

METHODS AND RELATED COMPOSITIONS FOR MANUFACTURING FOOD AND FEED**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application claims priority to U.S. Provisional Application No. 62/450,038, filed on January 24, 2017, and U.S. Provisional Application No. 62/584,011, filed on November 9, 2017, the contents of which are hereby incorporated herein by reference in their entireties.

BACKGROUND

Arthropods, such as crickets, cicadas, grasshoppers, ants, insect larvae, caterpillars, and scorpions, have many traditional and potential new uses in the production of food and feed for humans and animals, respectively. Insects as food and feed emerge as an especially relevant issue due to the rising cost of animal protein, food and feed insecurity, environmental pressures, population growth, and increasing demand for affordable and sustainable sources of nutrients for humans and animals (e.g., livestock). To cultivate beneficial arthropods for use in the food and feed industries, there is a need in the art for ways to promote the growth and fitness of such arthropods.

SUMMARY OF THE INVENTION

Disclosed herein are compositions and methods for modulating the fitness of insects for food and feed manufacturing. The composition includes an agent that alters a level, activity, or metabolism of one or more microorganisms resident in a host, the alteration resulting in a modulation in the host's fitness.

In one aspect, provided herein is a method for increasing a nutritional profile of an insect, the method including delivering an effective amount of methionine-producing bacteria to the insect.

In some embodiments, the insect is a cricket, a grasshopper, or a locust.

In some embodiments, the insect may be developmentally an embryo, larva, pupa, or adult.

In some embodiments, the delivery may include delivering the composition to at least one habitat where the insect grows, lives, reproduces, or feeds.

In some embodiments, the methionine-producing bacteria may be delivered in an insect comestible composition for ingestion by the insect.

In some embodiments, the methionine-producing bacteria may be formulated with an agriculturally acceptable carrier as a liquid, a solid, an aerosol, a paste, a gel, or a gas composition.

In some embodiments, the carrier may be a seed coating.

In a second aspect, provided herein is a modified insect comprising exogenous methionine-producing bacteria resident in the insect.

In some embodiments of the second aspect, the insect is developmentally an embryo, a larva, a pupa, or an adult.

In some embodiments of the second aspect, the methionine-producing bacteria alters microbiota in a gut and/or haemocoel of the insect.

In yet another aspect, the composition includes an agent that alters a level, activity, or metabolism of one or more microorganisms resident in an insect host, the alteration resulting in an increase in the insect host's fitness.

In some embodiments of any of the above compositions, the one or more microorganisms may be a bacterium or fungus resident in the host. In some embodiments, the bacterium resident in the host is at least one selected from the group consisting of *Candidatus spp*, *Buchenera spp*, *Blattabacterium spp*, *Baumania spp*, *Wigglesworthia spp*, *Wolbachia spp*, *Rickettsia spp*, *Orientia spp*, *Sodalis spp*,
 5 *Burkholderia spp*, *Cupriavidus spp*, *Frankia spp*, *Snirrhizobium spp*, *Streptococcus spp*, *Wolinella spp*, *Xylella spp*, *Erwinia spp*, *Agrobacterium spp*, *Bacillus spp*, *Paenibacillus spp*, *Streptomyces spp*, *Micrococcus spp*, *Corynebacterium spp*, *Acetobacter spp*, *Cyanobacteria spp*, *Salmonella spp*, *Rhodococcus spp*, *Pseudomonas spp*, *Lactobacillus spp*, *Enterococcus spp*, *Alcaligenes spp*, *Klebsiella spp*, *Paenibacillus spp*, *Arthrobacter spp*, *Corynebacterium spp*, *Brevibacterium spp*, *Thermus spp*,
 10 *Pseudomonas spp*, *Clostridium spp*, and *Escherichia spp*. In some embodiments, the fungus resident in the host is at least one selected from the group consisting of *Candida*, *Metschnikowia*, *Debaromyces*, *Starmerella*, *Pichia*, *Cryptococcus*, *Pseudozyma*, *Symbiotaphrina buchneri*, *Symbiotaphrina kochii*, *Scheffersomyces shehatae*, *Scheffersomyces stipites*, *Cryptococcus*, *Trichosporon*, *Amylostereum areolatum*, *Epichloe spp*, *Pichia pinus*, *Hansenula capsulate*, *Daldinia decipien*, *Ceratocytis spp*,
 15 *Ophiostoma spp*, and *Attamyces bromatificus*. In certain instances, the bacteria is a naturally occurring bacteria that is capable of producing nutrients (e.g., amino acids, e.g., methionine).

In any of the above compositions, the agent, which hereinafter may also be referred to as a modulating agent, may alter the growth, division, viability, metabolism, and/or longevity of the microorganism resident in the host. In any of the above embodiments, the modulating agent may
 20 decrease the viability of the one or more microorganisms resident in the host. In some embodiments, the modulating agent increases growth or viability of the one or more microorganisms resident in the host.

