaceticus</i>	<i>Actinoplanes consettensis</i>	<i>Arhodomonas aquaeolei</i>
<i>Acetobacter lovaniensis</i>	<i>Acinetobacter gerneri</i>	<i>Actinoplanes deccanensis</i>	Arsenophonus
<i>Acetobacter malorum</i>	<i>Acinetobacter haemolyticus</i>	<i>Actinoplanes derwentensis</i>	<i>Arsenophonus nasoniae</i>
<i>Acetobacter nitrogenifigens</i>	<i>Acinetobacter johnsonii</i>	<i>Actinoplanes digitatis</i>	
<i>Acetobacter oeni</i>	<i>Acinetobacter junii</i>	<i>Actinoplanes durhamensis</i>	Aminobacter
<i>Acetobacter orientalis</i>	<i>Acinetobacter lwoffii</i>	<i>Actinoplanes ferrugineus</i>	<i>Aminobacter aganoensis</i>
<i>Acetobacter orleanensis</i>	<i>Acinetobacter parvus</i>	<i>Actinoplanes globisporus</i>	<i>Aminobacter aminovorans</i>
<i>Acetobacter pasteurianus</i>	<i>Acinetobacter radioresistens</i>	<i>Actinoplanes humidus</i>	<i>Aminobacter niigataensis</i>
<i>Acetobacter pornorurn</i>	<i>Acinetobacter schindleri</i>	<i>Actinoplanes italicus</i>	Arthrobacter
<i>Acetobacter senegalensis</i>	<i>Acinetobacter soli</i>	<i>Actinoplanes liguriensis</i>	<i>Arthrobacter agilis</i>
<i>Acetobacter xylinus</i>	<i>Acinetobacter tandoii</i>	<i>Actinoplanes lobatus</i>	<i>Arthrobacter albus</i>
Acetobacterium	<i>Acinetobacter tjernbergiae</i>	<i>Actinoplanes missouriensis</i>	<i>Arthrobacter aureus</i>
<i>Acetobacterium baktii</i>	<i>Acinetobacter townieri</i>	<i>Actinoplanes palleronii</i>	<i>Arthrobacter chlorophenolicus</i>
<i>Acetobacterium carbinolicum</i>	<i>Acinetobacter ursingii</i>	<i>Actinoplanes philippinensis</i>	<i>Arthrobacter citreus</i>
	<i>Acinetobacter venetianus</i>	<i>Actinoplanes rectilineatus</i>	<i>Arthrobacter crystallopoietes</i>

FFS0002-1 WO

<i>Acetobacterium dehalogenans</i>	Acrocarpospora	<i>Actinoplanes regularis</i>	Ammoniphilus	<i>Arthrobacter cumminsi</i>
<i>Acetobacterium fimetarium</i>	<i>Acrocarpospora corrugata</i>	<i>Actinoplanes</i>	<i>Ammoniphilus oxalaticus</i>	<i>Arthrobacter globiformis</i>
<i>Acetobacterium malicum</i>	<i>Acrocarpospora</i>	<i>teichomyceticus</i>	<i>Ammoniphilus oxalivorans</i>	<i>Arthrobacter</i>
<i>Acetobacterium paludosum</i>	<i>macrocephala</i>	<i>Actinoplanes utahensis</i>		<i>histidinovorans</i>
<i>Acetobacterium tundrae</i>	<i>Acrocarpospora</i>	Actinopolyspora	Amphibacillus	<i>Arthrobacter ilicis</i>
<i>Acetobacterium wieringae</i>	<i>pleiomorpha</i>	<i>Actinopolyspora halophila</i>	<i>Amphibacillus xylanus</i>	<i>Arthrobacter luteus</i>
<i>Acetobacterium woodii</i>		<i>Actinopolyspora</i>		<i>Arthrobacter methylotrophus</i>
Acetofilamentum	Actibacter	<i>mortivallis</i>	Amphritea	<i>Arthrobacter mysorens</i>
<i>Acetofilamentum rigidum</i>	<i>Actibacter sediminis</i>		<i>Amphritea balenae</i>	<i>Arthrobacter nicotianae</i>
Acetohalobium	Actinoalloteichus	Actinosynnema	<i>Amphritea japonica</i>	<i>Arthrobacter nicotinovorans</i>
<i>Acetohalobium arabaticum</i>	<i>Actinoalloteichus</i>	<i>Actinosynnema mirum</i>		<i>Arthrobacter oxydans</i>
	<i>cyanogriseus</i>		Amycolatopsis	<i>Arthrobacter pascens</i>
Acetomicrobium	<i>Actinoalloteichus</i>	Actinotalea	<i>Amycolatopsis alba</i>	<i>Arthrobacter</i>
<i>Acetomicrobium faecale</i>	<i>hymeniacidonis</i>	<i>Actinotalea fermentans</i>	<i>Amycolatopsis albidoflavus</i>	<i>phenanthrenivorans</i>
<i>Acetomicrobium flavidium</i>	<i>Actinoalloteichus spitiensis</i>		<i>Amycolatopsis azurea</i>	<i>Arthrobacter</i>
		Aerococcus	<i>Amycolatopsis coloradensis</i>	<i>polychromogenes</i>
Acetonema	Actinobaccillus	<i>Aerococcus sanguinicola</i>	<i>Amycolatopsis lurida</i>	<i>Arthrobacter protophormiae</i>
<i>Acetonema longum</i>	<i>Actinobacillus capsulatus</i>	<i>Aerococcus urinae</i>	<i>Amycolatopsis mediterranei</i>	<i>Arthrobacter</i>
	<i>Actinobacillus delphinicola</i>	<i>Aerococcus urinaeequi</i>	<i>Amycolatopsis rifamycinica</i>	<i>psychrolactophilus</i>
Acetothermus	<i>Actinobacillus hominis</i>	<i>Aerococcus urinaehominis</i>	<i>Amycolatopsis rubida</i>	<i>Arthrobacter ramosus</i>
<i>Acetothermus paucivorans</i>	<i>Actinobacillus indolicus</i>	<i>Aerococcus viridans</i>	<i>Amycolatopsis sulphurea</i>	<i>Arthrobacter sulfonivorans</i>
			<i>Amycolatopsis tolypomycinica</i>	<i>Arthrobacter sulfureus</i>

FFS0002-1 WO

Acholeplasma	<i>Actinobacillus lignieresii</i>	Aeromicrobium	Anabaena	<i>Arthrobacter uratoxydans</i>
<i>Acholeplasma axanthum</i>	<i>Actinobacillus minor</i>	<i>Aeromicrobium erythreum</i>	<i>Anabaena cylindrica</i>	<i>Arthrobacter ureafaciens</i>
<i>Acholeplasma brassicae</i>	<i>Actinobacillus muris</i>		<i>Anabaena flos-aquae</i>	<i>Arthrobacter viscosus</i>
<i>Acholeplasma cavigenitalium</i>	<i>Actinobacillus</i>	Aeromonas	<i>Anabaena variabilis</i>	<i>Arthrobacter woluwensis</i>
<i>Acholeplasma equifetale</i>	<i>pleuropneumoniae</i>	<i>Aeromonas</i>		Asaia
<i>Acholeplasma granularum</i>	<i>Actinobacillus porcinus</i>	<i>allosaccharophila</i>	Anaerococcus	<i>Asaia bogorensis</i>
<i>Acholeplasma hippikon</i>	<i>Actinobacillus rossii</i>	<i>Aeromonas bestiarum</i>	<i>Anaerococcus burkinensis</i>	
<i>Acholeplasma laidlawii</i>	<i>Actinobacillus scotiae</i>	<i>Aeromonas caviae</i>		Asanoa
<i>Acholeplasma modicum</i>	<i>Actinobacillus seminis</i>	<i>Aeromonas encheleia</i>	Anaerobaculum	<i>Asanoa ferruginea</i>
<i>Acholeplasma morum</i>	<i>Actinobacillus succinogenes</i>	<i>Aeromonas</i>	<i>Anaerobaculum mobile</i>	
<i>Acholeplasma multilocale</i>	<i>Actinobacillus suis</i>	<i>enteropelogenes</i>		Asticcacaulis
<i>Acholeplasma oculi</i>	<i>Actinobacillus ureae</i>	<i>Aeromonas eucrenophila</i>	Anaerobiospirillum	<i>Asticcacaulis biprosthecium</i>
<i>Acholeplasma palmae</i>	Actinobaculum	<i>Aeromonas ichthiosmia</i>	<i>Anaerobiospirillum</i>	<i>Asticcacaulis excentricus</i>
<i>Acholeplasma parvum</i>	<i>Actinobaculum massiliense</i>	<i>Aeromonas jandaei</i>	<i>succiniciproducens</i>	
<i>Acholeplasma pleciae</i>	<i>Actinobaculum schaalii</i>	<i>Aeromonas media</i>	<i>Anaerobiospirillum thomasi</i>	Atopobacter
<i>Acholeplasma vituli</i>	<i>Actinobaculum suis</i>	<i>Aeromonas popoffii</i>		<i>Atopobacter phocae</i>
Achromobacter	<i>Actinomyces urinale</i>	<i>Aeromonas sobria</i>	Anaerococcus	
<i>Achromobacter denitrificans</i>	Actinocatenispora	<i>Aeromonas veronii</i>	<i>Anaerococcus hydrogenalis</i>	Atopobium
<i>Achromobacter insolitus</i>	<i>Actinocatenispora rupis</i>		<i>Anaerococcus lactolyticus</i>	<i>Atopobium fossor</i>
<i>Achromobacter piechaudii</i>	<i>Actinocatenispora</i>	Agrobacterium	<i>Anaerococcus prevotii</i>	<i>Atopobium minutum</i>
		<i>Agrobacterium</i>	<i>Anaerococcus tetradius</i>	<i>Atopobium parvulum</i>
		<i>gelatinovorum</i>	<i>Anaerococcus vaginalis</i>	<i>Atopobium rimae</i>
				<i>Atopobium vaginae</i>

FFS0002-1 WO

<i>Achromobacter ruhlandii</i>	<i>thailandica</i>	Agrococcus	Anaerofustis	Aureobacterium
<i>Achromobacter spanius</i>	<i>Actinocatenispora sera</i>	<i>Agrococcus citreus</i>	<i>Anaerofustis stercorihominis</i>	<i>Aureobacterium barkeri</i>
Acidaminobacter	Actinocorallia	<i>Agrococcus jenensis</i>	Anaeromusa	Aurobacterium
<i>Acidaminobacter hydrogenoformans</i>	<i>Actinocorallia aurantiaca</i>	Agromonas	<i>Anaeromusa acidaminophila</i>	<i>Aurobacterium liquefaciens</i>
Acidaminococcus	<i>Actinocorallia aurea</i>	<i>Agromonas oligotrophica</i>	Anaeromyxobacter	Avibacterium
<i>Acidaminococcus fermentans</i>	<i>Actinocorallia cavernae</i>	Agromyces	<i>Anaeromyxobacter</i>	<i>Avibacterium avium</i>
<i>Acidaminococcus intestinalis</i>	<i>Actinocorallia glomerata</i>	<i>Agromyces fucosus</i>	<i>dehalogenans</i>	<i>Avibacterium gallinarum</i>
Acidicaldus	<i>Actinocorallia herbida</i>	<i>Agromyces hippuratus</i>	Anaerorhabdus	<i>Avibacterium paragallinarum</i>
<i>Acidicaldus organivorans</i>	<i>Actinocorallia libanotica</i>	<i>Agromyces luteolus</i>	<i>Anaerorhabdus furcosa</i>	<i>Avibacterium volantium</i>
Acidimicrobium	<i>Actinocorallia longicatena</i>	<i>Agromyces mediolanus</i>	Anaerovirgula	Azoarcus
<i>Acidimicrobium ferrooxidans</i>	Actinomadura	<i>Agromyces ramosus</i>	<i>Anaerovirgula multivorans</i>	<i>Azoarcus indigenus</i>
Acidiphilium	<i>Actinomadura alba</i>	<i>Agromyces rhizosphaerae</i>	Ancalomicrobium	<i>Azoarcus tolueticus</i>
<i>Acidiphilium acidophilum</i>	<i>Actinomadura atramentaria</i>	Akkermansia	<i>Ancalomicrobium adetum</i>	<i>Azoarcus toluovorans</i>
<i>Acidiphilium angustum</i>	<i>Actinomadura bangladesensis</i>	<i>Akkermansia muciniphila</i>	Azohydromonas	<i>Azohydromonas australica</i>
<i>Acidiphilium cryptum</i>	<i>Actinomadura catellatispora</i>	Albidiferax	<i>Azohydromonas lata</i>	Azomonas
<i>Acidiphilium multivorum</i>	<i>Actinomadura chibensis</i>	<i>Albidiferax ferrireducens</i>	<i>Azomonas agilis</i>	
<i>Acidiphilium organovorum</i>	<i>Actinomadura citrea</i>	Albidovulum		
<i>Acidiphilium rubrum</i>	<i>Actinomadura coerulea</i>	<i>Albidovulum inexpectatum</i>		

FFS0002-1 WO

Acidisoma	<i>Actinomadura fibrosa</i>	Alcaligenes	Ancyllobacter	<i>Azomonas insignis</i>
<i>Acidisoma sibiricum</i>	<i>Actinomadura formosensis</i>	<i>Alcaligenes denitrificans</i>	<i>Ancyllobacter aquaticus</i>	<i>Azomonas macrocytogenes</i>
<i>Acidisoma tundrae</i>	<i>Actinomadura hibisca</i>	<i>Alcaligenes faecalis</i>		Azorhizobium
Acidisphaera	<i>Actinomadura kijaniata</i>		Aneurinibacillus	<i>Azorhizobium caulinodans</i>
<i>Acidisphaera rubrifaciens</i>	<i>Actinomadura latina</i>	Alcanivorax	<i>Aneurinibacillus</i>	
Acidithiobacillus	<i>Actinomadura livida</i>	<i>Alcanivorax borkumensis</i>	<i>aneurinilyticus</i>	Azorhizophilus
<i>Acidithiobacillus albertensis</i>	<i>Actinomadura</i>	<i>Alcanivorax jadensis</i>	<i>Aneurinibacillus migulanus</i>	<i>Azorhizophilus paspali</i>
<i>Acidithiobacillus caldus</i>	<i>luteofluorescens</i>		<i>Aneurinibacillus</i>	
<i>Acidithiobacillus ferrooxidans</i>	<i>Actinomadura macra</i>	Algicola	<i>thermoaerophilus</i>	Azospirillum
<i>Acidithiobacillus thiooxidans</i>	<i>Actinomadura madurae</i>	<i>Algicola bacteriolytica</i>		<i>Azospirillum brasilense</i>
Acidobacterium	<i>Actinomadura oligospora</i>	Alicyclobacillus	Angiococcus	<i>Azospirillum halopraeferens</i>
<i>Acidobacterium capsulatum</i>	<i>Actinomadura pelleiteri</i>	<i>Alicyclobacillus</i>	<i>Angiococcus disciformis</i>	<i>Azospirillum irakense</i>
	<i>Actinomadura rubrobrunea</i>	<i>disulfidooxidans</i>		Azotobacter
	<i>Actinomadura rugatobispora</i>	<i>Alicyclobacillus</i>	Angulomicrobium	<i>Azotobacter beijerinckii</i>
	<i>Actinomadura umbrina</i>	<i>sendaiensis</i>	<i>Angulomicrobium tetradrale</i>	<i>Azotobacter chroococcum</i>
	<i>Actinomadura verrucosospora</i>	<i>Alicyclobacillus vulcanalis</i>	Anoxybacillus	<i>Azotobacter nigricans</i>
	<i>Actinomadura vinacea</i>		<i>Anoxybacillus pushchinoensis</i>	<i>Azotobacter salinestris</i>
	<i>Actinomadura viridilutea</i>	Alisewanella	Aquabacterium	<i>Azotobacter vinelandii</i>
	<i>Actinomadura viridis</i>	<i>Alisewanella fetalis</i>	<i>Aquabacterium commune</i>	
	<i>Actinomadura yumaensis</i>		<i>Aquabacterium parvum</i>	

FFS0002-1 WO

Alkalibacillus
Alkalibacillus
haloalkaliphilus

Bacillus [see below]	Bacteroides	Bibersteinia	Borrelia	Brevinema
	<i>Bacteroides caccae</i>	<i>Bibersteinia trehalosi</i>	<i>Borrelia afzelii</i>	<i>Brevinema andersonii</i>
	<i>Bacteroides coagulans</i>		<i>Borrelia americana</i>	
	<i>Bacteroides eggerthii</i>	Bifidobacterium	<i>Borrelia burgdorferi</i>	Brevundimonas
	<i>Bacteroides fragilis</i>	<i>Bifidobacterium adolescentis</i>	<i>Borrelia carolinensis</i>	<i>Brevundimonas alba</i>
	<i>Bacteroides galacturonicus</i>	<i>Bifidobacterium angulatum</i>	<i>Borrelia coriaceae</i>	<i>Brevundimonas aurantiaca</i>
	<i>Bacteroides helcogenes</i>	<i>Bifidobacterium animalis</i>	<i>Borrelia garinii</i>	<i>Brevundimonas diminuta</i>
	<i>Bacteroides ovatus</i>	<i>Bifidobacterium asteroides</i>	<i>Borrelia japonica</i>	<i>Brevundimonas intermedia</i>
Bacteriovorax	<i>Bacteroides pectinophilus</i>	<i>Bifidobacterium bifidum</i>		<i>Brevundimonas subvibrioides</i>
<i>Bacteriovorax stolpii</i>	<i>Bacteroides pyogenes</i>	<i>Bifidobacterium boum</i>	Bosea	<i>Brevundimonas vancanneytii</i>
	<i>Bacteroides salyersiae</i>	<i>Bifidobacterium breve</i>	<i>Bosea minaitilanensis</i>	<i>Brevundimonas variabilis</i>
	<i>Bacteroides stercoris</i>	<i>Bifidobacterium catenulatum</i>	<i>Bosea thiooxidans</i>	<i>Brevundimonas vesicularis</i>
	<i>Bacteroides suis</i>	<i>Bifidobacterium choerinum</i>		
	<i>Bacteroides tectus</i>	<i>Bifidobacterium coryneforme</i>	Brachybacterium	Brochothrix
	<i>Bacteroides thetaiotaomicron</i>	<i>Bifidobacterium cuniculi</i>	<i>Brachybacterium</i>	<i>Brochothrix campestris</i>
	<i>Bacteroides uniformis</i>	<i>Bifidobacterium dentium</i>	<i>alimentarium</i>	<i>Brochothrix thermosphacta</i>
		<i>Bifidobacterium gallicum</i>	<i>Brachybacterium faecium</i>	
			<i>Brachybacterium</i>	