In any of the above embodiments, the modulating agent is a phage, a polypeptide, a small molecule, an antibiotic, a bacterium, or any combination thereof.

In some embodiments, the phage binds a cell surface protein on a bacterium resident in the host.
 25 In some embodiments, the phage is virulent to a bacterium resident in the host. In some embodiments, the phage is at least one selected from the group consisting of *Myoviridae*, *Siphoviridae*, *Podoviridae*, *Lipothirixviridae*, *Rudiviridae*, *Ampullaviridae*, *Bicaudaviridae*, *Clavaviridae*, *Corticoviridae*, *Cystoviridae*, *Fuselloviridae*, *Gluboloviridae*, *Guttaviridae*, *Inoviridae*, *Leviviridae*, *Microviridae*, *Plasmaviridae*, and *Tectiviridae*.

30 In some embodiments, the polypeptide is at least one of a bacteriocin, R-type bacteriocin, nodule C-rich peptide, antimicrobial peptide, lysin, or bacteriocyte regulatory peptide.

In some embodiments, the small molecule is a metabolite.

In some embodiments, the antibiotic is a broad-spectrum antibiotic.

In some embodiments, the modulating agent is a naturally occurring bacteria. In some
 35 embodiments, the bacteria is at least one selected from the group consisting of *Bartonella apis*, *Parasaccharibacter apium*, *Frischella perrara*, *Snodgrassella alvi*, *Gilliamella apicola*, *Bifidobacterium spp*, and *Lactobacillus spp*. In some embodiments, the bacterium is at least one selected from the group consisting of *Candidatus spp*, *Buchenera spp*, *Blattabacterium spp*, *Baumania spp*, *Wigglesworthia spp*, *Wolbachia spp*, *Rickettsia spp*, *Orientia spp*, *Sodalis spp*, *Burkholderia spp*, *Cupriavidus spp*, *Frankia*
 40 *spp*, *Snirrhizobium spp*, *Streptococcus spp*, *Wolinella spp*, *Xylella spp*, *Erwinia spp*, *Agrobacterium spp*,

Bacillus spp, Paenibacillus spp, Streptomyces spp, Micrococcus spp, Corynebacterium spp, Acetobacter spp, Cyanobacteria spp, Salmonella spp, Rhodococcus spp, Pseudomonas spp, Lactobacillus spp, Enterococcus spp, Alcaligenes spp, Klebsiella spp, Paenibacillus spp, Arthrobacter spp, Corynebacterium spp, Brevibacterium spp, Thermus spp, Pseudomonas spp, Clostridium spp, and Escherichia spp.

5 In any of the above compositions, host fitness may be measured by survival, reproduction, or metabolism of the host. In some embodiments, the modulating agent modulates the host's fitness by decreasing pesticidal susceptibility of the host (e.g., susceptibility to a pesticide listed in Table 12). In some embodiments, the pesticidal susceptibility is bactericidal or fungicidal susceptibility. In some embodiments, the pesticidal susceptibility is insecticidal susceptibility.

10 In any of the above compositions, the composition may include a plurality of different modulating agents. In some embodiments, the composition includes a modulating agent and a pesticidal agent (e.g., a pesticide listed in Table 12). In some embodiments, the pesticidal agent is a bactericidal or fungicidal agent. In some embodiments, the pesticidal agent is an insecticidal agent.

15 In any of the above compositions, modulating agent may be linked to a second moiety. In some embodiments, the second moiety is a modulating agent.

In any of the above compositions, the modulating agent may be linked to a targeting domain. In some embodiments, the targeting domain targets the modulating agent to a target site in the host. In some embodiments, the targeting domain targets the modulating agent to the one or more microorganisms resident in the host.

20 In any of the above compositions, the modulating agent may include an inactivating pre- or pro-sequence, thereby forming a precursor modulating agent. In some embodiments, the precursor modulating agent is converted to an active form in the host.

In any of the above compositions, the modulating agent may include a linker. In some embodiments, the linker is a cleavable linker.

25 In any of the above compositions, the composition may further include a carrier. In some instances, the carrier may be an agriculturally acceptable carrier.

In any of the above compositions, the composition may further include a host bait, a sticky agent, or a combination thereof. In some embodiments, the host bait is a comestible agent and/or a chemoattractant.

30 In any of the above compositions, the composition may be at a dose effective to modulate host fitness.

In any of the above embodiments, the modulating agent of the composition may be effective to increase production of a nutrient in the host relative to a reference level. In some embodiments, the modulating agent is a microorganism that produces the nutrient. In some embodiments, the microorganism is a bacterium. In some embodiments, the nutrient is a vitamin, a carbohydrate, an amino acid, or a polypeptide. In certain embodiments, the amino acid is methionine.

In any of the above compositions, the composition may be formulated for delivery to a microorganism inhabiting the gut of the host.

40 In any of the above compositions, the composition may be formulated for delivery to a microorganism inhabiting a bacteriocyte of the host and/or the gut of the host. In some embodiments, the

composition may be formulated for delivery to a plant. In some embodiments, the composition may be formulated for use in a host feeding station.