FFS0002-1 WO

<i>Bacteroides ureolyticus</i>	<i>Bifidobacterium gallinarum</i>	<i>paraconglomeratum</i>	Brucella
<i>Bacteroides vulgatus</i>	<i>Bifidobacterium indicum</i>	<i>Brachybacterium rhamnosum</i>	<i>Brucella canis</i>
Balnearium	<i>Bifidobacterium longum</i>	<i>Brachybacterium</i>	<i>Brucella neotomae</i>
<i>Balnearium lithotrophicum</i>	<i>Bifidobacterium</i>	<i>tyrofermentans</i>	Bryobacter
Balneatrix	<i>magnumBifidobacterium</i>		<i>Bryobacter aggregatus</i>
<i>Balneatrix alpica</i>	<i>merycicum</i>	Brachyspira	
Balneola	<i>Bifidobacterium minimum</i>	<i>Brachyspira alvinipulli</i>	
<i>Balneola vulgaris</i>	<i>Bifidobacterium</i>	<i>Brachyspira hyodysenteriae</i>	Burkholderia
Barnesiella	<i>pseudocatenulatum</i>	<i>Brachyspira innocens</i>	<i>Burkholderia ambifaria</i>
<i>Barnesiella viscericola</i>	<i>Bifidobacterium</i>	<i>Brachyspira murchii</i>	<i>Burkholderia andropogonis</i>
Bartonella	<i>pseudolongum</i>	<i>Brachyspira pilosicoli</i>	<i>Burkholderia anthina</i>
<i>Bartonella alsatica</i>	<i>Bifidobacterium pullorum</i>		<i>Burkholderia caledonica</i>
<i>Bartonella bacilliformis</i>	<i>Bifidobacterium ruminantium</i>	Bradyrhizobium	<i>Burkholderia caryophylli</i>
<i>Bartonella clarridgeiae</i>	<i>Bifidobacterium saeculare</i>	<i>Bradyrhizobium canariense</i>	<i>Burkholderia cenocepacia</i>
<i>Bartonella doshiae</i>	<i>Bifidobacterium subtile</i>	<i>Bradyrhizobium elkanii</i>	<i>Burkholderia cepacia</i>
<i>Bartonella elizabethae</i>	<i>Bifidobacterium</i>	<i>Bradyrhizobium japonicum</i>	<i>Burkholderia cocovenenans</i>
<i>Bartonella grahamii</i>	<i>thermophilum</i>	<i>Bradyrhizobium liaoningense</i>	<i>Burkholderia dolosa</i>
<i>Bartonella henselae</i>	Bilophila	<i>Bradyrhizobium liaoningense</i>	<i>Burkholderia fungorum</i>
	<i>Bilophila wadsworthia</i>	Brenneria	<i>Burkholderia glathei</i>
	Biostraticola	<i>Brenneria alni</i>	<i>Burkholderia glumae</i>
	<i>Biostraticola tofi</i>	<i>Brenneria nigrifluens</i>	<i>Burkholderia graminis</i>
			<i>Burkholderia kururiensis</i>

FFS0002-1 WO

<i>Bartonella rochalimae</i>		<i>Brenneria quercina</i>	<i>Burkholderia multivorans</i>
<i>Bartonella vinsonii</i>	Bizionia	<i>Brenneria quercina</i>	<i>Burkholderia phenazinium</i>
	<i>Bizionia argentinensis</i>	<i>Brenneria salicis</i>	<i>Burkholderia plantarii</i>
Bavariicoccus		Brevibacillus	<i>Burkholderia pyrrocinia</i>
<i>Bavariicoccus seileri</i>	Blastobacter	<i>Brevibacillus agri</i>	<i>Burkholderia silvaticola</i>
	<i>Blastobacter capsulatus</i>	<i>Brevibacillus borstelensis</i>	<i>Burkholderia stabilis</i>
Bdellovibrio	<i>Blastobacter denitrificans</i>	<i>Brevibacillus brevis</i>	<i>Burkholderia thailandensis</i>
<i>Bdellovibrio bacteriovorus</i>		<i>Brevibacillus centrosporus</i>	<i>Burkholderia tropica</i>
<i>Bdellovibrio exovorus</i>	Blastococcus	<i>Brevibacillus choshinensis</i>	<i>Burkholderia unamae</i>
Beggiatoa	<i>Blastococcus aggregatus</i>	<i>Brevibacillus invocatus</i>	<i>Burkholderia vietnamiensis</i>
<i>Beggiatoa alba</i>	<i>Blastococcus saxosidens</i>		
	Blastochloris	<i>Brevibacillus laterosporus</i>	Butiauxella
Beijerinckia	<i>Blastochloris viridis</i>	<i>Brevibacillus parabravis</i>	<i>Butiauxella agrestis</i>
<i>Beijerinckia dextrii</i>		<i>Brevibacillus reuszeri</i>	<i>Butiauxella brennerae</i>
<i>Beijerinckia fluminensis</i>	Blastomonas		<i>Butiauxella ferruginea</i>
<i>Beijerinckia indica</i>	<i>Blastomonas natatoria</i>	Brevibacterium	<i>Butiauxella gaviniae</i>
<i>Beijerinckia mobilis</i>		<i>Brevibacterium abidum</i>	<i>Butiauxella izardii</i>
	Blastopirellula	<i>Brevibacterium album</i>	<i>Butiauxella noackiae</i>
Belliella	<i>Blastopirellula marina</i>	<i>Brevibacterium aurantiacum</i>	<i>Butiauxella warmboldiae</i>
<i>Belliella baltica</i>		<i>Brevibacterium celere</i>	
	Blautia	<i>Brevibacterium epidermidis</i>	Butyrivibrio
Bellilinea	<i>Blautia coccoides</i>	<i>Brevibacterium</i>	<i>Butyrivibrio fibrisolvens</i>
<i>Bellilinea caldifistulae</i>	<i>Blautia hansenii</i>	<i>frigoritolerans</i>	

FFS0002-1 WO

Belnapia	<i>Blautia producta</i>	<i>Brevibacterium halotolerans</i>	<i>Butyrivibrio hungatei</i>
<i>Belnapia moubensis</i>	<i>Blautia wexlerae</i>	<i>Brevibacterium iodinum</i>	<i>Butyrivibrio proteoclasticus</i>
Bergeriella	Bogoriella	<i>Brevibacterium linens</i>	
<i>Bergeriella denitrificans</i>	<i>Bogoriella caseilytica</i>	<i>Brevibacterium lyticum</i>	
		<i>Brevibacterium mcbrellneri</i>	
Beutenbergia	Bordetella	<i>Brevibacterium otitidis</i>	
<i>Beutenbergia cavernae</i>	<i>Bordetella avium</i>	<i>Brevibacterium oxydans</i>	
	<i>Bordetella bronchiseptica</i>	<i>Brevibacterium paucivorans</i>	
	<i>Bordetella hinzii</i>	<i>Brevibacterium stationis</i>	
	<i>Bordetella holmesii</i>		
	<i>Bordetella parapertussis</i>		
	<i>Bordetella pertussis</i>		
	<i>Bordetella petrii</i>		
	<i>Bordetella trematum</i>		
Bacillus			
<i>B. acidiceler</i>		<i>B. taeanensis</i>	<i>B. lautus</i>
<i>B. acidicola</i>	<i>B. glucanolyticus</i>	<i>B. tequilensis</i>	<i>B. lehensis</i>
<i>B. acidiproducens</i>	<i>B. gordonae</i>	<i>B. thermantarcticus</i>	<i>B. lentimorbus</i>
<i>B. acidocaldarius</i>	<i>B. gothelii</i>	<i>B. thermoaerophilus</i>	<i>B. lentus</i>
<i>B. acidoterrestris</i>	<i>B. graminis</i>	<i>B. thermoamylovorans</i>	<i>B. licheniformis</i>
	<i>B. anthracis</i>		

FFS0002-1 WO

<i>B. aeolus</i>	<i>B. aquimaris</i>	<i>B. haloalkaliphilus</i>	<i>B. thermocatenulatus</i>	<i>B. ligniniphilus</i>
<i>B. aerius</i>	<i>B. arenosi</i>	<i>B. halochares</i>	<i>B. thermocloacae</i>	<i>B. litoralis</i>
<i>B. aerophilus</i>	<i>B. arseniciselenatis</i>	<i>B. halodenitrificans</i>	<i>B. thermocypriae</i>	<i>B. locisalis</i>
<i>B. agaradhaerens</i>	<i>B. arsenicus</i>	<i>B. halodurans</i>	<i>B. thermodenitrificans</i>	<i>B. luciferensis</i>
<i>B. agri</i>	<i>B. aurantiacus</i>	<i>B. halophilus</i>	<i>B. thermoglucosidasius</i>	<i>B. luteolus</i>
<i>B. aidingensis</i>	<i>B. arvi</i>	<i>B. halosaccharovorans</i>	<i>B. thermolactis</i>	<i>B. luteus</i>
<i>B. akibai</i>	<i>B. aryabhatai</i>	<i>B. hemicellulosilyticus</i>	<i>B. thermoleovorans</i>	<i>B. macauensis</i>
<i>B. alcalophilus</i>	<i>B. asahii</i>	<i>B. hemicentroti</i>	<i>B. thermophilus</i>	<i>B. macerans</i>
<i>B. algicola</i>	<i>B. atrophaeus</i>	<i>B. herbersteinensis</i>	<i>B. thermoruber</i>	<i>B. macquariensis</i>
<i>B. alginolyticus</i>	<i>B. axarquiensis</i>	<i>B. horikoshii</i>	<i>B. thermosphaericus</i>	<i>B. macyae</i>
<i>B. alkalidiazotrophicus</i>	<i>B. azotoformans</i>	<i>B. homeckiae</i>	<i>B. thiaminolyticus</i>	<i>B. malacitensis</i>
<i>B. alkalinitrilicus</i>	<i>B. azotoformans</i>	<i>B. horti</i>	<i>B. thioparans</i>	<i>B. mannanihyticus</i>
<i>B. alkalisediminis</i>	<i>B. badius</i>	<i>B. huizhouensis</i>	<i>B. thuringiensis</i>	<i>B. marisflavi</i>
<i>B. alkalitelluris</i>	<i>B. barbaricus</i>	<i>B. humi</i>	<i>B. tianshenii</i>	<i>B. marismortui</i>
<i>B. altitudinis</i>	<i>B. bataviensis</i>	<i>B. hwajinpoensis</i>	<i>B. trypoxylicola</i>	<i>B. marmarensis</i>
<i>B. alveayuensis</i>	<i>B. beijingensis</i>	<i>B. idriensis</i>	<i>B. tusciae</i>	<i>B. massiliensis</i>
<i>B. alvei</i>	<i>B. benzoovorans</i>	<i>B. indicus</i>	<i>B. validus</i>	<i>B. megaterium</i>
<i>B. amyloliquefaciens</i>	<i>B. beringensis</i>	<i>B. infantis</i>	<i>B. vallismortis</i>	<i>B. mesonae</i>
• <i>B.</i>	<i>B. berkeleyi</i>	<i>B. infernus</i>	<i>B. vedderi</i>	<i>B. methanolicus</i>
<i>a. subsp. amyloliquefaciens</i>	<i>B. beveridgei</i>	<i>B. insolitus</i>	<i>B. velezensis</i>	<i>B. methylotrophicus</i>
• <i>B. a. subsp. plantarum</i>	<i>B. bogoriensis</i>	<i>B. invictae</i>	<i>B. vietnamensis</i>	<i>B. migulanus</i>
	<i>B. boroniphilus</i>	<i>B. iranensis</i>	<i>B. vireti</i>	<i>B. mojavenensis</i>

FFS0002-1 WO

<i>B. diposauri</i>	<i>B. borstelensis</i>	<i>B. isabeliae</i>	<i>B. vulcani</i>	<i>B. mucilaginosus</i>
<i>B. drenensis</i>	<i>B. brevis Migula</i>	<i>B. isronensis</i>	<i>B. wakoensis</i>	<i>B. muralis</i>
<i>B. edaphicus</i>	<i>B. butanolivorans</i>	<i>B. jeotgali</i>	<i>B. weihenstephanensis</i>	<i>B. murimartini</i>
<i>B. ehimensis</i>	<i>B. canaverdii</i>	<i>B. kaustophilus</i>	<i>B. xiamenensis</i>	<i>B. mycoides</i>
<i>B. eiseniae</i>	<i>B. carboniphilus</i>	<i>B. kobensis</i>	<i>B. xiaoxiensis</i>	<i>B. naganoensis</i>
<i>B. enclensis</i>	<i>B. cecembensis</i>	<i>B. kochii</i>	<i>B. zhanjiangensis</i>	<i>B. nanhaiensis</i>
<i>B. endophyticus</i>	<i>B. cellulosityticus</i>	<i>B. kokeshiiformis</i>		<i>B. nanhaiisediminis</i>
<i>B. endoradicis</i>	<i>B. centrosporus</i>	<i>B. koreensis</i>	<i>B. peoriae</i>	<i>B. nealsonii</i>
<i>B. farraginis</i>	<i>B. cereus</i>	<i>B. korlensis</i>	<i>B. persepolensis</i>	<i>B. neidei</i>
<i>B. fastidiosus</i>	<i>B. chagannorensis</i>	<i>B. kribbensis</i>	<i>B. persicus</i>	<i>B. neizhouensis</i>
<i>B. fengquensis</i>	<i>B. chitinolyticus</i>	<i>B. krulwichiae</i>	<i>B. pervagus</i>	<i>B. niabensis</i>
<i>B. firmus</i>	<i>B. chondroitinus</i>	<i>B. laevolacticus</i>	<i>B. plakortidis</i>	<i>B. niacini</i>
<i>B. flexus</i>	<i>B. choshinensis</i>	<i>B. larvae</i>	<i>B. pocheonensis</i>	<i>B. novalis</i>
<i>B. foraminis</i>	<i>B. chungangensis</i>	<i>B. laterosporus</i>	<i>B. polygona</i>	<i>B. oceanisediminis</i>
<i>B. fordii</i>	<i>B. cibi</i>	<i>B. salexigens</i>	<i>B. polymyxa</i>	<i>B. odysseyi</i>
<i>B. formosus</i>	<i>B. circulans</i>	<i>B. saliphilus</i>	<i>B. popilliae</i>	<i>B. okhensis</i>
<i>B. fortis</i>	<i>B. clarkii</i>	<i>B. schlegelii</i>	<i>B. pseudocalophilus</i>	<i>B. okuhidensis</i>
<i>B. fumarioli</i>	<i>B. clausii</i>	<i>B. sediminis</i>	<i>B. pseudofirmus</i>	<i>B. oleronius</i>
<i>B. funiculus</i>	<i>B. coagulans</i>	<i>B. selenatarsenatis</i>	<i>B. pseudomycoides</i>	<i>B. oryzaecorticis</i>
<i>B. fusiformis</i>	<i>B. coahuilensis</i>	<i>B. selenitireducens</i>	<i>B. psychrodurans</i>	<i>B. oshimensis</i>
<i>B. galactophilus</i>	<i>B. cohnii</i>	<i>B. seohaenamensis</i>	<i>B. psychrophilus</i>	<i>B. pabuli</i>
	<i>B. composti</i>	<i>B. shacheensis</i>	<i>B. psychrosaccharolyticus</i>	<i>B. pakistanensis</i>
			<i>B. psychrotolerans</i>	

FFS0002-1 WO

<i>B. galactosidilyticus</i>	<i>B. curdlanolyticus</i>	<i>B. shackletonii</i>	<i>B. pulvifaciens</i>	<i>B. pallidus</i>
<i>B. galliciensis</i>	<i>B. cycloheptanicus</i>	<i>B. siamensis</i>	<i>B. pumilus</i>	<i>B. pallidus</i>
<i>B. gelatini</i>	<i>B. cytotoxicus</i>	<i>B. silvestris</i>	<i>B. purgationiresistens</i>	<i>B. panacisoli</i>
<i>B. gibsonii</i>	<i>B. daliensis</i>	<i>B. simplex</i>	<i>B. pycnus</i>	<i>B. panaciterrae</i>
<i>B. ginsengi</i>	<i>B. decisifrondis</i>	<i>B. siralis</i>	<i>B. qingdaonensis</i>	<i>B. pantothenicus</i>
<i>B. ginsengihumi</i>	<i>B. decolorationis</i>	<i>B. smithii</i>	<i>B. qingshengii</i>	<i>B. parabrevis</i>
<i>B. ginsengisoli</i>	<i>B. deserti</i>	<i>B. soli</i>	<i>B. reuszeri</i>	<i>B. paraflexus</i>
<i>B. globisporus</i> (eg, <i>B.</i>		<i>B. solimangrovi</i>	<i>B. rhizosphaerae</i>	<i>B. pasteurii</i>
<i>g. subsp. Globisporus</i> ; or <i>B.</i>		<i>B. solisalsi</i>	<i>B. rigui</i>	<i>B. patagoniensis</i>
<i>g. subsp. Marinus</i>)		<i>B. songklensis</i>	<i>B. ruris</i>	
		<i>B. sonorensis</i>	<i>B. safensis</i>	
		<i>B. sphaericus</i>	<i>B. salarius</i>	
		<i>B. sporothermodurans</i>		
		<i>B. stearothermophilus</i>		
		<i>B. stratosphericus</i>		
		<i>B. subterraneus</i>		
		<i>B. subtilis</i> (eg, <i>B.</i>		
		<i>s. subsp. Inaquosorum</i> ; or <i>B.</i>		
		<i>s. subsp. Spizizeni</i> ; or <i>B.</i>		
		<i>s. subsp. Subtilis</i>)		
Caenimonas	Campylobacter	Cardiobacterium	Catenuloplanes	Curtobacterium
<i>Caenimonas koreensis</i>	<i>Campylobacter coli</i>	<i>Cardiobacterium hominis</i>	<i>Catenuloplanes atrovinosus</i>	<i>Curtobacterium</i>