In any of the above compositions, the composition may be formulated as a liquid, a powder, granules, or nanoparticles. In some embodiments, the composition is formulated as one selected from the group consisting of a liposome, polymer, bacteria secreting peptide, and synthetic nanocapsule. In some embodiments, the synthetic nanocapsule delivers the composition to a target site in the host. In some embodiments, the target site is the gut of the host. In some embodiments, the target site is a bacteriocyte in the host.

In a further aspect, also provided herein are hosts that include any of the above compositions. In some embodiments, the host is an insect. In some embodiments, the insect is a species belonging to the order *Anoplura*, *Araneae*, *Blattodea*, *Coleoptera*, *Dermaptera*, *Dictyoptera*, *Diplura*, *Diptera*, *Embioptera*, *Ephemeroptera*, *Grylloblatodea*, *Hemiptera*, *Homoptera*, *Hymenoptera*, *Isoptera*, *Lepidoptera*, *Mantodea*, *Mecoptera*, *Neuroptera*, *Odonata*, *Orthoptera*, *Phasmida*, *Plecoptera*, *Protura*, *Psocoptera*, *Siphonaptera*, *Siphunculata*, *Thysanura*, *Strepsiptera*, *Thysanoptera*, *Trichoptera*, or *Zoraptera*. In certain embodiments, the insect is a cricket. In certain embodiments, the insect is a grasshopper. In certain embodiments, the insect is a locust.

In yet a further aspect, also provided herein is a system for modulating a host's fitness comprising a modulating agent that targets a microorganism that is required for a host's fitness, wherein the system is effective to modulate the host's fitness, and wherein the host is an insect. The modulating agent may include any of the compositions described herein. In some embodiments, the modulating agent is formulated as a powder. In some embodiments, the modulating agent is formulated as a solvent. In some embodiments, the modulating agent is formulated as a concentrate. In some embodiments, the modulating agent is formulated as a diluent. In some embodiments, the modulating agent is prepared for delivery by combining any of the previous compositions with a carrier.

In another aspect, also provided herein are methods for modulating the fitness of an insect using any of the compositions described herein. In one instance, the method of modulating the fitness of an insect host includes delivering the composition of any one of the previous claims to the host, wherein the modulating agent targets the one or more microorganisms resident in the host, and thereby modulates the host's fitness. In another instance, the method of modulating microbial diversity in an insect host includes delivering the composition of any one of the previous claims to the host, wherein the modulating agent targets the one or more microorganisms resident in the host, and thereby modulates microbial diversity in the host.

In some embodiments of any of the above methods, the modulating agent may alter the levels of the one or more microorganisms resident in the host. In some embodiments of any of the above methods, the modulating agent may alter the function of the one or more microorganisms resident in the host. In some embodiments, the one or more microorganisms may be a bacterium and/or fungus. In some embodiments, the one or more microorganisms are required for host fitness. In some embodiments, the one or more microorganisms are required for host survival.

In some embodiments of any of the above methods, the delivering step may include providing the modulating agent at a dose and time sufficient to effect the one or more microorganisms, thereby

modulating microbial diversity in the host. In some embodiments, the delivering step includes topical application of any of the previous compositions to a plant. In some embodiments, the delivering step includes providing the modulating agent through a genetically engineered plant. In some embodiments, the delivering step includes providing the modulating agent to the host as a comestible. In some
 5 embodiments, the delivering step includes providing a host carrying the modulating agent. In some
 10 embodiments the host carrying the modulating agent can transmit the modulating agent to one or more additional hosts.

 In some embodiments of any of the above methods, the composition is effective to increase health and/or survival of the host. In some embodiments, the composition is effective to increase host
 10 fitness, increase host lifespan, increase effective pollination, increase generation of a host product, increase host reproduction, or a combination thereof. In some embodiments, the composition is effective to decrease the host's sensitivity to a pesticidal agent (e.g., a pesticide listed in Table 12). In some
 15 embodiments, the pesticidal agent is a neonicotinoid. In some embodiments, the composition is effective to increase the host's resistance to an allelochemical agent produced by a plant. In some embodiments,
 20 the allelochemical agent is toxic to the host prior to delivery of the composition. In some embodiments, the allelochemical agent is caffeine, soyacystatin N, monoterpenes, diterpene acids, or phenolic compounds. In some embodiments, the composition is effective to increase nutrient production in the
 25 host, thereby increasing the nutrient content in the product derived from the host. In some embodiments, the nutrient is a vitamin, a carbohydrate, an amino acid, or a polypeptide.

 In some embodiments of any of the above methods, at least one part of the host may be used in the manufacture of a consumable product. In some embodiments of any of the above methods, the host
 30 is an insect. In some embodiments, the insect is a species belonging to the order *Anoplura*, *Araneae*, *Blattodea*, *Coleoptera*, *Dermaptera*, *Dictyoptera*, *Diplura*, *Diptera*, *Embioptera*, *Ephemeroptera*, *Grylloblatodea*, *Hemiptera*, *Homoptera*, *Hymenoptera*, *Isoptera*, *Lepidoptera*, *Mantodea*, *Mecoptera*,
 35 *Neuroptera*, *Odonata*, *Orthoptera*, *Phasmida*, *Plecoptera*, *Protura*, *Psocoptera*, *Siphonaptera*, *Siphunculata*, *Thysanura*, *Strepsiptera*, *Thysanoptera*, *Trichoptera*, or *Zoraptera*. In certain
 40 embodiments, the insect is a cricket. In certain embodiments, the insect is a grasshopper. In certain
 45 embodiments, the insect is a locust. In some embodiments, the product includes a food product for humans. In some embodiments, the product includes a nutritional supplement that supplements an
 50 animal feed or human food product. In some embodiments, the product includes feed for animals. In
 55 some embodiments, the animals are livestock or farm animals.

 In another aspect, provided herein is a method of making a human or animal food product, includes (a) providing a plurality (e.g., 2, >2, >5, >10, >100, >1000, >5,000, >10,000, > 50,000, >100,000)
 60 of host insects, (b) delivering an ingestible composition described herein to the plurality of host insects, in
 65 an amount effective to modulate one or more microorganisms resident in the plurality, and (c) processing
 70 the plurality (e.g., grinding, optionally admixing with a carrier or another food component) into a food, food additive or food supplement. In some embodiments, the ingestible composition comprises a
 75 microorganism. In some embodiments, the microorganism produces a nutrient, and the microorganism is
 80 effective to increase nutrient production in the host relative to a reference level. In some embodiments,

the microorganism is a bacterium. In some embodiments, the nutrient is a vitamin, a carbohydrate, an amino acid, or a polypeptide. In some embodiments, the amino acid is methionine.

In some embodiments of any of the above methods, the delivering step includes delivering any of the previous compositions to a plant. In some embodiments, the plant is an agricultural crop. In some
 5 embodiments, the crop is an unharvested crop at the time of delivery. In some embodiments, the crop is a harvested crop at the time of delivery. The some embodiments, the crop comprises harvested fruits or vegetables. In some embodiments, the composition is delivered in an amount and for a duration effective to increase growth of the crop. In some embodiments, the crop includes corn, soybean, or wheat plants.

In another aspect, also provided herein are screening assays to identify modulating agent that
 10 modulate the fitness of a host. In one instance, the screening assay to identify a modulating agent that modulates the fitness of a host, includes the steps of (a) exposing a microorganism that can be resident in the host to one or more candidate modulating agents and (b) identifying a modulating agent that increases or decreases the fitness of the host.

In some embodiments of the screening assay, the modulating agent is a microorganism resident
 15 in the host. In some embodiments, the microorganism is a bacterium. In some embodiments, the bacterium, when resident in the host, increases host fitness. In some embodiments, the bacterium degrades a pesticide (e.g., a pesticide listed in Table 12). In some embodiments, the pesticide is a neonicotinoid. In some embodiments, the bacterium secretes an amino acid. In some embodiments, wherein the amino acid is methionine.

In some embodiments of the screening assay, the modulating agent affects an allelochemical-degrading microorganism. In some embodiments, the modulating agent is a phage, an antibiotic, or a
 20 test compound. In some embodiments, the antibiotic is timentin or azithromycin.

In some embodiments of the screening assay, the host may be an invertebrate. In some
 25 embodiments, the invertebrate is an insect. In some embodiments, the insect is a cricket. In certain embodiments, the insect is a grasshopper. In certain embodiments, the insect is a locust.

In any of the above embodiments of the screening assay, host fitness may be modulated by modulating the host microbiota.

Definitions

As used herein, the term "bacteriocin" refers to a peptide or polypeptide that possesses anti-
 30 microbial properties. Naturally occurring bacteriocins are produced by certain prokaryotes and act against organisms related to the producer strain, but not against the producer strain itself. Bacteriocins contemplated herein include, but are not limited to, naturally occurring bacteriocins, such as bacteriocins produced by bacteria, and derivatives thereof, such as engineered bacteriocins, recombinantly expressed
 35 bacteriocins, and chemically synthesized bacteriocins. In some instances, the bacteriocin is a functionally active variant of the bacteriocins described herein. In some instances, the variant of the bacteriocin has at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a bacteriocin described herein or a
 40 naturally occurring bacteriocin.

As used herein, the term “bacteriocyte” refers to a specialized cell found in certain insects where intracellular bacteria reside with symbiotic bacterial properties.

As used herein, the term “effective amount” refers to an amount of a modulating agent (e.g., a phage, lysin, bacteriocin, small molecule, or antibiotic) or composition including said agent sufficient to effect the recited result, e.g., to increase or promote the fitness of a host organism (e.g., insect); to reach a target level (e.g., a predetermined or threshold level) of a modulating agent concentration inside a target host; to reach a target level (e.g., a predetermined or threshold level) of a modulating agent concentration inside a target host gut; to reach a target level (e.g., a predetermined or threshold level) of a modulating agent concentration inside a target host bacteriocyte; to modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host.