FFS0002-1 WO

Caldakalibacillus	<i>Campylobacter concisus</i>	Carnimonas	<i>Catenuloplanes castaneus</i>	<i>albidum</i>
<i>Caldakalibacillus uzonensis</i>	<i>Campylobacter curvus</i>	<i>Carnimonas nigrificans</i>	<i>Catenuloplanes crispus</i>	<i>Curtobacterium citreus</i>
	<i>Campylobacter fetus</i>		<i>Catenuloplanes indicus</i>	
Caldanaerobacter	<i>Campylobacter gracilis</i>	Carnobacterium	<i>Catenuloplanes japonicus</i>	
<i>Caldanaerobacter subterraneus</i>	<i>Campylobacter helveticus</i>	<i>Carnobacterium</i>	<i>Catenuloplanes nepalensis</i>	
	<i>Campylobacter hominis</i>	<i>alterfunditum</i>	<i>Catenuloplanes niger</i>	
Caldanaerobius	<i>Campylobacter hyointestinalis</i>	<i>Carnobacterium divergens</i>		
<i>Caldanaerobius fijiensis</i>	<i>Campylobacter jejuni</i>	<i>Carnobacterium funditum</i>	Chryseobacterium	
<i>Caldanaerobius</i>	<i>Campylobacter lari</i>	<i>Carnobacterium gallinarum</i>	<i>Chryseobacterium</i>	
<i>polysaccharolyticus</i>	<i>Campylobacter mucosalis</i>	<i>Carnobacterium</i>	<i>balustinum</i>	
<i>Caldanaerobius zeae</i>	<i>Campylobacter rectus</i>	<i>mltaromaticum</i>	Citrobacter	
Caldanaerovirga	<i>Campylobacter showae</i>	<i>Carnobacterium mobile</i>	<i>C. amalonaticus</i>	
<i>Caldanaerovirga acetigignens</i>	<i>Campylobacter sputorum</i>	<i>Carnobacterium viridans</i>	<i>C. braakii</i>	
	<i>Campylobacter upsaliensis</i>		<i>C. diversus</i>	
Caldicellulosiruptor	Capnocytophaga	Caryophanon	<i>C. farmeri</i>	
<i>Caldicellulosiruptor bescii</i>	<i>Capnocytophaga canimorsus</i>	<i>Caryophanon latum</i>	<i>C. freundii</i>	
<i>Caldicellulosiruptor kristjanssonii</i>	<i>Capnocytophaga cynodegmi</i>	<i>Caryophanon tenue</i>	<i>C. gillenii</i>	
<i>Caldicellulosiruptor owensensis</i>	<i>Capnocytophaga gingivalis</i>	Catellatospora	<i>C. koseri</i>	
	<i>Capnocytophaga granulosa</i>	<i>Catellatospora citrea</i>	<i>C. murlinae</i>	
	<i>Capnocytophaga haemolytica</i>	<i>Catellatospora</i>	<i>C. pasteurii⁽¹⁾</i>	
	<i>Capnocytophaga ochracea</i>	<i>methionotrophica</i>	<i>C. rodentium</i>	
	<i>Capnocytophaga sputigena</i>		<i>C. sedlakii</i>	

Catenococcus

C. werkmanii
C. youngae

Catenococcus thiocycli

Clostridium

(see below)

Coccochloris

Coccochloris elabens

Corynebacterium

Corynebacterium flavescens
Corynebacterium variabile

Clostridium

Clostridium absonum, *Clostridium aceticum*, *Clostridium acetireducens*, *Clostridium acetobutylicum*, *Clostridium acidisoli*, *Clostridium aciditolerans*, *Clostridium acidurici*, *Clostridium aerotolerans*, *Clostridium aestuarii*, *Clostridium akagii*, *Clostridium aldenense*, *Clostridium aldrichii*, *Clostridium algidicarni*, *Clostridium algidixylanolyticum*, *Clostridium algifacis*, *Clostridium algoriphilum*, *Clostridium alkallicellulosi*, *Clostridium aminophilum*, *Clostridium aminovalericum*, *Clostridium amygdalinum*, *Clostridium amylolyticum*, *Clostridium arbuti*, *Clostridium arcticum*, *Clostridium argentinense*, *Clostridium asparagiforme*, *Clostridium aurantibutyricum*, *Clostridium autoethanogenum*, *Clostridium baratii*, *Clostridium barkeri*, *Clostridium bartlettii*, *Clostridium beijerinckii*, *Clostridium bifermentans*, *Clostridium boltea*, *Clostridium bornimense*, *Clostridium botulinum*, *Clostridium bowmanii*, *Clostridium bryanii*, *Clostridium butyricum*, *Clostridium cadaveris*, *Clostridium caenicola*, *Clostridium caminithermale*, *Clostridium carboxidivorans*, *Clostridium carnis*, *Clostridium cavendishii*, *Clostridium celatatum*, *Clostridium celerecrescens*, *Clostridium cellobioparum*, *Clostridium cellulofragmentans*, *Clostridium cellulolyticum*, *Clostridium cellulosi*, *Clostridium cellulovorans*, *Clostridium chartatabidum*, *Clostridium chauvoei*, *Clostridium chromiireducens*, *Clostridium citroniae*, *Clostridium clariflavum*, *Clostridium clostridioforme*, *Clostridium coccoides*, *Clostridium cochlearium*, *Clostridium colletant*, *Clostridium colicanis*,

Clostridium colinum, *Clostridium collagenovorans*, *Clostridium cylindrosporum*, *Clostridium difficile*, *Clostridium diolis*, *Clostridium disporicum*,
Clostridium drakei, *Clostridium durum*, *Clostridium estertheticum*, *Clostridium estertheticum estertheticum*, *Clostridium estertheticum laramiense*,
Clostridium fallax, *Clostridium felsineum*, *Clostridium fervidum*, *Clostridium fimetarium*, *Clostridium formicaceticum*, *Clostridium frigidicarnis*, *Clostridium*
frigoris, *Clostridium ganghwense*, *Clostridium gasigenes*, *Clostridium ghonii*, *Clostridium glycolicum*, *Clostridium glycyrrhizinilyticum*, *Clostridium grantii*,
Clostridium haemolyticum, *Clostridium halophilum*, *Clostridium hastiforme*, *Clostridium hathewayi*, *Clostridium herbivorans*, *Clostridium hiranonis*,
Clostridium histolyticum, *Clostridium homopropionicum*, *Clostridium huakuii*, *Clostridium hungatei*, *Clostridium hydrogeniformans*, *Clostridium*
hydroxybenzoicum, *Clostridium hylemonae*, *Clostridium jejuense*, *Clostridium indolis*, *Clostridium innocuum*, *Clostridium intestinale*, *Clostridium irregulare*,
Clostridium isatidis, *Clostridium josui*, *Clostridium kluyveri*, *Clostridium lactatifermentans*, *Clostridium lacusfryxellense*, *Clostridium laramiense*, *Clostridium*
lavalense, *Clostridium lentocellum*, *Clostridium lentoputrescens*, *Clostridium leptum*, *Clostridium limosum*, *Clostridium litorale*, *Clostridium lituseburense*,
Clostridium ljungdahlii, *Clostridium lortetii*, *Clostridium lundense*, *Clostridium magnum*, *Clostridium malenominatum*, *Clostridium manganotii*, *Clostridium*
mayombei, *Clostridium methoxybenzovorans*, *Clostridium methylpentosum*, *Clostridium neopropionicum*, *Clostridium nexile*, *Clostridium nitrophenolicum*,
Clostridium novyi, *Clostridium oceanicum*, *Clostridium orbiscindens*, *Clostridium oroticum*, *Clostridium oxalicum*, *Clostridium papyrosolvans*, *Clostridium*
paradoxum, *Clostridium paraperfringens* (Alias: *C. welchii*), *Clostridium paraputrificum*, *Clostridium pascui*, *Clostridium pasteurianum*, *Clostridium*
peptidivorans, *Clostridium perenne*, *Clostridium perfringens*, *Clostridium pfennigii*, *Clostridium phytofermentans*, *Clostridium piliforme*, *Clostridium*
polysaccharolyticum, *Clostridium populei*, *Clostridium propionicum*, *Clostridium proteoclasticum*, *Clostridium proteolyticum*, *Clostridium psychrophilum*,
Clostridium puniceum, *Clostridium purinilyticum*, *Clostridium putrefaciens*, *Clostridium putrificum*, *Clostridium quercicolum*, *Clostridium quinii*, *Clostridium*
ramosum, *Clostridium rectum*, *Clostridium roseum*, *Clostridium saccharobutylicum*, *Clostridium saccharogumia*, *Clostridium saccharolyticum*, *Clostridium*
saccharoperbutylacetonicum, *Clostridium sardiniense*, *Clostridium sartagoforme*, *Clostridium scatologenes*, *Clostridium schirmacherense*, *Clostridium*
scindens, *Clostridium septicum*, *Clostridium sordellii*, *Clostridium sphenoides*, *Clostridium spiroforme*, *Clostridium sporogenes*, *Clostridium*
sporosphaeroides, *Clostridium stercorarium*, *Clostridium stercorarium leptospartum*, *Clostridium stercorarium stercorarium*, *Clostridium stercorarium*
thermolacticum, *Clostridium sticklandii*, *Clostridium straminisolvans*, *Clostridium subterminale*, *Clostridium sufflavum*, *Clostridium sulfidigenes*, *Clostridium*
symbiosum, *Clostridium tagluense*, *Clostridium tepidiprofundii*, *Clostridium termitidis*, *Clostridium tetani*, *Clostridium tetanomorphum*,

Clostridium thermacetivum, *Clostridium thermautotrophicum*, *Clostridium thermoacetalophilum*, *Clostridium thermobutyricum*, *Clostridium thermocellum*, *Clostridium thermocopriae*, *Clostridium thermohydrosulfuricum*, *Clostridium thermolacticum*, *Clostridium thermopalmarum*, *Clostridium thermopaperyolyticum*, *Clostridium thermosaccharolyticum*, *Clostridium thermosuccinogenes*, *Clostridium thermosulfurigenes*, *Clostridium thiosulfatireducens*, *Clostridium tyrobutyricum*, *Clostridium uliginosum*, *Clostridium ultunense*, *Clostridium villosum*, *Clostridium vincentii*, *Clostridium viride*, *Clostridium xylanolyticum*, *Clostridium xylanovorans*

Dactylosporangium	Deinococcus	Delftia	Echinicola
<i>Dactylosporangium aurantiacum</i>	<i>Deinococcus aerius</i>	<i>Delftia acidovorans</i>	<i>Echinicola pacifica</i>
<i>Dactylosporangium fulvum</i>	<i>Deinococcus apachensis</i>	Desulfovibrio	<i>Echinicola vietnamensis</i>
<i>Dactylosporangium matsuzakiense</i>	<i>Deinococcus aquaticus</i>	<i>Desulfovibrio desulfuricans</i>	
<i>Dactylosporangium roseum</i>	<i>Deinococcus aquatilis</i>	Diplococcus	
<i>Dactylosporangium thailandense</i>	<i>Deinococcus caeni</i>	<i>Diplococcus pneumoniae</i>	
<i>Dactylosporangium vinaceum</i>	<i>Deinococcus radiodurans</i>		
	<i>Deinococcus radiophilus</i>		
Enterobacter	<i>Enterobacter kobei</i>	Faecalibacterium	Flavobacterium
<i>E. aerogenes</i>	<i>E. ludwigii</i>	<i>Faecalibacterium prausnitzii</i>	<i>Flavobacterium antarcticum</i>
<i>E. amnigenus</i>	<i>E. mori</i>	Fangia	<i>Flavobacterium aquatile</i>
<i>E. agglomerans</i>	<i>E. nimipressuralis</i>	<i>Fangia hongkongensis</i>	<i>Flavobacterium</i>
<i>E. arachidis</i>	<i>E. oryzae</i>	Fastidiosipila	<i>aquidurensis</i>
<i>E. asburiae</i>	<i>E. pulveris</i>	<i>Fastidiosipila sanguinis</i>	<i>Flavobacterium balustinum</i>
<i>E. cancerogenus</i>	<i>E. pyrinus</i>	Fusobacterium	<i>Flavobacterium croceum</i>
<i>E. cloacae</i>	<i>E. radicitans</i>	<i>Fusobacterium nucleatum</i>	<i>Flavobacterium cucumis</i>

FFS0002-1 WO

<i>E. cowanii</i>	<i>E.aylorae</i>	<i>Flavobacterium</i>
<i>E. dissolvens</i>	<i>E. turicensis</i>	<i>daejeonense</i>
<i>E. gergoviae</i>	<i>E. sakazakii</i>	<i>Flavobacterium defluvii</i>
<i>E. helveticus</i>	Enterococcus	<i>Flavobacterium degerlachei</i>
<i>E. hormaechei</i>	<i>Enterococcus durans</i>	<i>Flavobacterium</i>
<i>E. intermedius</i>	<i>Enterococcus faecalis</i>	<i>denitrificans</i>
	<i>Enterococcus faecium</i>	<i>Flavobacterium filum</i>
	Erwinia	<i>Flavobacterium flevense</i>
	<i>Erwinia hapontici</i>	<i>Flavobacterium frigidarium</i>
	Escherichia	<i>Flavobacterium mizutaii</i>
	<i>Escherichia coli</i>	<i>Flavobacterium</i>
		<i>okeanokoites</i>
Gaetbulibacter	Haemophilus	Janibacter
<i>Gaetbulibacter saemankumensis</i>	<i>Haemophilus aegyptius</i>	<i>Janibacter anophelis</i>
Gallibacterium	<i>Haemophilus aphrophilus</i>	<i>Janibacter corallicola</i>
<i>Gallibacterium anatis</i>	<i>Haemophilus felis</i>	<i>Janibacter limosus</i>
Gallicola	<i>Haemophilus gallinarum</i>	<i>Janibacter melonis</i>
<i>Gallicola barnesae</i>	<i>Haemophilus haemolyticus</i>	<i>Janibacter terrae</i>
Garciella	<i>Haemophilus influenzae</i>	Jannaschia
<i>Garciella nitratreducens</i>	<i>Haemophilus paracuniculus</i>	<i>Jannaschia cystaugens</i>

FFS0002-1 WO

Geobacillus	<i>Haemophilus parahaemolyticus</i>	<i>Idiomarina seosinensis</i>	<i>Jannaschia helgolandensis</i>
<i>Geobacillus thermoglucosidasius</i>	<i>Haemophilus parainfluenzae</i>	<i>Idiomarina zobellii</i>	<i>Jannaschia pohangensis</i>
<i>Geobacillus stearothermophilus</i>	<i>Haemophilus</i>	Ignatzschineria	<i>Jannaschia rubra</i>
Geobacter	<i>paraphrohaemolyticus</i>	<i>Ignatzschineria larvae</i>	
<i>Geobacter bemiidjensis</i>	<i>Haemophilus parasuis</i>		Janthinobacterium
<i>Geobacter bremensis</i>	<i>Haemophilus pittmaniae</i>	Ignavigranum	<i>Janthinobacterium</i>
<i>Geobacter chappelii</i>	Hafnia	<i>Ignavigranum ruoffiae</i>	<i>agaricidamnosum</i>
<i>Geobacter grbiciae</i>	<i>Hafnia alvei</i>	Ilumatobacter	<i>Janthinobacterium lividum</i>
<i>Geobacter hydrogenophilus</i>	Hahella	<i>Ilumatobacter fluminis</i>	Jejuia
<i>Geobacter lovleyi</i>	<i>Hahella ganghwensis</i>	Ilyobacter	<i>Jejuia pallidilutea</i>
<i>Geobacter metallireducens</i>	Halalkalibacillus	<i>Ilyobacter delafieldii</i>	Jeotgalibacillus
<i>Geobacter pelophilus</i>	<i>Halalkalibacillus halophilus</i>	<i>Ilyobacter insuetus</i>	<i>Jeotgalibacillus</i>
<i>Geobacter pickeringii</i>	Helicobacter	<i>Ilyobacter polytropus</i>	<i>alimentarius</i>
<i>Geobacter sulfurreducens</i>	<i>Helicobacter pylori</i>	<i>Ilyobacter tartaricus</i>	Jeotgalicoccus
Geodermatophilus			<i>Jeotgalicoccus halotolerans</i>
<i>Geodermatophilus obscurus</i>			
Gluconacetobacter			
<i>Gluconacetobacter xylinus</i>			
Gordonia			
<i>Gordonia rubripertincta</i>			

Kaistia	Labeledella	<i>Listeria ivanovii</i>	Micrococcus	Nesterenkonia
<i>Kaistia adipata</i>	<i>Labeledella gwakjiensis</i>	<i>L. marthii</i>	<i>Micrococcus luteus</i>	<i>Nesterenkonia holobia</i>
<i>Kaistia soli</i>	Labrenzia	<i>L. monocytogenes</i>	<i>Micrococcus lylae</i>	Nocardia
Kangiella	<i>Labrenzia aggregata</i>	<i>L. newyorkensis</i>	Moraxella	<i>Nocardia argentinensis</i>
<i>Kangiella aquimarina</i>	<i>Labrenzia alba</i>	<i>L. riparia</i>	<i>Moraxella bovis</i>	<i>Nocardia corallina</i>
<i>Kangiella koreensis</i>	<i>Labrenzia alexandrii</i>	<i>L. rocourtae</i>	<i>Moraxella nonliquefaciens</i>	<i>Nocardia</i>
	<i>Labrenzia marina</i>	<i>L. seeligeri</i>	<i>Moraxella osloensis</i>	<i>otitidiscavitarum</i>
Kerstesia	Labrys	<i>L. weihenstephanensis</i>	Nakamurella	
<i>Kerstesia gyiorum</i>	<i>Labrys methylaminiphilus</i>	<i>L. welshimeri</i>	<i>Nakamurella multipartita</i>	
Kiloniella	<i>Labrys miyagiensis</i>	Listonella	Nannocystis	
<i>Kiloniella laminariae</i>	<i>Labrys monachus</i>	<i>Listonella anguillarum</i>	<i>Nannocystis pusilla</i>	
Klebsiella	<i>Labrys okinawensis</i>	Macrococcus	Natranaerobius	
<i>K. granulomatis</i>	<i>Labrys portucalensis</i>	<i>Macrococcus bovicus</i>	<i>Natranaerobius</i>	
<i>K. oxytoca</i>		Marinobacter	<i>thermophilus</i>	
<i>K. pneumoniae</i>	Lactobacillus	<i>Marinobacter algicola</i>	<i>Natranaerobius trueperi</i>	
<i>K. terrigena</i>	[see below]	<i>Marinobacter bryozoorum</i>	Naxibacter	
<i>K. varicola</i>	Laceyella	<i>Marinobacter flavimaris</i>	<i>Naxibacter alkalitolerans</i>	
Kluyvera	<i>Laceyella putida</i>	Meiothermus	Neisseria	
<i>Kluyvera ascorbata</i>	Lechevalieria	<i>Meiothermus ruber</i>	<i>Neisseria cinerea</i>	
Kocuria	<i>Lechevalieria aerocolonigenes</i>	Methylophilus	<i>Neisseria denitrificans</i>	
<i>Kocuria rosea</i>	Legionella	<i>Methylophilus</i>	<i>Neisseria gonorrhoeae</i>	
<i>Kocuria varians</i>	[see below]	<i>methylotrophus</i>	<i>Neisseria lactamica</i>	