As used herein, the term “fitness” refers to the ability of a host organism to survive, and/or to produce surviving offspring. Fitness of an organism may be measured by one or more parameters, including, but not limited to, life span, nutrient production, reproductive rate, mobility, body weight, and metabolic rate. Fitness may additionally be measured based on measures of activity or product output.

As used herein, the term “gut” refers to any portion of a host’s gut, including, the foregut, midgut, or hindgut of the host.

As used herein, the term “host” refers to an organism (e.g., insect) carrying resident microorganisms (e.g., endogenous microorganisms, endosymbiotic microorganisms (e.g., primary or secondary endosymbionts), commensal organisms, and/or pathogenic microorganisms).

As used herein “increasing host fitness” or “promoting host fitness” refers to any favorable alteration in host physiology, or any activity carried out by said host, as a consequence of administration of a modulating agent, including, but not limited to, any one or more of the following desired effects: (1) increasing a population of a host by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (2) increasing the reproductive rate of a host (e.g., insect) by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (3) increasing the mobility of a host (e.g., insect) by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (4) increasing the body weight of a host (e.g., insect) by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (5) increasing the metabolic rate or activity of a host (e.g., insect) by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (6) increasing production of host byproducts by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; (7) increasing nutrient content of the host (e.g., insect) (e.g., protein, fatty acids, or amino acids) by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more; or (8) increasing host resistance to pesticides by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or more. An increase in host fitness can be determined in comparison to a host organism to which the modulating agent has not been administered.

The term “insect” includes any organism belonging to the phylum *Arthropoda* and to the class *Insecta* or the class *Arachnida*, in any stage of development, i.e., immature and adult insects.

As used herein, “lysin” also known as endolysin, autolysin, murein hydrolase, peptidoglycan hydrolase, or cell wall hydrolase refers to a hydrolytic enzyme that can lyse a bacterium by cleaving peptidoglycan in the cell wall of the bacterium. Lysins contemplated herein include, but are not limited to,

naturally occurring lysins, such as lysins produced by phages, lysins produced by bacteria, and derivatives thereof, such as engineered lysins, recombinantly expressed lysins, and chemically synthesized lysins. A functionally active variant of the bacteriocin may have at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 5 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a synthetic, recombinant, or naturally derived bacteriocin, including any described herein.

As used herein, the term “microorganism” refers to bacteria or fungi. Microorganisms may refer to microorganisms resident in a host organism (e.g., endogenous microorganisms, endosymbiotic 10 microorganisms (e.g., primary or secondary endosymbionts)) or microorganisms exogenous to the host, including those that may act as modulating agents. As used herein, the term “target microorganism” refers to a microorganism that is resident in the host and impacted by a modulating agent, either directly or indirectly.

As used herein, the term “modulating agent” or “agent” refers to an agent that is capable of 15 altering the levels and/or functioning of microorganisms resident in a host organism (e.g., insect), and thereby modulate (e.g., increase) the fitness of the host organism (e.g., insect).

As used herein, “increasing a nutritional profile of an insect” refers to increased production of a nutrient that may increase protein content, body mass, and/or overall nutritional value of the insect.

As used herein, the term “pesticide” or “pesticidal agent” refers to a substance that can be used 20 in the control of agricultural, environmental, or domestic/household pests, such as insects, fungi, bacteria, or viruses. The term “pesticide” is understood to encompass naturally occurring or synthetic insecticides (larvicides or adulticides), insect growth regulators, acaricides (miticides), nematocides, ectoparasiticides, bactericides, fungicides, or herbicides (substance which can be used in agriculture to control or modify plant growth). Further examples of pesticides or pesticidal agents are listed in Table 12. In some 25 instances, the pesticide is an allelochemical. As used herein, “allelochemical” or “allelochemical agent” is a substance produced by an organism that can effect a physiological function (e.g., the germination, growth, survival, or reproduction) of another organism (e.g., a host insect).

As used herein, the term “peptide,” “protein,” or “polypeptide” encompasses any chain of naturally or non-naturally occurring amino acids (either D- or L-amino acids), regardless of length (e.g., at least 2, 30 3, 4, 5, 6, 7, 10, 12, 14, 16, 18, 20, 25, 30, 40, 50, 100, or more amino acids), the presence or absence of post-translational modifications (e.g., glycosylation or phosphorylation), or the presence of, e.g., one or more non-amino acyl groups (for example, sugar, lipid, etc.) covalently linked to the peptide, and includes, for example, natural proteins, synthetic, or recombinant polypeptides and peptides, hybrid molecules, peptoids, or peptidomimetics.

As used herein, “percent identity” between two sequences is determined by the BLAST 2.0 35 algorithm, which is described in Altschul et al., (1990) J. Mol. Biol. 215:403-410. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information.