FFS0002-1 WO

Kurthia	Listeria	Microbacterium	
<i>Kurthia zopfii</i>	<i>L. aquatica</i>	<i>Microbacterium</i>	<i>Neisseria mucosa</i>
	<i>L. booriae</i>	<i>ammoniaophilum</i>	<i>Neisseria sicca</i>
	<i>L. cornellensis</i>	<i>Microbacterium arborescens</i>	<i>Neisseria subflava</i>
	<i>L. fleischmannii</i>		Neptunomonas
	<i>L. floridensis</i>	<i>Microbacterium liquefaciens</i>	<i>Neptunomonas japonica</i>
	<i>L. grandensis</i>	<i>Microbacterium oxydans</i>	
	<i>L. grayi</i>		
	<i>L. innocua</i>		
Lactobacillus			
<i>L. acetotolerans</i>	<i>L. cateniformis</i>	<i>L. mali</i>	<i>L. parakefiri</i>
<i>L. acidifarinae</i>	<i>L. ceti</i>	<i>L. manihotivorans</i>	<i>L. paralimentarius</i>
<i>L. acidipiscis</i>	<i>L. coleohominis</i>	<i>L. mindensis</i>	<i>L. paraplantarum</i>
<i>L. acidophilus</i>	<i>L. collinoides</i>	<i>L. mucosae</i>	<i>L. pentosus</i>
<i>Lactobacillus agilis</i>	<i>L. composti</i>	<i>L. murinus</i>	<i>L. perolens</i>
<i>L. algidus</i>	<i>L. concavus</i>	<i>L. nagelii</i>	<i>L. plantarum</i>
<i>L. alimentarius</i>	<i>L. coryniformis</i>	<i>L. namurensis</i>	<i>L. pontis</i>
<i>L. amylolyticus</i>	<i>L. crispatus</i>	<i>L. nantensis</i>	<i>L. protectus</i>
<i>L. amylophilus</i>	<i>L. crustorum</i>	<i>L. oligofermentans</i>	<i>L. psittaci</i>
<i>L. amylophilicus</i>	<i>L. curvatus</i>	<i>L. oris</i>	<i>L. remini</i>
<i>L. amylovorus</i>		<i>L. panis</i>	<i>L. reuteri</i>
			<i>L. sakei</i>
			<i>L. salivarius</i>
			<i>L. sanfranciscensis</i>
			<i>L. satsumensis</i>
			<i>L. secdiphilus</i>
			<i>L. sharpeae</i>
			<i>L. siliginis</i>
			<i>L. spicheri</i>
			<i>L. suebicus</i>
			<i>L. thailandensis</i>
			<i>L. ultunensis</i>

FFS0002-1 WO

<i>L. animalis</i>	<i>L. delbrueckii</i> subsp.	<i>L. pantheris</i>	<i>L. rhamnosus</i>	<i>L. vaccinostercus</i>
<i>L. antri</i>	<i>bulgaricus</i>	<i>L. parabrevis</i>	<i>L. rimae</i>	<i>L. vaginalis</i>
<i>L. apodemi</i>	<i>L. delbrueckii</i> subsp.	<i>L. parabuchneri</i>	<i>L. rogosa</i>	<i>L. versmoldensis</i>
<i>L. aviarius</i>	<i>delbrueckii</i>	<i>L. paracasei</i>	<i>L. rossiae</i>	<i>L. vini</i>
<i>L. bif fermentans</i>	<i>L. delbrueckii</i> subsp. <i>lactis</i>	<i>L. paracollinoides</i>	<i>L. ruminis</i>	<i>L. vitulinus</i>
<i>L. brevis</i>	<i>L. dextrinicus</i>	<i>L. parafarraginis</i>	<i>L. saerinneri</i>	<i>L. zeae</i>
<i>L. buchneri</i>	<i>L. diolivorans</i>	<i>L. homohiochii</i>	<i>L. jensenii</i>	<i>L. zymae</i>
<i>L. camelliae</i>	<i>L. equi</i>	<i>L. iners</i>	<i>L. johnsonii</i>	<i>L. gastricus</i>
<i>L. casei</i>	<i>L. equigenerosi</i>	<i>L. ingluviei</i>	<i>L. kalixensis</i>	<i>L. ghanensis</i>
<i>L. kitasatonis</i>	<i>L. farraginis</i>	<i>L. intestinalis</i>	<i>L. kefirano faciens</i>	<i>L. graminis</i>
<i>L. kunkei</i>	<i>L. farciminis</i>	<i>L. fuchuensis</i>	<i>L. kefirii</i>	<i>L. hammesii</i>
<i>L. leichmannii</i>	<i>L. fermentum</i>	<i>L. gallinarum</i>	<i>L. kimchii</i>	<i>L. hamsteri</i>
<i>L. lindneri</i>	<i>L. formicalis</i>	<i>L. gasserii</i>	<i>L. helveticus</i>	<i>L. harbinensis</i>
<i>L. malefermentans</i>	<i>L. fructivorans</i>		<i>L. hilgardii</i>	<i>L. hayakitenensis</i>
	<i>L. frumenti</i>			

Legionella

<i>Legionella adelaidensis</i>	<i>Legionella drancourtii</i>	<i>Candidatus Legionella jeonii</i>	<i>Legionella quinlivanii</i>
<i>Legionella anisa</i>	<i>Legionella dresdenensis</i>	<i>Legionella jordanis</i>	<i>Legionella rowbothamii</i>
<i>Legionella beliardensis</i>	<i>Legionella drozanskii</i>	<i>Legionella lansingensis</i>	<i>Legionella rubrilucens</i>
<i>Legionella birminghamsensis</i>	<i>Legionella dumoffii</i>	<i>Legionella londiniensis</i>	<i>Legionella sainthelensis</i>
<i>Legionella bozemanae</i>	<i>Legionella erythra</i>	<i>Legionella longbeachae</i>	<i>Legionella santacrucis</i>

FFS0002-1 WO

<i>Legionella brunensis</i>	<i>Legionella fairfieldensis</i>	<i>Legionella lytica</i>	<i>Legionella shakespearei</i>
<i>Legionella busanensis</i>	<i>Legionella fallonii</i>	<i>Legionella maceachernii</i>	<i>Legionella spiritensis</i>
<i>Legionella cardiaca</i>	<i>Legionella feeleii</i>	<i>Legionella massiliensis</i>	<i>Legionella steelei</i>
<i>Legionella cherrii</i>	<i>Legionella geestiana</i>	<i>Legionella micdadei</i>	<i>Legionella steigerwaltii</i>
<i>Legionella cincinnatiensis</i>	<i>Legionella genomospecies</i>	<i>Legionella monrovia</i>	<i>Legionella taurinensis</i>
<i>Legionella clemsonensis</i>	<i>Legionella gormanii</i>	<i>Legionella moravica</i>	<i>Legionella tucsonensis</i>
<i>Legionella donaldsonii</i>	<i>Legionella gratiana</i>	<i>Legionella nagasakiensis</i>	<i>Legionella tunisiensis</i>
	<i>Legionella gresilensis</i>	<i>Legionella nautarum</i>	<i>Legionella wadsworthii</i>
	<i>Legionella hackeliae</i>	<i>Legionella norrlandica</i>	<i>Legionella waltersii</i>
	<i>Legionella impletisoli</i>	<i>Legionella oakridgensis</i>	<i>Legionella worsleiensis</i>
	<i>Legionella israelensis</i>	<i>Legionella parisiensis</i>	<i>Legionella yabuuchiiae</i>
	<i>Legionella jamestowniensis</i>	<i>Legionella pittsburghensis</i>	
		<i>Legionella pneumophila</i>	
		<i>Legionella quateirensis</i>	

Oceanibulbus	Paenibacillus	Prevotella	Quadrifphaera
<i>Oceanibulbus indolifex</i>	<i>Paenibacillus thiaminolyticus</i>	<i>Prevotella albensis</i>	<i>Quadrifphaera granulorum</i>
Oceanicaulis	Pantoea	<i>Prevotella amnii</i>	Quatrionococcus
<i>Oceanicaulis alexandrii</i>	<i>Pantoea agglomerans</i>	<i>Prevotella bergensis</i>	<i>Quatrionococcus</i>
Oceanicola		<i>Prevotella bivia</i>	<i>australiensis</i>
<i>Oceanicola batsensis</i>	Paracoccus	<i>Prevotella brevis</i>	
	<i>Paracoccus alcaliphilus</i>	<i>Prevotella bryantii</i>	

FFS0002-1 WO

<i>Oceanicola granulosis</i>	Paucimonas	<i>Prevotella buccae</i>	Quinella
<i>Oceanicola nanhaiensis</i>	<i>Paucimonas lenoignei</i>	<i>Prevotella buccalis</i>	<i>Quinella ovalis</i>
Oceanimonas	Pectobacterium	<i>Prevotella copri</i>	
<i>Oceanimonas baumannii</i>	<i>Pectobacterium aroidearum</i>	<i>Prevotella dentalis</i>	Ralstonia
Oceaniserpentilla	<i>Pectobacterium atrosepticum</i>	<i>Prevotella denticola</i>	<i>Ralstonia eutropha</i>
<i>Oceaniserpentilla haliotis</i>	<i>Pectobacterium</i>	<i>Prevotella disiens</i>	<i>Ralstonia insidiosa</i>
Oceanisphaera	<i>betavascolorum</i>	<i>Prevotella histicola</i>	<i>Ralstonia mannitolilytica</i>
<i>Oceanisphaera donghaensis</i>	<i>Pectobacterium cacticida</i>	<i>Prevotella intermedia</i>	<i>Ralstonia pickettii</i>
<i>Oceanisphaera litoralis</i>	<i>Pectobacterium carnegeiana</i>	<i>Prevotella maculosa</i>	<i>Ralstonia</i>
Oceanithermus	<i>Pectobacterium carotovorum</i>	<i>Prevotella marshii</i>	<i>pseudosolanacearum</i>
<i>Oceanithermus desulfurans</i>	<i>Pectobacterium chrysanthemi</i>	<i>Prevotella melaninogenica</i>	<i>Ralstonia syzygii</i>
<i>Oceanithermus profundus</i>	<i>Pectobacterium cypripedii</i>	<i>Prevotella micans</i>	<i>Ralstonia solanacearum</i>
Oceanobacillus	<i>Pectobacterium rhapontici</i>	<i>Prevotella multififormis</i>	Ramlibacter
<i>Oceanobacillus caeni</i>	<i>Pectobacterium wasabiae</i>	<i>Prevotella nigrescens</i>	<i>Ramlibacter henchirensis</i>
Oceanospirillum	Planococcus	<i>Prevotella oralis</i>	<i>Ramlibacter tataouinensis</i>
<i>Oceanospirillum linum</i>	<i>Planococcus citreus</i>	<i>Prevotella oris</i>	
	Planomicrobium	<i>Prevotella oulorum</i>	Raoultella
	<i>Planomicrobium okeanokoites</i>	<i>Prevotella pallens</i>	<i>Raoultella ornithinolytica</i>
	Plesiomonas	<i>Prevotella salivae</i>	<i>Raoultella planticola</i>
	<i>Plesiomonas shigelloides</i>	<i>Prevotella stercorea</i>	<i>Raoultella terrigena</i>
	Proteus	<i>Prevotella tamerae</i>	Rathayibacter
	<i>Proteus vulgaris</i>	<i>Prevotella timonensis</i>	<i>Rathayibacter caricis</i>

FFS0002-1 WO

<i>Prevotella veroralis</i>	<i>Rathayibacter festucae</i>
Providencia	<i>Rathayibacter iranicus</i>
<i>Providencia stuartii</i>	<i>Rathayibacter rathayi</i>
Pseudomonas	<i>Rathayibacter toxicus</i>
<i>Pseudomonas aeruginosa</i>	<i>Rathayibacter tritici</i>
<i>Pseudomonas alcaligenes</i>	Rhodobacter
<i>Pseudomonas anguillispetica</i>	<i>Rhodobacter sphaeroides</i>
<i>Pseudomonas fluorescens</i>	Ruegeria
<i>Pseudalteromonas</i>	<i>Ruegeria gelatinovorans</i>
<i>haloplanktis</i>	
<i>Pseudomonas mendocina</i>	
<i>Pseudomonas</i>	
<i>pseudocaligenes</i>	
<i>Pseudomonas putida</i>	
<i>Pseudomonas tutzeri</i>	
<i>Pseudomonas syringae</i>	
Psychrobacter	
<i>Psychrobacter faecalis</i>	
<i>Psychrobacter</i>	
<i>phenylpyruvicus</i>	

Saccharococcus	Sagittula	Sanguibacter	Stenotrophomonas	Tatlockia
<i>Saccharococcus thermophilus</i>	<i>Sagittula stellata</i>	<i>Sanguibacter keddiei</i>	<i>Stenotrophomonas maltophilia</i>	<i>Tatlockia maceachernii</i>
Saccharomonospora	Salegentibacter	<i>Sanguibacter suarezii</i>	Streptococcus	<i>Tatlockia micdadei</i>
<i>Saccharomonospora azurea</i>	<i>Salegentibacter salegens</i>	Saprospira	[also see below]	Tenacibaculum
<i>Saccharomonospora cyanea</i>	Salimicrobium	<i>Saprospira grandis</i>		<i>Tenacibaculum</i>
<i>Saccharomonospora viridis</i>	<i>Salimicrobium album</i>	Sarcina		<i>amylyticum</i>
Saccharophagus	Salinibacter	<i>Sarcina maxima</i>	Streptomyces	<i>Tenacibaculum discolor</i>
<i>Saccharophagus degradans</i>	<i>Salinibacter ruber</i>	<i>Sarcina ventriculi</i>	<i>Streptomyces achromogenes</i>	<i>Tenacibaculum gallaicum</i>
Saccharopolyspora	Salinicoccus	Sebaldella	<i>Streptomyces cesalbus</i>	<i>Tenacibaculum lutimaris</i>
<i>Saccharopolyspora erythraea</i>	<i>Salinicoccus alkaliphilus</i>	<i>Sebaldella termitidis</i>	<i>Streptomyces cesaepitosus</i>	<i>Tenacibaculum mesophilum</i>
<i>Saccharopolyspora gregorii</i>	<i>Salinicoccus hispanicus</i>		<i>Streptomyces cesedistaticus</i>	<i>Tenacibaculum</i>
<i>Saccharopolyspora hirsuta</i>	<i>Salinicoccus roseus</i>	Serratia	<i>Streptomyces ceseifolius</i>	<i>skagerrakense</i>
<i>Saccharopolyspora hordei</i>	Salinispora	<i>Serratia fonticola</i>	<i>Streptomyces fimbriatus</i>	Tepidanaerobacter
<i>Saccharopolyspora rectivirgula</i>	<i>Salinispora arenicola</i>	<i>Serratia marcescens</i>	<i>Streptomyces fradiae</i>	<i>Tepidanaerobacter</i>
<i>Saccharopolyspora spinosa</i>	<i>Salinispora tropica</i>	Sphaerotilus	<i>Streptomyces fulvissimus</i>	<i>syntrophicus</i>
<i>Saccharopolyspora taberi</i>	Salinivibrio	<i>Sphaerotilus natans</i>	<i>Streptomyces griseoruber</i>	Tepidibacter
Saccharothrix	<i>Salinivibrio costicola</i>		<i>Streptomyces griseus</i>	<i>Tepidibacter</i>
<i>Saccharothrix australiensis</i>			<i>Streptomyces lavendulae</i>	<i>formicigenes</i>
<i>Saccharothrix coerulescens</i>			<i>Streptomyces</i>	
			<i>phaeochromogenes</i>	
			<i>Streptomyces</i>	

<i>Saccharothrix espanaensis</i>	Salmonella	Sphingobacterium	<i>thermodiastaticus</i>	<i>Tepidibacter</i>
<i>Saccharothrix longispora</i>	<i>Salmonella bongori</i>	<i>Sphingobacterium multivorum</i>	<i>Streptomyces tubercidicus</i>	<i>thalassicus</i>
<i>Saccharothrix mutabilis</i>	<i>Salmonella enterica</i>	Staphylococcus	Thermus	Thermus
<i>Saccharothrix syringae</i>	<i>Salmonella subterranea</i>	[see below]	<i>Thermus aquaticus</i>	<i>Thermus aquaticus</i>
<i>Saccharothrix tangerinus</i>	<i>Salmonella typhi</i>		<i>Thermus filiformis</i>	<i>Thermus filiformis</i>
<i>Saccharothrix texasensis</i>			<i>Thermus thermophilus</i>	<i>Thermus thermophilus</i>
Staphylococcus				
<i>S. arlettae</i>	<i>S. equorum</i>	<i>S. microti</i>	<i>S. schleiferi</i>	
<i>S. agnetis</i>	<i>S. felis</i>	<i>S. muscae</i>	<i>S. sciuri</i>	
<i>S. aureus</i>	<i>S. fleurettii</i>	<i>S. nepalensis</i>	<i>S. simiae</i>	
<i>S. auricularis</i>	<i>S. gallinarum</i>	<i>S. pasteurii</i>	<i>S. simulans</i>	
<i>S. capitis</i>	<i>S. haemolyticus</i>	<i>S. petrasii</i>	<i>S. stepanovicii</i>	
<i>S. caprae</i>	<i>S. hominis</i>	<i>S. pettenkoferi</i>	<i>S. succinus</i>	
<i>S. carnosus</i>	<i>S. hyicus</i>	<i>S. piscifermentans</i>	<i>S. vitulinus</i>	
<i>S. caseolyticus</i>	<i>S. intermedius</i>	<i>S. pseudintermedius</i>	<i>S. warneri</i>	
<i>S. chromogenes</i>	<i>S. kloosii</i>	<i>S. pseudolugdunensis</i>	<i>S. xylosus</i>	
<i>S. cohnii</i>	<i>S. leei</i>	<i>S. pulvereri</i>		
<i>S. condimentii</i>	<i>S. lentus</i>	<i>S. rostri</i>		
<i>S. delphini</i>	<i>S. lugdunensis</i>	<i>S. saccharolyticus</i>		
<i>S. devriesei</i>	<i>S. lutrae</i>	<i>S. saprophyticus</i>		
<i>S. epidermidis</i>				

FFS0002-1 WO

S. lyticans
S. massiliensis

Streptococcus

<i>Streptococcus agalactiae</i>	<i>Streptococcus infantarius</i>	<i>Streptococcus orisratti</i>	<i>Streptococcus thermophilus</i>
<i>Streptococcus anginosus</i>	<i>Streptococcus iniae</i>	<i>Streptococcus parasanguinis</i>	<i>Streptococcus sanguinis</i>
<i>Streptococcus bovis</i>	<i>Streptococcus intermedius</i>	<i>Streptococcus peroris</i>	<i>Streptococcus sobrinus</i>
<i>Streptococcus canis</i>	<i>Streptococcus lactarius</i>	<i>Streptococcus pneumoniae</i>	<i>Streptococcus suis</i>
<i>Streptococcus constellatus</i>	<i>Streptococcus milleri</i>	<i>Streptococcus</i>	<i>Streptococcus uberis</i>
<i>Streptococcus downei</i>	<i>Streptococcus mitis</i>	<i>pseudopneumoniae</i>	<i>Streptococcus vestibularis</i>
<i>Streptococcus dysgalactiae</i>	<i>Streptococcus mutans</i>	<i>Streptococcus pyogenes</i>	<i>Streptococcus viridans</i>
<i>Streptococcus equines</i>	<i>Streptococcus oralis</i>	<i>Streptococcus ratti</i>	<i>Streptococcus</i>
<i>Streptococcus faecalis</i>	<i>Streptococcus tigurinus</i>	<i>Streptococcus salivarius</i>	<i>zooepidemicus</i>
<i>Streptococcus ferus</i>			

Uliginosibacterium

	Vagococcus	Vibrio	Virgibacillus	Xanthobacter
	<i>Vagococcus carniphilus</i>	<i>Vibrio aerogenes</i>	<i>Virgibacillus</i>	<i>Xanthobacter agilis</i>
<i>Uliginosibacterium gangwonense</i>	<i>Vagococcus elongatus</i>	<i>Vibrio aestuarius</i>	<i>halodenitrificans</i>	<i>Xanthobacter</i>
Ulvibacter	<i>Vagococcus fessus</i>	<i>Vibrio albensis</i>	<i>Virgibacillus</i>	<i>aminoxidans</i>
<i>Ulvibacter litoralis</i>	<i>Vagococcus fluvialis</i>	<i>Vibrio alginolyticus</i>	<i>pantothenticus</i>	<i>Xanthobacter</i>
		<i>Vibrio campbellii</i>		<i>autotrophicus</i>

Umezawaea	<i>Vagococcus lutrae</i>	<i>Vibrio cholerae</i>	<i>Xanthobacter flavus</i>
<i>Umezawaea tangerina</i>	<i>Vagococcus salmoninarum</i>	<i>Vibrio cincinnatiensis</i>	<i>Xanthobacter tagetidis</i>
Undibacterium		<i>Vibrio coralliilyticus</i>	<i>Xanthobacter viscosus</i>
<i>Undibacterium pigrum</i>	Variovorax	<i>Vibrio cyclitrophicus</i>	Xanthomonas
Ureaplasma	<i>Variovorax boronicumulans</i>	<i>Vibrio diazotrophicus</i>	<i>Xanthomonas</i>
<i>Ureaplasma urealyticum</i>	<i>Variovorax dokdonensis</i>	<i>Vibrio fluvialis</i>	<i>albilineans</i>
	<i>Variovorax paradoxus</i>	<i>Vibrio furnissii</i>	<i>Xanthomonas alfalfae</i>
Ureibacillus	<i>Variovorax soli</i>	<i>Vibrio gazogenes</i>	<i>Xanthomonas</i>
<i>Ureibacillus composti</i>	Veillonella	<i>Vibrio halotitoli</i>	<i>arboricola</i>
<i>Ureibacillus suwonensis</i>	<i>Veillonella atypica</i>	<i>Vibrio harveyi</i>	<i>Xanthomonas</i>
<i>Ureibacillus terrenus</i>	<i>Veillonella caviae</i>	<i>Vibrio ichthyenteri</i>	<i>axonopodis</i>
<i>Ureibacillus thermophilus</i>	<i>Veillonella criceti</i>	<i>Vibrio mediterranei</i>	<i>Xanthomonas</i>
<i>Ureibacillus thermosphaericus</i>	<i>Veillonella dispar</i>	<i>Vibrio metschnikovii</i>	<i>campestris</i>
	<i>Veillonella montpellierensis</i>	<i>Vibrio mytili</i>	<i>Xanthomonas citri</i>
	<i>Veillonella parvula</i>	<i>Vibrio natriegens</i>	<i>Xanthomonas codiae</i>
	<i>Veillonella ratti</i>	<i>Vibrio navarrensis</i>	<i>Xanthomonas</i>
	<i>Veillonella rodentium</i>	<i>Vibrio nereis</i>	<i>cucurbitae</i>
	Venenivibrio	<i>Vibrio nigripulchritudo</i>	<i>Xanthomonas</i>
	<i>Venenivibrio stagnispumantis</i>	<i>Vibrio ordalii</i>	<i>euvesicatoria</i>
		<i>Vibrio orientalis</i>	<i>Xanthomonas fragariae</i>
		<i>Vibrio parahaemolyticus</i>	<i>Xanthomonas fuscans</i>
		<i>Vibrio pectenica</i>	<i>Xanthomonas gardneri</i>
			<i>thlassocola</i>

Verminephrobacter	<i>Vibrio penaeicida</i>	Wolbachia	<i>Xanthomonas hortorum</i>
<i>Verminephrobacter eiseniae</i>	<i>Vibrio proteolyticus</i>	<i>Wolbachia persica</i>	<i>Xanthomonas hyacinthi</i>
	<i>Vibrio shilonii</i>		<i>Xanthomonas perforans</i>
	<i>Vibrio splendidus</i>		<i>Xanthomonas phaseoli</i>
	<i>Vibrio tubiashii</i>		<i>Xanthomonas pisi</i>
Verrucomicrobium	<i>Vibrio vulnificus</i>	Wolinella	<i>Xanthomonas populi</i>
<i>Verrucomicrobium spinosum</i>		<i>Wolinella succinogenes</i>	<i>Xanthomonas theicola</i>
			<i>Xanthomonas translucens</i>
		Zobellia	<i>Xanthomonas vesicatoria</i>
		<i>Zobellia galactanivorans</i>	
		<i>Zobellia uliginosa</i>	Xylella
			<i>Xylella fastidiosa</i>
		Zoogloea	Xylophilus
		<i>Zoogloea ramigera</i>	<i>Xylophilus ampelinus</i>
		<i>Zoogloea resiniphila</i>	
Xenophilus	<i>Yersinia mollaretii</i>	Zooshikella	Zobellella
<i>Xenophilus azovorans</i>	<i>Yersinia philomiragia</i>	<i>Zooshikella ganghwensis</i>	<i>Zobellella denitrificans</i>
Xenorhabdus	<i>Yersinia pestis</i>		<i>Zobellella taiwanensis</i>
<i>Xenorhabdus beddingii</i>			

FFS0002-1 WO

<i>Xenorhabdus bovienii</i>	Yaniella	<i>Yersinia pseudotuberculosis</i>	
<i>Xenorhabdus cabanillasii</i>	<i>Yaniella flava</i>	<i>Yersinia rohdei</i>	Zunongwangia
<i>Xenorhabdus doucetiae</i>	<i>Yaniella halotolerans</i>	<i>Yersinia ruckeri</i>	<i>Zunongwangia profunda</i>
<i>Xenorhabdus griffinae</i>			Zeaxanthinibacter
<i>Xenorhabdus hominickii</i>	Yeosuana	Yokenella	<i>Zeaxanthinibacter</i>
<i>Xenorhabdus koppenhoeferi</i>	<i>Yeosuana aromativorans</i>	<i>Yokenella regensburgei</i>	<i>enoshimensis</i>
<i>Xenorhabdus nematophila</i>			Zhibengliuella
<i>Xenorhabdus poinarii</i>	Yersinia	Yonghaparkia	<i>Zhibengliuella</i>
Xylanibacter	<i>Yersinia alldovae</i>	<i>Yonghaparkia alkaliphila</i>	<i>halotolerans</i>
<i>Xylanibacter oryzae</i>	<i>Yersinia bercovieri</i>	Zavarzinia	Xylanibacterium
	<i>Yersinia enterocolitica</i>	<i>Zavarzinia compransoris</i>	<i>Xylanibacterium ulmi</i>
	<i>Yersinia entomophaga</i>		<i>Zymophilus paucivorans</i>
	<i>Yersinia frederiksenii</i>		<i>Zymophilus raffinosisvorans</i>
	<i>Yersinia intermedia</i>		
	<i>Yersinia kristensenii</i>		

FFS0002-1 WO

Table 3: *Pseudomonas* Species & Strains Comprising *PSPTO_0477* or an Orthologue of *PSPTO_0477*

Pseudomonas Species & Strains Comprising an Orthologue of *PSPTO_0477* obtained by the BLASTN comparison with non-redundant nucleotide database in NCBI.

Description	Max Score	Total Score	Query Cover	E value	Per. Ident	Accession
<i>Pseudomonas syringae</i> pv. tomato strain delta IV,IX chromosome	2660	2660	100%	0	100%	CP047072.1
<i>Pseudomonas syringae</i> pv. tomato strain delta VI chromosome	2660	2660	100%	0	100%	CP047071.1
<i>Pseudomonas syringae</i> pv. tomato strain delta X chromosome, complete genome	2660	2660	100%	0	100%	CP047073.1
<i>Pseudomonas syringae</i> pv. tomato str. DC3000, complete genome	2660	2660	100%	0	100%	AE016853.1
<i>Pseudomonas syringae</i> strain Ps25 chromosome	2615	2615	100%	0	99%	CP034558.1
<i>Pseudomonas syringae</i> pv. tomato strain B13-200 chromosome, complete genome	2615	2615	100%	0	99%	CP019871.1
<i>Pseudomonas syringae</i> pv. avii isolate CFBP3846 genome assembly, chromosome: 1	2577	2577	100%	0	99%	LT963402.1
<i>Pseudomonas avellanae</i> strain R2leaf chromosome, complete genome	2316	2316	100%	0	96%	CP026562.1
<i>Pseudomonas syringae</i> group genomosp. 3 isolate CFBP6411 genome assembly, chromosome: I	2316	2316	100%	0	96%	LT963408.1
<i>Pseudomonas syringae</i> pv. actinidiae str. Shaanxi_M228 chromosome, complete genome	2305	2305	100%	0	96%	CP032631.1
<i>Pseudomonas syringae</i> pv. actinidiae strain P155 chromosome, complete genome	2305	2305	100%	0	96%	CP032871.1
<i>Pseudomonas syringae</i> pv. actinidiae strain MAFF212063 chromosome, complete genome	2305	2305	100%	0	96%	CP024712.1
<i>Pseudomonas syringae</i> pv. actinidiae strain CRAFRU 14.08, complete genome	2305	2305	100%	0	96%	CP019732.1

FFS0002-1 WO

Pseudomonas syringae pv. actinidiae strain CRAFRU 12.29, complete genome	2305	2305	100%	0	96%	CP019730.1
Pseudomonas syringae pv. actinidiae ICMP 9853, complete genome	2305	2305	100%	0	96%	CP018202.1
Pseudomonas syringae pv. actinidiae strain NZ-47, complete genome	2305	2305	100%	0	96%	CP017009.1
Pseudomonas syringae pv. actinidiae strain NZ-45, complete genome	2305	2305	100%	0	96%	CP017007.1
Pseudomonas syringae pv. actinidiae ICMP 18884, complete genome	2305	2305	100%	0	96%	CP011972.2
Pseudomonas syringae pv. actinidiae ICMP 18708, complete genome	2305	2305	100%	0	96%	CP012179.1
Pseudomonas syringae pv. maculicola str. ES4326 chromosome, complete genome	1951	1951	100%	0	91%	CP047260.1
Pseudomonas coronafaciens strain X-1 chromosome, complete genome	1912	1912	100%	0	91%	CP050260.1
Pseudomonas coronafaciens pv. coronafaciens strain B19001 chromosome, complete genome	1912	1912	100%	0	91%	CP046441.1
Pseudomonas coronafaciens pv. oryzae str. 1_6 chromosome, complete genome	1895	1895	100%	0	90%	CP046035.1
Pseudomonas syringae CC1557, complete sequence	1857	1857	100%	0	90%	CP007014.1
Pseudomonas syringae strain 31R1 genome assembly, chromosome: 1	1845	1845	100%	0	90%	LT629769.1
Pseudomonas cerasi isolate PL963 genome assembly, chromosome: 1	1829	1829	100%	0	90%	LT963395.1
Pseudomonas sp. 58 isolate Sour cherry (Prunus cerasus) symptomatic leaf genome assembly, chromosome: 1	1829	1829	100%	0	90%	LT222319.1
Pseudomonas syringae UMAF0158, complete genome	1829	1829	100%	0	90%	CP005970.1
Pseudomonas syringae pv. syringae strain Pss9097 chromosome, complete genome	1823	1823	100%	0	90%	CP026568.1

FFS0002-1 WO

Pseudomonas syringae UB303 chromosome, complete genome	1812	1812	100%	0	89%	CP047267.1
Pseudomonas syringae USA011 chromosome, complete genome	1812	1812	100%	0	89%	CP045799.1
Pseudomonas syringae pv. syringae isolate CFBP4215 genome assembly, chromosome: 1	1812	1812	100%	0	89%	LT962480.1
Pseudomonas syringae pv. syringae B728a, complete genome	1812	1812	100%	0	89%	CP000075.1
Pseudomonas sp. KUIN-1 DNA, complete genome	1807	1807	100%	0	89%	AP020337.1
Pseudomonas syringae pv. syringae B301D, complete genome	1807	1807	100%	0	89%	CP005969.1
Pseudomonas syringae pv. syringae isolate CFBP2118 genome assembly, chromosome: 1	1801	1801	100%	0	89%	LT962481.1
Pseudomonas amygdali pv. tabaci str. ATCC 11528 chromosome, complete genome	1790	1790	100%	0	89%	CP042804.1
Pseudomonas syringae strain CFBP 2116 genome assembly, chromosome: 1	1762	1762	100%	0	89%	LT985192.1
Pseudomonas amygdali pv. morsprunorum strain R15244 chromosome, complete genome	1762	1762	100%	0	89%	CP026558.1
Pseudomonas syringae isolate CFBP3840 genome assembly, chromosome: 1	1762	1762	100%	0	89%	LT963409.1
Pseudomonas sp. KBS0707 chromosome, complete genome	1757	1757	100%	0	89%	CP041754.1
Pseudomonas savastanoi pv. savastanoi NCPPB 3335, complete genome	1757	1757	100%	0	89%	CP008742.1
Pseudomonas amygdali pv. lachrymans strain NM002, complete genome	1757	1757	100%	0	89%	CP020351.1
Pseudomonas savastanoi pv. phaseolicola 1448A chromosome, complete genome	1757	1757	100%	0	89%	CP000058.1
Pseudomonas amygdali pv. lachrymans str. M301315 chromosome, complete genome	1751	1751	100%	0	89%	CP031225.1

FFS0002-1 WO

Pseudomonas syringae pv. cerasicola isolate CFBP6109 genome assembly, chromosome: 1	1751	1751	100%	0	89%	LT963391.1
Pseudomonas syringae pv. pisi str. PP1 chromosome, complete genome	1746	1746	100%	0	89%	CP034078.1
Pseudomonas syringae pv. lapsa strain ATCC 10859, complete genome	1740	1740	100%	0	88%	CP013183.1
Pseudomonas syringae pv. syringae HS191, complete genome	1724	1724	100%	0	88%	CP006256.1
Pseudomonas syringae pv. atrofaciens strain LMG5095 chromosome, complete genome	1712	1712	100%	0	88%	CP028490.1
Pseudomonas viridiflava strain CFBP 1590 genome assembly, chromosome: I	1602	1602	100%	0	87%	LT855380.1
Pseudomonas asturiensis strain CC1524 chromosome, complete genome	1568	1568	100%	0	86%	CP047265.1
Pseudomonas cichorii JBC1, complete genome	1544	1544	99%	0	86%	CP007039.1
Paucimonas lemoignei strain NCTC10937 genome assembly, chromosome: 1	1447	1447	100%	0	85%	LS483371.1
Pseudomonas sp. StFLB209 DNA, complete genome	1203	1203	93%	0	83%	AP014637.1
Pseudomonas putida strain PP112420, complete genome	1155	1155	99%	0	81%	CP017073.1
Pseudomonas putida GB-1 chromosome, complete genome	1155	1155	99%	0	81%	CP000926.1
Pseudomonas sp. MRSN12121, complete genome	1151	1151	97%	0	82%	CP010892.1
Pseudomonas chlororaphis subsp. chlororaphis strain DSM 50083 chromosome, complete genome	1146	1146	97%	0	82%	CP027712.1
Pseudomonas sp. 09C 129 chromosome	1146	1146	97%	0	82%	CP025261.1
Pseudomonas chlororaphis strain PCL1606, complete genome	1140	1140	96%	0	82%	CP011110.1
Pseudomonas chlororaphis subsp. aureofaciens strain ChPhzTR36 chromosome, complete genome	1134	1134	97%	0	81%	CP027721.1
Pseudomonas chlororaphis strain TAMOak81 chromosome, complete genome	1133	1133	97%	0	81%	CP027713.1

FFS0002-1 WO

Pseudomonas chlororaphis subsp. aurantiaca strain JD37, complete genome	1129	2159	98%	0	81%	CP009290.1
Pseudomonas chlororaphis subsp. aurantiaca strain K27 chromosome, complete genome	1123	1123	97%	0	81%	CP027745.1
Pseudomonas chlororaphis subsp. aurantiaca strain M71 chromosome, complete genome	1123	2072	97%	0	81%	CP027744.1
Pseudomonas chlororaphis subsp. aurantiaca strain CW2 chromosome, complete genome	1123	1123	97%	0	81%	CP027743.1
Pseudomonas chlororaphis subsp. aurantiaca strain M12 chromosome, complete genome	1123	1123	97%	0	81%	CP027715.1
Pseudomonas chlororaphis isolate 189, complete genome	1123	1123	96%	0	81%	CP014867.1
Pseudomonas chlororaphis subsp. aurantiaca strain B-162 chromosome	1118	1118	97%	0	81%	CP050510.1
Pseudomonas chlororaphis subsp. aurantiaca strain PCM 2210 chromosome, complete genome	1118	1118	97%	0	81%	CP027717.1
Pseudomonas chlororaphis subsp. aurantiaca strain DSM 19603 chromosome, complete genome	1118	1118	97%	0	81%	CP027746.1
Pseudomonas chlororaphis subsp. aurantiaca strain 464 chromosome, complete genome	1118	1118	97%	0	81%	CP027742.1
Pseudomonas chlororaphis subsp. aurantiaca strain 449 chromosome, complete genome	1118	1118	97%	0	81%	CP027741.1
Pseudomonas chlororaphis strain ATCC 17415 chromosome, complete genome	1118	1118	97%	0	81%	CP027714.1
Pseudomonas chlororaphis strain LMG 21630 genome assembly, chromosome: I	1118	1118	96%	0	81%	LT629747.1
Pseudomonas chlororaphis strain UFB2, complete genome	1114	1114	97%	0	81%	CP011020.1
Pseudomonas chlororaphis subsp. aurantiaca strain zm-1 chromosome, complete genome	1112	1112	97%	0	81%	CP048051.1
Pseudomonas chlororaphis subsp. aurantiaca strain ARS 38 chromosome, complete genome	1112	1112	97%	0	81%	CP045221.1