As used herein, the term “bacteriophage” or “phage” refers to a virus that infects and replicates in bacteria. Bacteriophages replicate within bacteria following the injection of their genome into the 40 cytoplasm and do so using either a lytic cycle, which results in bacterial cell lysis, or a lysogenic (non-

lytic) cycle, which leaves the bacterial cell intact. The phage may be a naturally occurring phage isolate, or an engineered phage, including vectors, or nucleic acids that encode either a partial phage genome (e.g., including at least all essential genes necessary to carry out the life cycle of the phage inside a host bacterium) or the full phage genome.

5 As used herein, the term "plant" refers to whole plants, plant organs, plant tissues, seeds, plant cells, seeds, or progeny of the same. Plant cells include, without limitation, cells from seeds, suspension cultures, embryos, meristematic regions, callus tissue, leaves, roots, shoots, gametophytes, sporophytes, pollen, or microspores. Plant parts include differentiated or undifferentiated tissues including, but not limited to the following: roots, stems, shoots, leaves, pollen, seeds, tumor tissue, and various forms of
10 cells and culture (e.g., single cells, protoplasts, embryos, or callus tissue). The plant tissue may be in a plant or in a plant organ, tissue, or cell culture. In addition, a plant may be genetically engineered to produce a heterologous protein or RNA, for example, of any of the modulating agents in the methods or compositions described herein.

The terms "obtainable by", "producible by" or the like are used to indicate that a claim or
15 embodiment refers to compound, composition, product, etc. per se, i.e. that the compound, composition, product, etc. can be obtained or produced by a method which is described for manufacture of the compound, composition, product, etc., but that the compound, composition, product, etc. may be obtained or produced by other methods than the described one as well. The terms "obtained by," "produced by," or the like indicate that the compound, composition, product, is obtained or produced by a recited specific
20 method. It is to be understood that the terms "obtainable by," "producible by" and the like also disclose the terms "obtained by", "produced by" and the like as a preferred embodiment of "obtainable by", "producible by" and the like.

Other features and advantages of the invention will be apparent from the following Detailed Description and the Claims.

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BRIEF DESCRIPTION OF THE FIGURES

The figures are meant to be illustrative of one or more features, aspects, or embodiments of the invention and are not intended to be limiting.

Fig. 1 is a graph showing the time to reach adulthood from embryos in *Drosophila melanogaster*.
30 Embryos of *Drosophila melanogaster* were either raised on diet seeded with *Corynebacterium glutamicum* (a strain that produces glutamate – *C. glutamicum* Glu) or on axenic diet without any bacteria. The percentage of adults emerging from their pupa was measured every 12 hours from the time of the emergence of the first adult. The organisms raised on bacteria supplemented diet reach adulthood faster than their bacteria free counterparts.

35 Fig. 2A is a graph showing the effects of male gender on the developmental rate differences in *Drosophila melanogaster*. The adults emerging from Fig. 1 were sexed and their rate of emergence was plotted.

Fig. 2B is a graph showing the effects of female gender on the developmental rate differences in *Drosophila melanogaster*. The adults emerging from Fig. 1 were sexed and their rate of emergence was
40 plotted. The enhancement in the rate of development in the females due to the presence of bacteria in

the diet is significantly more than in their male counterparts. The benefits of the presence of bacteria in the fly diet are higher in the females compared to the males.

Fig. 3 is a graph showing *C. glutamicum* strains promoted larval biomass. Larvae raised on diet supplemented with *C. glutamicum* strains either producing glutamate or methionine are bigger than those raised on sterile diet or diet supplemented with *Escherichia coli*. The areas of the larvae are measured as the number of pixels in the images of the larvae. The medians and the 95% confidence intervals are shown as lines on the graph.

Fig. 4 is a panel of graphs showing the results of a Seahorse flux assay for bacterial respiration. Bacteria were grown to logarithmic phase and loaded into Seahorse XFe96 plates for temporal measurements of oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) as described in methods. Treatments were injected into the wells after approximately 20 minutes and bacteria were monitored to detect changes in growth. Rifampicin = 100 µg/mL; Chloramphenicol = 25 µg/mL; Phages (T7 for *E. coli* and ΦSmVL-C1 for *Serratia marcescens*) were lysates diluted either 1:2 or 1:100 in SM Buffer. The markers on each line are solely provided as indicators of the condition to which each line corresponds, and are not indicative of data points

Fig. 5 is a graph showing phage against *S. marcescens* reduced fly mortality. Flies that were pricked with *S. marcescens* were all dead within a day, whereas a sizeable portion of the flies that were pricked with both *S. marcescens* and the phage survived for five days after the treatment. Almost all of the control flies which were not treated in anyway survived till the end of the experiment. Log-rank test was used to compare the curves for statistical significance, asterisk denotes $p < 0.0001$.