FFS0002-1 WO

Pseudomonas chlororaphis strain B25 chromosome, complete genome	1112	1112	97%	0	81%	CP027753.1
Pseudomonas chlororaphis strain Pb-St2 chromosome, complete genome	1112	1112	97%	0	81%	CP027716.1
Pseudomonas chlororaphis subsp. aurantiaca DNA, complete genome, strain: StFRB508	1112	1112	97%	0	81%	AP014623.1
Pseudomonas chlororaphis subsp. aureofaciens strain C50 chromosome, complete genome	1107	1107	97%	0	81%	CP027722.1
Pseudomonas chlororaphis subsp. aurantiaca strain Q16 chromosome, complete genome	1107	1107	97%	0	81%	CP027718.1
Pseudomonas chlororaphis subsp. piscium strain DSM 21509 chromosome, complete genome	1107	1107	97%	0	81%	CP027707.1
Pseudomonas chlororaphis strain Lzh-T5 chromosome, complete genome	1107	1107	97%	0	81%	CP025309.1
Pseudomonas chlororaphis strain DSM 21509 genome assembly, chromosome: I	1107	1107	96%	0	81%	LT629761.1
Pseudomonas chlororaphis subsp. aureofaciens strain DSM 6698 chromosome, complete genome	1096	1096	97%	0	81%	CP027720.1
Pseudomonas chlororaphis strain ATCC 13985 genome assembly, chromosome: I	1096	1096	96%	0	81%	LT629738.1
Pseudomonas sp. R32 chromosome, complete genome	1090	1090	97%	0	81%	CP019396.1
Pseudomonas putida strain 1290 chromosome, complete genome	1090	1090	99%	0	81%	CP039371.1
Pseudomonas chlororaphis subsp. piscium strain ChPhzTR44 chromosome, complete genome	1090	1090	97%	0	81%	CP027711.1
Pseudomonas chlororaphis subsp. piscium strain ChPhzS140 chromosome, complete genome	1090	1090	97%	0	81%	CP027740.1
Pseudomonas chlororaphis subsp. piscium strain ToZa7 chromosome, complete genome	1090	1090	97%	0	81%	CP027739.1
Pseudomonas chlororaphis subsp. piscium strain ChPhzS135 chromosome, complete genome	1090	1090	97%	0	81%	CP027738.1

FFS0002-1 WO

Pseudomonas chlororaphis subsp. piscium strain PCL1607 chromosome, complete genome	1090	1090	97%	0	81%	CP027737.1
Pseudomonas chlororaphis subsp. piscium strain PCL1391 chromosome, complete genome	1090	1090	97%	0	81%	CP027736.1
Pseudomonas chlororaphis subsp. piscium strain DTR133 chromosome, complete genome	1090	1090	97%	0	81%	CP027735.1
Pseudomonas chlororaphis subsp. piscium strain SLPH10 chromosome, complete genome	1090	1090	97%	0	81%	CP027710.1
Pseudomonas putida S13.1.2, complete genome	1090	1090	99%	0	81%	CP010979.1

Table 4: Non-Pseudomonas Species & Strains Comprising an Orthologue of *PSPTO_0477* (BLASTN Results)

Description	Total		Query	E	Per.	
	Max Score	Score	Cover	value	Ident	Accession
Paucimonas lemoignei strain NCTC10937 genome assembly, chromosome: 1	1447	1447	100%	0	85%	LS483371.1
Stenotrophomonas rhizophila strain GA1 chromosome, complete genome	1018	1018	98%	0	80%	CP031729.1
Enterococcus faecalis strain V583 genome	996	996	98%	0	79%	CP022312.1
Uncultured bacterium 182_02_C03 genomic sequence	736	736	77%	0	79%	KJ802934.1

Table 5: *Pseudomonas* Species & Strains Comprising *PSPTO_820* or an Orthologue of *PSPTO_820* (BLASTN Results)

Description	Total		Query	E	Per.	
	Max Score	Score	Cover	value	Ident	Accession
Pseudomonas syringae pv. tomato str. DC3000, complete genome	5746	5746	100%	0	100%	AE016853.1
Pseudomonas syringae pv. tomato strain delta IV,IX chromosome	5746	5746	100%	0	100%	CP047072.1
Pseudomonas syringae pv. tomato strain delta VI chromosome	5746	5746	100%	0	100%	CP047071.1
Pseudomonas syringae pv. tomato strain delta X chromosome, complete genome	5746	5746	100%	0	100%	CP047073.1

FFS0002-1 WO

Pseudomonas syringae pv. tomato strain B13-200 chromosome, complete genome	5674	5674	100%	0	100%	CP019871.1
Pseudomonas syringae strain Ps25 chromosome	5674	5674	100%	0	100%	CP034558.1
Pseudomonas syringae pv. avii isolate CFBP3846 genome assembly, chromosome: 1	5651	5651	100%	0	99%	LT963402.1
Pseudomonas syringae pv. actinidiae ICMP 18708, complete genome	5164	5164	98%	0	97%	CP012179.1
Pseudomonas syringae pv. actinidiae ICMP 18884, complete genome	5164	5164	98%	0	97%	CP011972.2
Pseudomonas syringae pv. actinidiae str. Shaanxi_M228 chromosome, complete genome	5164	5164	98%	0	97%	CP032631.1
Pseudomonas syringae pv. actinidiae strain CRAFRU 12.29, complete genome	5164	5164	98%	0	97%	CP019730.1
Pseudomonas syringae pv. actinidiae strain CRAFRU 14.08, complete genome	5164	5164	98%	0	97%	CP019732.1
Pseudomonas syringae pv. actinidiae strain MAFF212063 chromosome, complete genome	5164	5164	98%	0	97%	CP024712.1
Pseudomonas syringae pv. actinidiae strain NZ-45, complete genome	5164	5164	98%	0	97%	CP017007.1
Pseudomonas syringae pv. actinidiae strain NZ-47, complete genome	5164	5164	98%	0	97%	CP017009.1
Pseudomonas syringae pv. actinidiae strain P155 chromosome, complete genome	5164	5164	98%	0	97%	CP032871.1
Pseudomonas syringae pv. actinidiae ICMP 9853, complete genome	5169	5169	98%	0	97%	CP018202.1
Pseudomonas avellanae strain R2leaf chromosome, complete genome	5145	5145	98%	0	97%	CP026562.1
Pseudomonas syringae group genomosp. 3 isolate CFBP6411 genome assembly, chromosome: 1	5068	5068	98%	0	97%	LT963408.1
Pseudomonas syringae pv. cerasicola isolate CFBP6109 genome assembly, chromosome: 1	4109	4109	98%	0	91%	LT963391.1
Pseudomonas amygdali pv. morsprunorum strain R15244 chromosome, complete genome	4071	4071	98%	0	91%	CP026558.1
Pseudomonas syringae isolate CFBP3840 genome assembly, chromosome: 1	4071	4071	98%	0	91%	LT963409.1
Pseudomonas syringae strain CFBP 2116 genome assembly, chromosome: 1	4071	4071	98%	0	91%	LT985192.1
Pseudomonas amygdali pv. tabaci str. ATCC 11528 chromosome, complete genome	4048	4048	98%	0	91%	CP042804.1
Pseudomonas amygdali pv. lachrymans str. M301315 chromosome, complete genome	4043	4043	98%	0	91%	CP031225.1
Pseudomonas amygdali pv. lachrymans strain NM002, complete genome	4043	4043	98%	0	91%	CP020351.1
Pseudomonas savastanoi pv. savastanoi NCPPB 3335, complete genome	4039	4039	98%	0	91%	CP008742.1

FFS0002-1 WO

Pseudomonas savastanoi pv. phaseolicola 1448A chromosome, complete genome	4010	4010	98%	0	90%	CP000058.1
Pseudomonas sp. KBS0707 chromosome, complete genome	4010	4010	98%	0	90%	CP041754.1
Pseudomonas syringae pv. maculicola str. ES4326 chromosome, complete genome	3509	3509	98%	0	87%	CP047260.1
Pseudomonas syringae CC1557, complete sequence	3496	6991	97%	0	87%	CP007014.1
Pseudomonas coronafaciens pv. oryzae str. 1_6 chromosome, complete genome	3367	3367	98%	0	87%	CP046035.1
Pseudomonas coronafaciens pv. coronafaciens strain B19001 chromosome, complete genome	3356	3356	98%	0	87%	CP046441.1
Pseudomonas coronafaciens strain X-1 chromosome, complete genome	3356	3356	98%	0	87%	CP050260.1
Pseudomonas sp. LPH1, complete genome	2562	2562	98%	0	82%	CP017290.1
Pseudomonas aeruginosa DSM 50071, complete genome	2477	2477	97%	0	81%	CP012001.1
Pseudomonas aeruginosa genome assembly NCTC10332, chromosome : 1	2477	2477	97%	0	81%	LN831024.1
Pseudomonas aeruginosa isolate B10W, complete genome	2466	2466	97%	0	81%	CP017969.1
Pseudomonas aeruginosa strain AR_455 chromosome, complete genome	2466	2466	97%	0	81%	CP030328.1
Pseudomonas aeruginosa strain Pa58, complete genome	2466	2466	97%	0	81%	CP021775.1
Pseudomonas aeruginosa strain PABLO48 chromosome, complete genome	2466	2466	97%	0	81%	CP039293.1
Pseudomonas aeruginosa strain PASGNDM345, complete genome	2466	2466	97%	0	81%	CP020703.1
Pseudomonas aeruginosa strain PASGNDM699, complete genome	2466	2466	97%	0	81%	CP020704.1
Pseudomonas aeruginosa strain PB368 chromosome, complete genome	2466	2466	97%	0	81%	CP025050.1
Pseudomonas aeruginosa strain PB369 chromosome, complete genome	2466	2466	97%	0	81%	CP025049.1
Pseudomonas aeruginosa strain S04 90 genome	2466	2466	97%	0	81%	CP011369.1
Pseudomonas aeruginosa strain T2436 chromosome, complete genome	2466	2466	97%	0	81%	CP039988.1
Pseudomonas aeruginosa strain 60503 chromosome, complete genome	2460	2460	97%	0	81%	CP041774.1
Pseudomonas aeruginosa strain BAMCPA07-48, complete genome	2460	2460	97%	0	81%	CP015377.1
Pseudomonas aeruginosa strain NCTC13715 genome assembly, chromosome: 1	2460	2460	97%	0	81%	LR134330.1
Pseudomonas aeruginosa strain ST773 chromosome, complete genome	2460	2460	97%	0	81%	CP041945.1
Pseudomonas aeruginosa strain AR_0353 chromosome, complete genome	2466	2466	98%	0	81%	CP027172.1
Pseudomonas aeruginosa strain WPB099 chromosome	2466	2466	98%	0	81%	CP031878.1
Pseudomonas aeruginosa strain WPB100 chromosome	2466	2466	98%	0	81%	CP031877.1

FFS0002-1 WO

Pseudomonas aeruginosa strain WPB101 chromosome	2466	2466	98%	0	81%	CP031876.1
Pseudomonas aeruginosa isolate PA14Or_reads genome assembly, chromosome: PA14OR	2455	2455	97%	0	81%	LT608330.1
Pseudomonas aeruginosa strain 243931 chromosome, complete genome	2455	2455	97%	0	81%	CP041772.1
Pseudomonas aeruginosa strain 24Pae112 chromosome, complete genome	2455	2455	97%	0	81%	CP029605.1
Pseudomonas aeruginosa strain 268 chromosome, complete genome	2455	2455	97%	0	81%	CP032761.1
Pseudomonas aeruginosa strain AR_0354 chromosome, complete genome	2455	2455	97%	0	81%	CP027171.1
Pseudomonas aeruginosa strain CCUG 51971 chromosome, complete genome	2455	2455	97%	0	81%	CP043328.1
Pseudomonas aeruginosa strain E90 chromosome, complete genome	2455	2455	97%	0	81%	CP044006.1
Pseudomonas aeruginosa strain FDAARGOS_571 chromosome, complete genome	2455	2455	97%	0	81%	CP033833.1
Pseudomonas aeruginosa strain H26023 chromosome, complete genome	2455	2455	97%	0	81%	CP033685.1
Pseudomonas aeruginosa strain L10, complete genome	2455	2455	97%	0	81%	CP019338.1
Pseudomonas aeruginosa strain MRSN12280 chromosome, complete genome	2455	2455	97%	0	81%	CP028162.1
Pseudomonas aeruginosa strain PAK genome assembly, chromosome: 1	2455	2455	97%	0	81%	LR657304.1
Pseudomonas aeruginosa strain W60856, complete genome	2455	2455	97%	0	81%	CP008864.2
Pseudomonas aeruginosa UCBPP-PA14 chromosome	2455	2455	97%	0	81%	CP034244.1
Pseudomonas aeruginosa UCBPP-PA14, complete genome	2455	2455	97%	0	81%	CP000438.1
Pseudomonas salegens strain CECT 8338 genome assembly, chromosome: I	2462	2462	97%	0	81%	LT629787.1
Pseudomonas aeruginosa DNA, complete genome, strain: IOMTU 133	2449	2449	97%	0	81%	AP017302.1
Pseudomonas aeruginosa NCGM2.S1 DNA, complete genome	2455	2455	98%	0	81%	AP012280.1
Pseudomonas aeruginosa PAK chromosome, complete genome	2455	2455	98%	0	81%	CP020659.1
Pseudomonas aeruginosa strain GIMC5002:PAT-169 chromosome	2455	2455	98%	0	81%	CP043549.1
Pseudomonas aeruginosa strain M1608, complete genome	2455	2455	98%	0	81%	CP008862.2
Pseudomonas aeruginosa strain M37351, complete genome	2455	2455	98%	0	81%	CP008863.1
Pseudomonas aeruginosa strain PA-VAP-3 chromosome	2449	2449	98%	0	81%	CP028330.1
Pseudomonas aeruginosa VRFA04, complete genome	2438	2438	98%	0	81%	CP008739.2
Pseudomonas aeruginosa strain AR_0095 chromosome, complete genome	2422	2422	98%	0	81%	CP027538.1
Pseudomonas otitidis MirB4 DNA, complete genome						AP022642.1

FFS0002-1 WO

Table 6: Non-*Pseudomonas* Species & Strains Comprising an Orthologue of *PSPTO_820* (BLASTN Results)

Description	Max Score	Total Score	Query Cover	E value	Per. Ident	Accession
Azotobacter chroococcum strain B3, complete genome	2942	2942	98%	0	84%	CP011835.1
Azotobacter chroococcum NCIMB 8003, complete genome	2935	2935	98%	0	84%	CP010415.1
Azotobacter salinestris strain KACC 13899 chromosome, complete genome	2795	2795	98%	0	83%	CP045302.1
Lysobacter gummosus strain 3.2.11, complete genome	2497	2497	97%	0	82%	CP011131.1
Variovorax sp. PBL-H6 genome assembly, chromosome: 1	2473	2473	98%	0	81%	LR594659.1
Xanthomonas arboricola pv. juglandis strain Xaj 417 genome	2431	2431	98%	0	81%	CP012251.1
Xanthomonas arboricola strain 17, complete genome	2431	2431	98%	0	81%	CP011256.1
Xanthomonas arboricola pv. pruni strain 15-088 chromosome, complete genome	2425	2425	98%	0	81%	CP044334.1
Burkholderia cenocepacia MCO-3 chromosome 3, complete sequence	2438	2438	98%	0	81%	CP000960.1
Xanthomonas citri pv. glycines strain 2098 chromosome, complete genome	2409	2409	98%	0	81%	CP041965.1
Burkholderia cenocepacia AU 1054 chromosome 1, complete sequence	2412	2412	98%	0	81%	CP000378.1
Burkholderia cenocepacia HI2424 chromosome 3, complete sequence	2412	2412	98%	0	81%	CP000460.1
Burkholderia cenocepacia strain CR318 chromosome 3, complete sequence	2412	2412	98%	0	81%	CP017240.1
Xanthomonas axonopodis pv. phaseoli strain ISO18C8, complete genome	2392	2392	98%	0	81%	CP012063.1
Xanthomonas axonopodis pv. phaseoli strain ISO98C12, complete genome	2392	2392	98%	0	81%	CP012057.1
Xanthomonas sp. ISO98C4, complete genome	2392	2392	98%	0	81%	CP012060.1
Burkholderia cenocepacia strain FDAARGOS_720 chromosome 1	2407	2407	98%	0	81%	CP050980.1
Paraburkholderia terricola strain mHS1 chromosome mHS1_A, complete sequence	2399	2399	98%	0	81%	CP024941.1
Xanthomonas axonopodis pv. dieffenbachiae LMG 695 genome	2375	2375	98%	0	81%	CP014347.1
Ralstonia solanacearum strain UA-1591 chromosome	2383	2383	98%	0	81%	CP034195.1
Paraburkholderia sprentiae WSM5005 chromosome 1, complete sequence	2386	2386	98%	0	81%	CP017561.1

FFS0002-1 WO						
Variovorax paradoxus S110 chromosome 2, complete sequence	2374	2374	97%	0	81%	CP001636.1
Cupriavidus basilensis strain 4G11 chromosome secondary, complete sequence	2372	2888	98%	0	81%	CP010537.1
Xanthomonas campestris pv. campestris MAFF302021 DNA, complete genome	2364	2364	98%	0	81%	AP019684.1
Burkholderia lata strain A05 chromosome 3, complete sequence	2368	2368	98%	0	81%	CP024945.1
Burkholderia pyrrocinia strain mHSR5 chromosome mHSR5_B, complete sequence	2351	2351	97%	0	81%	CP024903.1
Ralstonia pseudosolanacearum strain CRMrs218, complete genome	2359	2359	98%	0	81%	CP021764.1
Xanthomonas euvesicatoria strain LMG930, complete genome	2348	2348	98%	0	81%	CP018467.1
Burkholderia ambifaria MC40-6 chromosome 3, complete sequence	2355	2355	98%	0	81%	CP001027.1
Xanthomonas perforans strain LH3 chromosome, complete genome	2331	2331	98%	0	81%	CP018475.1
Cupriavidus taiwanensis isolate Cupriavidus taiwanensis STM 3679 genome assembly, chromosome: I	2322	2322	97%	0	81%	LT984803.1
Cupriavidus necator N-1 plasmid pBB1, complete sequence	2316	2316	98%	0	80%	CP002879.1

Table 7: Inventory of Predicted MDR Transporters from the RND (Pfam PF00873) Superfamily Encoded in PsPto genome

NCBI ID	NCBI gene description	Notes
RND-type:		
PSPTO_0375	Cation efflux family protein	
*	AcrB/AcrD/AcrF family protein	
PSPTO_0820		
PSPTO_1308	AcrB/AcrD/AcrF family protein	
PSPTO_2592	Aliphatic isothiocyanate resistance protein SaxG; AcrB/AcrD/AcrF family	Putative ortholog of <i>P. aeruginosa</i> PAO1 MexD
PSPTO_2755	AcrB/AcrD/AcrF family protein	
PSPTO_3100	Aliphatic isothiocyanate resistance protein SaxF; AcrB/AcrD/AcrF family	Putative ortholog of <i>P. aeruginosa</i> PAO1 MexF
PSPTO_3302	AcrB/AcrD/AcrF family protein	
PSPTO_4304	Isothiocyanate resistance protein SaxB	Putative ortholog of <i>P. aeruginosa</i> PAO1 MexB
PSPTO_5191	TpsC transporter	