DETAILED DESCRIPTION

Provided herein are methods and compositions for food and feed applications, e.g., for altering a level, activity, or metabolism of one or more microorganisms resident in a host insect, the alteration resulting in an increase in the fitness of the host. The invention features a composition that includes a modulating agent (e.g., phage, peptide, small molecule, antibiotic, or combinations thereof) that can alter the host's microbiota in a manner that is beneficial to the host. By promoting favorable microbial levels, microbial activity, microbial metabolism, and/or microbial diversity, the modulating agent described herein may be used to increase the fitness of a variety of insects utilized in human food and animal feed industries.

The methods and compositions described herein are based, in part, on the examples which illustrate how different agents, for example methionine-producing microorganisms, can be used in insect hosts such as a cricket, a fly, a grasshopper, or a locust, to indirectly improve the health (e.g., increase methionine content, body mass, development rate, and/or survival) of these hosts by altering the level, activity or metabolism of microorganisms within these hosts. Methionine-producing microorganisms are a representative example of amino acid-producing microorganisms and more generally are representative of nutrient-producing microorganisms, and other microorganisms of this type may be useful in the invention. On this basis, the present disclosure describes a variety of different approaches for the use of agents that alter a level, activity, or metabolism of one or more microorganisms resident in a host, the alteration resulting in a modulation in the host's fitness.

I. Hosts

i. Insects

The host of any of the compositions or methods described herein may be any organism
 5 belonging to the phylum *Arthropoda* (e.g., insects), including any arthropods described herein. In some instances, the host may be an insect or an arachnid that may be cultivated for a consumable product (e.g., food or feed). For example, the host may be a moth, butterfly, fly, cricket, grasshopper, locust, spider, or beetle. In some instances, the host is in the order *Anoplura*, *Araneae*, *Blattodea*, *Coleoptera*, *Dermaptera*, *Dictyoptera*, *Diplura*, *Diptera*, *Embioptera*, *Ephemeroptera*, *Grylloblatodea*, *Hemiptera*,
 10 *Homoptera*, *Hymenoptera*, *Isoptera*, *Lepidoptera*, *Mantodea*, *Mecoptera*, *Neuroptera*, *Odonata*, *Orthoptera*, *Phasmida*, *Plecoptera*, *Protura*, *Psocoptera*, *Siphonaptera*, *Siphunculata*, *Thysanura*, *Strepsiptera*, *Thysanoptera*, *Trichoptera*, or *Zoraptera*.

In some examples, the host is a black soldier fly (*Hermetia illucens*), a common house fly, a lesser mealworm, a weaver ant, a silkworm (*Bombyx mori*), a grasshopper, a Chinese grasshopper
 15 (*Acrida cinerea*), a yellow mealworm (*Clarias gariepinns*), a moth (*Anaphe infracta* or *Bombyx mori*), *Spodoptera littoralis*, a house cricket, a termite, a palm weevil (*Rhynchophorus ferrugineus*), a giant water bug (*Lethocerus indicus*), a water beetle, a termite (*Macrotermes subhyalinus*), a drugstore beetle (*Stegobium paniceum*), *Imbrasia belina*, *Rhynchophorus phoenicis*, *Oryctes rhinoceros*, *Macrotermes bellicosus*, *Ruspolia differens*, *Oryctes Monoceros*, or *Oecophylla smaragdina*.

20 In particular instances, the modulating agents disclosed herein may be used to increase the fitness of crickets, grasshoppers, or locusts.

The host may be at any stage developmentally. For instance, the host may be an embryo, a larva, a pupa, or an adult.

25 ii. Host Fitness

The methods and compositions provided herein may be used to increase the fitness of any of the hosts described herein. The increase in fitness may arise from any alterations in microorganisms resident in the host, wherein the alterations are a consequence of administration of a modulating agent and have beneficial or advantageous effects on the host.

30 In some instances, the increase in host fitness may manifest as an improvement in the physiology of the host (e.g., improved health or survival) as a consequence of administration of a modulating agent. In some instances, the fitness of an organism may be measured by one or more parameters, including, but not limited to, reproductive rate, lifespan, mobility, fecundity, body weight, metabolic rate or activity, or survival in comparison to a host organism to which the modulating agent has
 35 not been administered. For example, the methods or compositions provided herein may be effective to improve the overall health of the host or to improve the overall survival of the host in comparison to a host organism to which the modulating agent has not been administered. In some instances, the improved survival of the host is about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% greater relative to a reference level (e.g., a level found in a host that does not receive
 40 a modulating agent). In some instances, the methods and compositions are effective to increase host

reproduction (e.g., reproductive rate) in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods and compositions are effective to increase other physiological parameters, such as mobility, body weight, life span, fecundity, or metabolic rate, by about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% relative to a reference level (e.g., a level found in a host that does not receive a modulating agent).