Table 8: Summary of log reduction in the pathogen *Pto* DC3000 load by the active GBTM compared with the control GBTM (see Example 1)

Experiment	Average CFU/cm ²	Reduction in target pathogen load (CFU/ cm ²)	Percentage (%) Reduction in <i>Pto</i> DC3000 load	Log (CFU/ cm ²)	Log reduction in pathogen (<i>Pto</i> DC3000) load*
Biological replicate-1					
<i>Pto</i> DC3000 control	2.0E+05	-		5	-
Plant control GB TM 1	1.19E+05	-		5	-
Plant active GB TM 1	5.5E+03	1.14E+05	95	4	1.3
Biological replicate-2					
<i>Pto</i> DC3000 control	1.6E+04	-		4	-
Plant control GB TM 1	1.6E+04	-		4	-
Plant active GB TM 1	2.7E+02	1.6E+04	98	2	1.8
Biological replicate-3					
<i>Pto</i> DC3000 control	6.9E+04	-		5	-
Plant control GB TM 1	3.0E+05	-		5	-
Plant active GB TM 1	2.9E+03	3.0E+05	99	3	2.0
Average log reduction					1.7
Biological replicate-1					
<i>Pto</i> DC3000 control	6.8E+04	-		5	-
Plant control GB TM 2	3.2E+05	-		6	-
Plant active GB TM 2	1.4E+04	3.0E+05	96	4	1.4
Biological replicate 2					

<i>Pto</i> DC3000 control	4.6E+05	-		6	-
Plant control GB™ 2	9.0E+04	-		5	-
Plant active GB™ 2	7.2E+03	8.3E+04	92	4	1.1
Biological replicate 3					
<i>Pto</i> DC3000 control	4.8E+05	-		6	-
Plant control GB™ 2	7.2E+04	-		5	-
Plant active GB™ 2	6.3E+03	6.5E+04	91	4	1.1
Average log reduction					1.2

Table 9: Durability of Anti-Bacterial Response Delivered by Conjugation

Experiment	CFU/mL Day 1	CFU/mL Day 7	Percentage (%) kill active GB- Day 1	% kill active GB-Day 7	Difference in % kill
Pfu 896 Guided Biotic vs. <i>Pto</i> DC3000					
Experiment 1					
Pathogen only. <i>Pto</i> DC3000	8.05E+03	4.69E+05			
Non Active Guided Biotic	2.06E+04	1.16E+05			
Active Guided Biotic	2.49E+02	1.94E+03	98.8	98.3	-0.5
Experiment 2					
Pathogen only. <i>Pto</i> DC3000	7.68E+02	1.57E+04			
Non Active Guided Biotic	8.16E+02	6.34E+04			
Active Guided Biotic#	3.26E+01	1.00E+00	96.0	100.0	4
Experiment 3					
Pathogen only. <i>Pto</i> DC3000	7.40E+02	3.15E+05			
Non-Active Guided Biotic	9.16E+04	1.16E+06			
Active Guided Biotic	1.36E+02	1.08E+04	99.9	99.1	-0.8
Average % kill					0.9
Pfu 887 Guided Biotic vs. <i>Pto</i> DC3000					
Experiment 1					
Pathogen only. <i>Pto</i> DC3000	7.40E+02	3.15E+05			
Non-Active Guided Biotic	2.57E+04	1.17E+06			
Active Guided Biotic	1.80E+02	1.27E+04	99.3	98.9	-0.4
Experiment 2					
Pathogen only. <i>Pto</i> DC3000	1.15E+04	1.96E+06			
Non-Active Guided Biotic	9.17E+03	1.55E+05			
Active Guided Biotic	6.38E+02	1.97E+03	93.0	98.7	5.7
Experiment 3					

Pathogen only. <i>Pto</i> DC3000	1.15E+04	1.96E+06			
Non-Active Guided Biotic	1.48E+03	2.45E+05			
Active Guided Biotic	3.15E+02	4.71E+03	78.8	98.1	19.3
Average % kill					8.2
Formula/key:					
Percentage (%) kill by active GB = (CFU/mL of nonactive GB - CFU/mL of active GB)/CFU/mL of nonactive GB*100					
Difference in % killing = Percentage (%) kill active GB at Day 7- % kill active GB at Day 1)					
Average % kill = Average of difference in % kill of triplicate experiments					
# 0E+0 changed to 1E+0 to calculate log CFU/mL					

NUCLEOTIDE AND PROTEIN SEQUENCES

>PSPTO_0820 (SEQ ID NO: 1)

ATGAGCGAAGGTCGTTTCAACCTGTCAGTGCTGGCCGTGCGCGAGCGCTCGATCACCTG
TTCCTGATTTGCCTGATTTTCGCTGGCCGGGGTCATTGCCT
TTTTCAAACCTGGGCCGCGCCGAAGACCCGGCCTTCACGGTCAAGGTAATGACCGTGCGTGT
CGGTCTGGCCGGGCGCAACCGCCCAGGAGATGCAGGATCA
GGTGGCGGAGAAGATCGAAAAGCGCCTTCAGGAAGTGGTACGACCGCACCGAAA
CCTACACGCGGCCTGGCATGGCATTACAAACCTGACCCTG
CTCGACAGCACGCCGCCGTCGCAAGTGCCGGATGAGTTTTATCAGGCACGCAAGAAAAT
CGGTGACGAGGCCATGACGCTTCCGGCCGGGGTGATCGGGC
CGATGGTCAACGACGAGTATTCGGACGTTACTTTTCGCGCTGTTTCGCGCTCAAGGCCAAAG
GCGAGCCGCAGCGCGTGCTGGCACGTGACGCCGAATCGCT
GCGCCAGCGCCTGCTGCATGTGCCGGGCGTGAAGAAGGTCAACATCGTGGGCGAGCAGC
CCGAGCGCATCTACGTCGAGTTCTCCACGAGCGACTGGCA
ACGCTGGGTATCAGCCCGCAAGAGGTATTTGCCGCGCTGAATAATCAGAATGCGCTTACC
CCGGCAGGCTCGGTGAAACCCGTGGGCCGAGGTGTTCA
TTCGGCTCGACGGCGCTTTTCGATGAGCTGCAGAAGATCCGCGATACGCCGGTTGTGGCTC
AGGGCCGCACGCTGAAGCTGGCGGACATTGCCACGGTCAA
ACGCGGTTACGAAGACCCGGCAACGTTTCATGATTCGCAACGGCGGCGAGCCGGCACTGT
TGCTGGGGATCGTCATGCGCGATGGCTGGAACGGGCTGGAC
CTTGGAAGGCGCTGGATCATGAGGTGGGCGCGATCAACGCCGAGCTGCCCTTGGGCAT

GAGCCTGAACAAGGTCACGGACCAGGCCGTCAACATCAGTT
CGGCGGTTCGATGAGTTCATGATCAAGTTTTTCGTCGCATTGCTGGTGGTCATGCTGGTCT
GCTTTATCAGCATGGGCTGGCGTGTGGGCGTTGTGGTGGC
TGCCGCCGTACCGCTGACCCTGGCGGTGGTCTTCGTGATCATGGCCATGAGCGGCAAGAA
TTTCGACCGCATTACATTGGGTTCACTGATTCTGGCGCTC
GGGCTGCTGGTCGACGACGCGATCATCGCCATCGAAATGATGGTGGTGAAGATGGAAGA
AGGTTACGACCGCATCGCGGCTCTGCGTACGCTGGAGCC
ACACCGCCGCGCCCATGTTATCCGGCACCTGGTCACCGCTGTCGGCTTCATGCCCAACG
GTTTTGCGCGCTCCACGGCAGGCGAATACACCAGCAACAT
GTTCTGGATCGTCGGTATCGCGCTGATTGCCTCATGGGTGGTCGCGGTGTTTTTCACACCG
TATCTGGGCGTGAAACTGTTGCCTGAGGTGAAGCAGGTC
GAAGGCGGACATGCAACGCTTTACGACACCCACGCTACAACCGTTTCCGCCGGGTCTG
GCACGCGTCATTGCAGGCAAGTGGCTGGTCGAGGTTTCGG
TCATCGGGTTGTTTCGTCTGGCAGTGCTGGGCATGGGGCTGGTCAAGAAACAGTTTTTTTC
CGGTGTCCGACCGCCAGAGGTGCTGGTCGAACTGCAGAT
GCCTTACGGCACCTCGATTGCTCAAACCAGCGCGGCCGCGGCCAAAGTGGAAGCTGGC
TGGCCGAGCAGGCAGAAGCCGGGATCGTCACCGCTACATT
GGCCAGGGCGCGCCACGTTTCTACATGGCGATGGGGCCGGAATTACCTGACCCGTCATTT
GCCAAGATCGTGGTGCACCGACAGCCAGGAACAGCGCG
AGACACTGAAACACCGCTTGCGTCAGGCTATTTCCGAAGGGCTGGCTGGCGAGGCGCAA
GTGCGCGTCACGCAACTGGTCTTCGGCCCGTATTACCCCTA
CCCGGTGCGCTACCGCGTTACTGGCCATGACCCGGACACACTGCGCAGCATTGCGGCGCA
GGTGCAACAGGTGCTGAGCGCCAGCCGATGATGCGCACC
GTCAATACTGACTGGGGCACGCGCACCCCAACGCTGCATTTACCTTGCAACAGGACCG
GATGCAGGCCATCGGGTTGAGTTCCAGCCAGGTCGCGCAAC
AATTGCAGTTCCTGCTGACCGGCCTGCCGGTTACGGCGGTGCGCGAGGACATTGCGACCG
TGCAGGTGGTTGCCCGCTCGGCTGGCGACACCCGACTGGA
TCCGGCAAAAATCATGGACTTCACCCTCACAGGCGTCGATGGGCAACGTGTTCCGCTGTC
GCAGATCGGTGCAGTCGATGTGCGCATGGAAGAGCCGGTC
ATGCGCCGGCGCGACCGCACGCCAACCATACCGTACGGGGCGACATCGCCGACGGCCT
GCAACCGCCAGATGTATCGACGGCCATTACCCGGCAGTTGC
AGCCCATCATCGACACGCTGCCAGTGGCTATCGGATCGATCAGGCAGGTTCAATCGAG
GAATCCGGCAAGGCAATGGCGGCGATGTTGCCACTGTTCCC
GATCATGCTGGCGGTACGCTGATCATCCTGATTCTGCAGGTGCGTTCGATATCGGCCAT
GGTCATGGTGTCTTGACAGCCCGCTGGGGCTGATCGGT
GTGGTGCCTACGCTGATCCTCTTTCAGCAGCCCTTCGGCATCAATGCACTGGTCGGGCTG

ATCGCACTGTCCGGCATTCTGATGCGCAACACGCTGATCC
TGATCGGCCAGATCCACCACAATGAACAGGCGGGGCTCGACCCGTTTCAGGCCGTGGTC
GAAGCCACCGTACAACGTGCGCGCCCGGTGATACTGACAGC
GCTGGCCGCCATTCTGGCGTTTATCCCCCTCACCCATTCCGGTGTCTGGGGCACGCTGGCC
TACACGCTGATCGGCGGCACATTCGCCGGTACGGTGCTG
ACCCTGGTGTTCCTGCGGCAATGTACTCGATCTGGTTCAGGATCAGGCCCCGATGGCAAC
GAGCGGCCGCAAGGCGGTCAATTCCTTGTCACAGGTAAAG GGGTGAGCTAG

>AcrB/AcrD/AcrF family protein (encoded by PSPTO_0820) (SEQ ID NO: 2)

MSEGRFNLSVLAVRERSITLFLICLISLAGVIAFFKLGRAEDPAFTVKVMTVVSVPWPGATAQE
MQDQVAEKIEKRLQELRWYDRTEYTRPGMAFTTLTLLDSTPPSQVPDEFYQARKKIGDEA
MTLPAGVIGPMVNDEYSDVTFALFALKAKGEPQRLARDAESLRQRLHVPGVKKVNIVGE
QPERIYVEFSHERLATLGISPQEVFAALNNQNALTPAGSVETRGPQVFIRLDGAFDELQKIRDT
PVVAQGRTLKLADIATVKRGYEDPATFMIRNGGEPALLLGIVMRDGNGLDLGKALDHEVG
AINAELPLGMSLNKVTDAQVNISAVDEFMIKFFVALLVVMLVCFISMGWRVGVVVAAP
LTLAVVFVIMAMSGKNFDRITLGSLLALGLLVDDAIIAIEMMVVKMEEGYDRIAASAYAWS
HTAAPMLSGTLVTAVGFMPNGFARSTAGEYTSNMFWIVGIALIASWVAVFFTPYLGVKLLP
EVKQVEGGHATLYDTPRYNRFRRVLARVIAGKWLVAAGSVIGLFLVAVLGMGLVKKQFFPVS
DRPEVLVELQMPYGTSAQTSAAAAKVESWLAEQAEAGIVTAYIGQGAPRFYMAMGPELPD
PSFAKIVVRTDSQEQRETLKHRLRQAISEGLAGEAQVRVTQLVFGPYSPYPVAYRVTGHDPD
TLRSIAAQVQQVLSASPMRTVNTDWGTRTPTLHFTLQQDRMQAIGLSSSQVAQQLQFLLT
GLPVTAVREDIRTVQVVARSDTRLDPAKIMDFLTGVDGQVRVPLSQIGAVDVRMEEPVM
RRRDRTPTITVRGDIADGLQPPDVSTAIRQLQPIIDTLPSGYRIDQAGSIEESGKAMAAMLPLF
PIMLAVTLIILQVRSISAMVMVFLTSPLGLIGVVPTLILFQQPFGINALVGLIALSGILMRNTLI
LIGQIHNEQAGLDPFQAVVEATVQRARPVILTALAAILAIFPLTHSVFWGTLAYTLIGGTGAG
TVLTLVFLPAMYSIWFRIRPDGNERPQGGHSLSTGKGV

>PSPTO_4977 (SEQ ID NO: 3)

ATGTTGCGCAAACCTTCGTTGGTCGTGGCTGTTTCGTTGGCGTCCAGCGGACTGACCTGG
GCTGCCGACTTGCCGCTGCCAACCAAAACCGGTCTGTTGA
ATGTGTATCAGCAGGCGGTAGACAACAACGCCGACCTCGCGGCCTCGCGTGCCGATTAC
GATGCCCCGAAGGAAGCCGTGCCACAGGCCCGAGCCGGCCT
GCTGCCGAATATTTCCGGCAGTGTCAGAACACCAACACCCGCACCAGCATCGACCGCC
CCAGCGCCGTGGCGACCCGCAGCGGCACGGTTTATCAGGCC
ACCCTGAGCCAGCCGATCTTTCGCGCCGACCGCTGGTTCAGTTGCAGGCTGCCGAAGCG
GTCAACGAACAGGCCGCGCTGGAAGTGTGCGGCCACCGAGC

AGAACCTGATCCTGCAATCGGCGCAGAGCTATTTTCAGTGTGTTGCGCGCGCAGGACAATC
TGGCCTCGACCAAGGCTGAGGAAGCGGCGTTCAAACGCCA
GCTCGATCAGGCCAACGAACGCTTCGATGTCGGTCTGTCAGACAAGACCGATGTGCTGC
AGGCCCAGGCCAGCTACGACACCTCGCGCGCCAGCCGGCTG
ATCGCCAGGCGTCAGGTGGACGATGCCTTTTCAGGCGCTGGTGACCCTGACCAATCGCGA
ATACAACTCCATCGAAGGCATCGTGCACACCTTGCCGGTGC
TGGCACCAACGCCCAACGACGCCAAGGCCTGGGTGGATACGGCAGCGCAACAAAACCTC
AACCTGCTGGCCAGCAACTACGCCGTCAGCGCTGCCGAAGA
AACCCTGCGCCAGCGCAAGGCCGGGCACGCGCCACCCTTGATGCCGTGGCGACTTACC
AGCGTGCGCACAACGATGCATTGGGTTTCAACAACCCCAAC
TACACCGGGCAAAATTACGGCGGCGACGTCGAGCAACGCAGCATTGGCGTGCAGTTGAA
TATCCCGATCTACAGCGGCGGCCTGACCAGTTCACAGGTGC
GTGAGGCTTATTCGCGCCTGAGCCAGAGCGAGCAGCGCCGCGAAAGCCTGCGACGTCAG
GTGGTGGAACACCCGTAACCTGCACCGTGCGGTGAACAC
TGATGTCGAGCAGGTTTCAGGCGCGCAAACAGTCGATCATCTCCAACCAGAGTGCGCTGG
AAGCCACGGAAATCGGCTATCAGGTGCGCACCCGCAACATC
GTCGATGTGCTGGACGCCCAGCGTCAGTTGTATGCCTCGGTGCGTGACTACAACAACACG
CGCTATGACTACATCCTCGACAACCTGCGCCTCAAGCAGG
CAGCGGGCACCTGAACCCGGGCGACTTGCAGGACCTGTCACGCTACCTCAAACCGGAC
TACAACCCGGACAAGGACTTCCTGCCGCCGGATTGCGCGAC
TGCAGCGCAGAAGAATTTTCGAGCGGCCGGCGCAGCGCTGA

>Outer membrane efflux protein TolC (encoded by PSPTO_4977) (SEQ ID NO: 4)

MLRKLSLVVAVSLASSGLTWAADLPLPTKTGLLNQYQAVDNNADLAASRADYDARKEAV
PQARAGLLPNISGSVQNTNTRTSIDRPSAVATRSGTVYQATLSQPIFRADRFQQLQAAEAVNE
QAALELSATEQNLILQSAQSYFSVLRAQDNLASTKAEEAAFKRQLDQANERFDVGLSDKTDV
LQAQASYDTSRASRLIARRQVDDAFQALVTLTNREYNSIEGIVHTLPVLAPTPNDAKAWVDT
AAQQNLNLLASNYAVSAAEETLRQRKAGHAPTLDAVATYQRGDNDALGFNNPNYTGQNYG
GDVEQRSIGVQLNIPIYSGGLTSSQVREAYSRLSQSEQRRESLRRQVVENTRNLHRAVNTDVE
QVQARKQSIISNQSALATEIGYQVGTNRNIVDLDAQRQLYASVRDYNTRYDYILDNLRLK
QAAGTLNPGDLQDLSRYLKPDPNPKDFLPPDLATAAQKNFERPAQR

CLAIMS:

1. A method of killing a bacterial target cell, the cell comprising at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, the method comprising contacting the target cell with a carrier bacterial cell, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent that is toxic to the target cell, wherein the carrier cell conjugates to the target cell and the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell is killed.
2. The method of claim 1, wherein the agent comprises a CRISPR/Cas system or component thereof.
3. The method of claim 2, wherein the agent is a crRNA or guide RNA that guides a Cas nuclease in the target cell to a target protospacer sequence, wherein the Cas cuts the target sequence and the target cell is killed.
4. The method of claim 3, wherein the target sequence is a chromosomal sequence of the target cell.
5. The method of any preceding claim, wherein the plasmid encodes a or said Cas nuclease, optionally a Cas9, Cas3 or Cpf1.
6. The method of any preceding claim, wherein the target cell comprises an RND efflux pump of a strain selected from
 - (i) Azotobacter chroococcum NCIMB 8003, Azotobacter chroococcum strain B3, Azotobacter salinestris strain KACC 13899, Burkholderia ambifaria MC40-6, Burkholderia cenocepacia AU 1054 chromosome 1, Burkholderia cenocepacia HI2424 chromosome 3, Burkholderia cenocepacia MC0-3, Burkholderia cenocepacia strain CR318 chromosome 3, Burkholderia cenocepacia strain FDAARGOS_720, Burkholderia lata strain A05, Burkholderia pyrrocinia strain mHSR5, Cupriavidus basilensis strain 4G11, Cupriavidus necator N-1 plasmid pBB1, Cupriavidus taiwanensis STM 3679, Lysobacter gummosus strain 3.2.11, Paraburkholderia sprentiae WSM5005, Paraburkholderia terricola strain mHS1, Ralstonia pseudosolanacearum strain CRMRS218, Ralstonia solanacearum strain UA-1591, Variovorax paradoxus S110, Variovorax sp. PBL-H6, Xanthomonas arboricola pv. juglandis strain Xaj 417,

Xanthomonas arboricola pv. *pruni* strain 15-088, *Xanthomonas arboricola* strain 17, *Xanthomonas axonopodis* pv. *dieffenbachiae* LMG 695, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO18C8, *Xanthomonas axonopodis* pv. *phaseoli* strain ISO98C12, *Xanthomonas campestris* pv. *campestris* MAFF302021, *Xanthomonas citri* pv. *glycines* strain 2098, *Xanthomonas euvesicatoria* strain LMG930, *Xanthomonas perforans* strain LH3 and *Xanthomonas* sp. ISO98C4, which strains have NCBI Accession Numbers respectively of CP010415.1, CP011835.1, CP045302.1, CP001027.1, CP000378.1, CP000460.1, CP000960.1, CP017240.1, CP050980.1, CP024945.1, CP024903.1, CP010537.1, CP002879.1, LT984803.1, CP011131.1, CP017561.1, CP024941.1, CP021764.1, CP034195.1, CP001636.1, LR594659.1, CP012251.1, CP044334.1, CP011256.1, CP014347.1, CP012063.1, CP012057.1, AP019684.1, CP041965.1, CP018467.1, CP018475.1 and CP012060.1, or an orthologue or homologue of such a pump;

- (ii) *Pseudomonas aeruginosa* strain: IOMTU 133, *Pseudomonas aeruginosa* DSM 50071, *Pseudomonas aeruginosa* genome assembly NCTC10332, *Pseudomonas aeruginosa* isolate B10W, *Pseudomonas aeruginosa* isolate PA14Or, *Pseudomonas aeruginosa* NCGM2.S1, *Pseudomonas aeruginosa* PAK, *Pseudomonas aeruginosa* strain 243931, *Pseudomonas aeruginosa* strain 24Pae112, *Pseudomonas aeruginosa* strain 268, *Pseudomonas aeruginosa* strain 60503, *Pseudomonas aeruginosa* strain AR_0095, *Pseudomonas aeruginosa* strain AR_0353, *Pseudomonas aeruginosa* strain AR_0354, *Pseudomonas aeruginosa* strain AR_455, *Pseudomonas aeruginosa* strain BAMCPA07-48, *Pseudomonas aeruginosa* strain CCUG 51971, *Pseudomonas aeruginosa* strain E90, *Pseudomonas aeruginosa* strain FDAARGOS_571, *Pseudomonas aeruginosa* strain GIMC5002:PAT-169, *Pseudomonas aeruginosa* strain H26023, *Pseudomonas aeruginosa* strain L10, *Pseudomonas aeruginosa* strain M1608, *Pseudomonas aeruginosa* strain M37351, *Pseudomonas aeruginosa* strain MRSN12280, *Pseudomonas aeruginosa* strain NCTC13715, *Pseudomonas aeruginosa* strain Pa58, *Pseudomonas aeruginosa* strain PABL048, *Pseudomonas aeruginosa* strain PAK, *Pseudomonas aeruginosa* strain PASGNDM345, *Pseudomonas aeruginosa* strain PASGNDM699, *Pseudomonas aeruginosa* strain PA-VAP-3, *Pseudomonas aeruginosa* strain PB368, *Pseudomonas aeruginosa* strain PB369, *Pseudomonas aeruginosa* strain S04 90, *Pseudomonas aeruginosa* strain ST773, *Pseudomonas aeruginosa* strain T2436, *Pseudomonas aeruginosa* strain W60856, *Pseudomonas aeruginosa* strain WPB099, *Pseudomonas aeruginosa* strain WPB100, *Pseudomonas aeruginosa* strain WPB101, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* UCBPP-PA14, *Pseudomonas aeruginosa* VRFP404, *Pseudomonas amygdali* pv. *lachrymans* str. M301315, *Pseudomonas amygdali* pv.

lachrymans strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas avellanae* strain R2leaf, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas coronafaciens* pv. *oryzae* str. 1_6, *Pseudomonas coronafaciens* strain X-1, *Pseudomonas otitidis* MrB4, *Pseudomonas salegens* strain CECT 8338, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas savastanoi* pv. *savastanoi* NCPPB 3335, *Pseudomonas* sp. KBS0707, *Pseudomonas* sp. LPH1, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* group genomosp. 3 isolate CFBP6411, *Pseudomonas syringae* isolate CFBP3840, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *actinidiae* ICMP 18884, *Pseudomonas syringae* pv. *actinidiae* ICMP 9853, *Pseudomonas syringae* pv. *actinidiae* str. Shaanxi_M228, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 12.29, *Pseudomonas syringae* pv. *actinidiae* strain CRAFRU 14.08, *Pseudomonas syringae* pv. *actinidiae* strain MAFF212063, *Pseudomonas syringae* pv. *actinidiae* strain NZ-45, *Pseudomonas syringae* pv. *actinidiae* strain NZ-47, *Pseudomonas syringae* pv. *actinidiae* strain P155, *Pseudomonas syringae* pv. *avii* isolate CFBP3846, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *tomato* str. DC3000, *Pseudomonas syringae* pv. *tomato* strain B13-200, *Pseudomonas syringae* pv. *tomato* strain delta IV/IX, *Pseudomonas syringae* pv. *tomato* strain delta VI, *Pseudomonas syringae* pv. *tomato* strain delta X, *Pseudomonas syringae* strain CFBP 2116 and *Pseudomonas syringae* strain Ps25, which strains have NCBI Accession Numbers respectively of AP017302.1, CP012001.1, LN831024.1, CP017969.1, LT608330.1, AP012280.1, CP020659.1, CP041772.1, CP029605.1, CP032761.1, CP041774.1, CP027538.1, CP027172.1, CP027171.1, CP030328.1, CP015377.1, CP043328.1, CP044006.1, CP033833.1, CP043549.1, CP033685.1, CP019338.1, CP008862.2, CP008863.1, CP028162.1, LR134330.1, CP021775.1, CP039293.1, LR657304.1, CP020703.1, CP020704.1, CP028330.1, CP025050.1, CP025049.1, CP011369.1, CP041945.1, CP039988.1, CP008864.2, CP031878.1, CP031877.1, CP031876.1, CP034244.1, CP000438.1, CP008739.2, CP031225.1, CP020351.1, CP026558.1, CP042804.1, CP026562.1, CP046441.1, CP046035.1, CP050260.1, AP022642.1, LT629787.1, CP000058.1, CP008742.1, CP041754.1, CP017290.1, CP007014.1, LT963408.1, LT963409.1, CP012179.1, CP011972.2, CP018202.1, CP032631.1, CP019730.1, CP019732.1, CP024712.1, CP017007.1, CP017009.1, CP032871.1, LT963402.1, LT963391.1, CP047260.1, AE016853.1, CP019871.1, CP047072.1, CP047071.1, CP047073.1, LT985192.1 and CP034558.1, or an orthologue or homologue of such a pump;

- (iii) *Stenotrophomonas rhizophila* strain GA1, *Enterococcus faecalis* strain V583 and *Paucimonas lemoignei* strain NCTC10937, which strains have NCBI Accession Numbers respectively CP031729.1, CP022312.1 and LS483371.1, or an orthologue or homologue of such a pump; or
 - (iv) *Pseudomonas amygdali* pv. *lachrymans* strain NM002, *Pseudomonas amygdali* pv. *morsprunorum* strain R15244, *Pseudomonas amygdali* pv. *tabaci* str. ATCC 11528, *Pseudomonas asturiensis* strain CC1524, *Pseudomonas avellanae* strain R2, *Pseudomonas cerasi* isolate PL963, *Pseudomonas chlororaphis* strain PCL1606, *Pseudomonas chlororaphis* subsp. *aurantiaca* strain JD37, *Pseudomonas chlororaphis* subsp. *aureofaciens* strain ChPhzTR36, *Pseudomonas chlororaphis* subsp. *chlororaphis* strain DSM 50083, *Pseudomonas chlororaphis* subsp. *piscium* strain DSM 21509, *Pseudomonas cichorii* JBC1, *Pseudomonas coronafaciens* pv. *coronafaciens* strain B19001, *Pseudomonas putida* GB-1 chromosome, *Pseudomonas savastanoi* pv. *phaseolicola* 1448A, *Pseudomonas* sp. 09C 129, *Pseudomonas syringae* CC1557, *Pseudomonas syringae* pv. *actinidiae* ICMP 18708, *Pseudomonas syringae* pv. *cerasicola* isolate CFBP6109, *Pseudomonas syringae* pv. *lapse* strain ATCC 10859, *Pseudomonas syringae* pv. *maculicola* str. ES4326, *Pseudomonas syringae* pv. *pisi* str. PP1, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* pv. *syringae* B301D, *Pseudomonas syringae* UMAF0158 and *Pseudomonas viridiflava* strain CFBP 1590, which strains have NCBI Accession Numbers respectively of CP020351.1, CP026558.1, CP042804.1, CP047265.1, CP026562.1, LT963395.1, CP011110.1, CP009290.1, CP027721.1, CP027712.1, CP027707.1, CP007039.1, CP046441.1, CP000926.1, CP000058.1, CP025261.1, CP007014.1, CP012179.1, LT963391.1, CP013183.1, CP047260.1, CP034078.1, CP005969.1, AE016853.1, CP005970.1 and LT855380.1, or an orthologue or homologue of such a pump.
7. The method of any preceding claim, wherein the efflux pump comprises a protein produced by a strain listed in claim 6.
8. The method of any preceding claim, wherein the efflux pump comprises a protein encoded by a *Pseudomonas syringae* gene selected from PSPTO_0820, PSPTO_4977, PSPTO_02375, PSPTO_1308, PSPTO_2592, PSPTO_2755, PSPTO_3100, PSPTO_3302, PSPTO_430 or PSPTO_5191, or an orthologue or homologue thereof.

9. The method of any preceding claim, wherein the efflux pump comprises a protein encoded by
- (a) *Pseudomonas syringae* PSPTO_0820 or PSPTO_4977 gene or an orthologue or homologue thereof; or
 - (b) A nucleotide sequence selected from SEQ ID NO: 1 and 3, or a nucleotide sequence that is at least 70% identical to SEQ ID NO: 1 or 3.
10. The method of any one of claims 1 to 7, wherein the efflux pump is a Mex efflux pump (optionally a MexAB-OprM efflux pump, MexCD-OprJ efflux pump, MexEF-OprN efflux pump or MexXY efflux pump), AdeABC efflux pump, AcrAD-TolC efflux pump, AcrAB-TolC efflux pump, AcrABZ-TolC efflux pump, AcrA efflux pump, ArcB efflux pump, AcrC efflux pump, AcrD efflux pump, AcrAB efflux pump, AcrEF efflux pump, AcrF efflux pump, CmeABC efflux pump, VexB efflux pump, VexD efflux pump, VexK efflux pump, adeABC efflux pump, adeIJK efflux pump, MdsABC efflux pump or MdtABC efflux pump.
11. The method of any preceding claim, wherein the carrier cell is a *Pseudomonas* cell, optionally a *P. fluorescens* cell.
12. The method of any preceding claim, wherein the carrier cell comprises a Chitinase class I exoenzyme and/or the carrier cell genome encodes a Chitinase class I exoenzyme.
13. The method of any preceding claim, wherein the carrier cell comprises a *pepI* gene.
14. The method of any preceding claim, wherein the carrier cell is a motile bacterial cell.
15. The method of any preceding claim, wherein the target cell is a *Pseudomonas* (optionally a *P. fluorescens* or *P. aeruginosa*) cell, *Erwinia* (optionally *E. carotovora*), *Xanthomonas*, *Agrobacterium*, *Burkholderia*, *Clavibacterium*, *Enterobacter*, *Pantoea*, *Pectobacterium* (eg, *P. atrosepticum*), *Rhizobium*, *Streptomyces* (eg, *S. scabies*), *Xylella* (eg, *X. fastidiosa*), *Candidatus* (eg, *C. liberibacter*), *Phytoplasma*, *Ralstonia* (eg, *R. solanacearum*), or *Dickeya* (eg, *D. dadantii*) cell.

16. The method of any preceding claim, wherein the method is carried out *in vitro* or *ex vivo*.
17. The method of any preceding claim, wherein the target cell is comprised by
 - (a) a plant microbiome,
 - (b) an animal or human microbiome; or
 - (c) a soil, manure, food or beverage microbiome.
18. The method of claim 17(a), wherein the cell is comprised by a plant leaf, stem, root, seed, bulb, flower or fruit microbiome.
19. The method of any preceding claim, wherein the target cell is a cell of a species found in soil.
20. The method of any preceding claim, wherein the method is carried out using a first cell population comprising a plurality of carrier cells that are contacted with a second cell population comprising a plurality of target cells, wherein copies of said plasmid are conjugatively transferred from carrier cells into target cells, whereby some or all of the cells of the second population are killed.
21. The method of claim 20, wherein at least 90% of the target cells are killed.
22. A method of increasing the biomass of a plant or part thereof, the method comprising carrying out the method of claim 20 or 21, wherein the plant comprises said target cells (optionally on leaves and/or stems thereof or comprised by the apoplast of the plant), whereby target cells are killed and said biomass is increased.
23. The method of claim 22, wherein leaf, fruit, ear, seed, grain, head, pod, stem, trunk, tuber and/or root biomass is increased.
24. A method of promoting germination of a plant seed, the method comprising carrying out the method of claim 20 or 21, wherein the plant seed comprises said target cells, whereby target cells are killed and germination is promoted.

25. A method of increasing leaf chlorophyll production in a plant, the method comprising carrying out the method of claim 20 or 21, wherein the plant comprises said target cells (optionally on leaves and/or stems thereof, or comprised by the apoplast of the plant), whereby target cells are killed and chlorophyll is increased in the plant.
26. A method for reducing a biofilm comprised by a subject or comprised on a surface, wherein the biofilm comprises target cells, wherein the method comprises carrying out the method of claim 20 or 21, thereby killing the target cells in the biofilm or reducing the growth or proliferation of target cells, optionally wherein the method is carried out *ex vivo* or *in vitro*.
27. The method of Claim 26, wherein the subject is a human or animal, optionally wherein the surface is a lung surface.
28. The method of Claim 26 wherein the subject is a plant, optionally wherein the biofilm is comprised by a leaf, trunk, root or stem of the plant.
29. The method of Claim 26, wherein the surface is comprised by a domestic or industrial apparatus or container.
30. A carrier bacterial cell for use in a method of killing a bacterial target cell according to any preceding claim, wherein the carrier cell comprises a conjugative plasmid, the plasmid encoding an antibacterial agent that is toxic in the target cell, wherein the carrier cell is capable of conjugating to the target cell wherein the plasmid is transferred into the target cell, wherein the agent is expressed in the target cell and the target cell is killed.
31. The carrier cell of claim 30, wherein the carrier cell and/or the target cell is according any one of claims 1 to 29.
32. A pharmaceutical composition comprising a plurality of carrier cells of claim 30 or 31 for administration to a human or animal subject for killing a plurality of bacterial target cells comprised by the subject, wherein each target cell comprises at least one Resistance-Nodulation-

Cell Division (RND)-efflux pump whereby each target cell is an antibiotic resistant cell, wherein plasmids encoding the antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and an antibiotic resistant infection of bacterial target cells is treated or prevented in the subject.

33. The composition of claim 32, wherein at least 90% of said target cells are killed.
34. A method of treating or preventing a disease or condition in a plant, the method comprising contacting the plant (eg, one or more stems and/or one or more leaves of the plant) with a composition comprising a plurality of carrier cells of claim 30 or 31, wherein the plant comprises target bacterial cells that mediate the disease or condition, wherein each target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein plasmids encoding the antibacterial agent are introduced from carrier cells into target cells by conjugation and said antibacterial agent is produced in target cells, whereby target cells are killed and the disease or condition is treated or prevented.
35. Use of a carrier cell of claim 30 or 31 in the manufacture of a composition, for killing a bacterial target cell *ex vivo* or wherein the target cell is not comprised by a human or animal (eg, the target cell is comprised by a plant or soil), wherein the target cell comprises at least one Resistance-Nodulation-Cell Division (RND)-efflux pump, wherein the target cell is contacted with the carrier cell and the carrier cell conjugates to the target cell, whereby the plasmid is introduced into the target cell, wherein the antibacterial agent is expressed in the target cell and the target cell is killed.
36. The use of claim 35, wherein the carrier cell and/or the target cell is according any one of claims 1 to 29.
37. The use of claim 35 or 36, wherein the use comprises using a plurality of said carrier cells to kill a plurality of said target cells, wherein the use is for killing at least 90% of the target cells.

38. The use of claim 35, 36 or 37, wherein the use comprises using a plurality of said carrier cells to kill a plurality of said target cells, wherein the target cells are comprised by a plant or plant environment (eg, soil) and the killing
- a) increases (or is for increasing) the biomass of the plant or part thereof (eg, leaf, fruit, ear, seed, grain, head, pod, stem, trunk, tuber and/or root biomass is increased);
 - b) promotes (or is for promoting) germination of one or more seeds of the plant;
 - c) increases (or is for increasing) the amount of leaf chlorophyll of the plant; and/or
 - d) reduces (or is for reducing) a biofilm comprised by the plant, wherein the biofilm comprises target cells (eg, *Pseudomonas* cells).