In some instances, the increase in host fitness may manifest as an increase in the production of one or more nutrients in the host (e.g., vitamins, carbohydrates, amino acids, or polypeptides) in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may be effective to increase the production of nutrients in the host (e.g., vitamins, carbohydrates, amino acids, or polypeptides) by about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% relative to a reference level (e.g., a level found in a host that does not receive a modulating agent). In some instances, the methods or compositions provided herein may increase nutrients in the host by increasing the production of nutrients by one or more microorganisms (e.g., endosymbiont) in the host in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the increase in host fitness may manifest as a decrease in the host's sensitivity to a pesticidal agent (e.g., a pesticide listed in Table 12) and/or an increase in the host's resistance to a pesticidal agent (e.g., a pesticide listed in Table 12) in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may be effective to decrease the host's sensitivity to a pesticidal agent by about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% relative to a reference level (e.g., a level found in a host that does not receive a modulating agent). The pesticidal agent may be any pesticidal agent known in the art, including insecticidal agents. In some instances, the pesticidal agent is a neonicotinoid. In some instances, the methods or compositions provided herein may decrease the host's sensitivity to a pesticidal agent (e.g., a pesticide listed in Table 12) by increasing the host's ability to metabolize or degrade the pesticidal agent into usable substrates in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the increase in host fitness may manifest as a decrease in the host's sensitivity to an allelochemical agent and/or an increase in the host's resistance to an allelochemical agent in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may be effective to increase the host's resistance to an allelochemical agent by about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% relative to a reference level (e.g., a level found in a host that does not receive a modulating agent). In some instances, the allelochemical agent is caffeine, soyacystatin N, monoterpenes, diterpene acids, or phenolic compounds in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may decrease the host's sensitivity to an allelochemical agent by increasing the host's ability to metabolize or degrade the allelochemical agent into usable substrates in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the methods or compositions provided herein may be effective to increase the host's resistance to parasites or pathogens (e.g., fungal, bacterial, or viral pathogens; or parasitic mites) in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may be effective to increase the host's resistance to a pathogen or parasite (e.g., fungal, bacterial, or viral pathogens; or parasitic mites) by about 2%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or greater than 100% relative to a reference level (e.g., a level found in a host that does not receive a modulating agent).

In some instances, the increase in host fitness may manifest as other fitness advantages, such as improved tolerance to certain environmental factors (e.g., a high or low temperature tolerance), improved ability to survive in certain habitats, or an improved ability to sustain a certain diet (e.g., an improved ability to metabolize soy vs corn) in comparison to a host organism to which the modulating agent has not been administered. In some instances, the methods or compositions provided herein may be effective to increase host fitness in any plurality of ways described herein. Further, the modulating agent may increase host fitness in any number of host classes, orders, families, genera, or species (e.g., 1 host species, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 500, or more host species). In some instances, the modulating agent acts on a single host class, order, family, genus, or species.

Host fitness may be evaluated using any standard methods in the art. In some instances, host fitness may be evaluated by assessing an individual host. Alternatively, host fitness may be evaluated by assessing a host population. For example, an increase in host fitness may manifest as an increase in successful competition against other insects, thereby leading to an increase in the size of the host population.

iii. Host insects in feed/food production

Upon reaching a desired life stage, the host may be harvested and, if desired, processed for use in the manufacture of a consumable product. In some instances, the harvested insect may be distributed in a whole form (e.g., as the whole, unprocessed insect) as a consumable product. In some instances, the whole harvested insect is processed (e.g., ground up) and distributed as a consumable product. Alternatively, one or more parts of the insect (e.g., one or more body parts or one or more substances) may be extracted from the insect for use in the manufacture of a consumable product.

The consumable product may be any product safe for human or animal consumption (e.g., ingestion). In some instances, the host may be used in the manufacture of a feed for an animal. In some instances, the animal is livestock or a farm animal (e.g., chicken, cow, horse, or pig). In some instances, the animal is a bird, reptile, amphibian, mammal, or fish. In some instances, the host may be used in the manufacture of a product that replaces the normal feed of an animal. Alternatively, the host may be used in the manufacture of a product that supplements the normal feed of an animal. The host may also be used in the manufacture of a food, food additive, or food ingredient for humans. In some instances, the host is used in the manufacture of a nutritional supplement (e.g., protein supplement) for humans.

The host may be a wild or domesticated insect. Additionally, the host may be at any developmental stage at the time of delivering or applying the compositions described herein. Further, the

host may be at any developmental stage at the time of harvesting the host for use in the manufacture of a consumable product. In some instances, the host is a larva, pupa, or adult insect at the time of harvesting, using, processing, or manufacturing. The delivery of the modulating agent and the harvesting steps may occur at the same time or different times.

5 In some instances, an insect species is selected based upon their natural nutritional profile. In some instances, the modulating agent is used to improve the nutritional profile of the insect, wherein the modulating agent leads to an increased production of a nutrient in comparison to a host organism to which the modulating agent has not been administered. Examples of nutrients include vitamins, carbohydrates, amino acids, polypeptides, or fatty acids. In some instances, the increased production
10 may arise from increased production of a nutrient by a microorganism resident in the host. Alternatively, the increased production may arise from increased production of a nutrient by the host insect itself, wherein the host has increased fitness following delivery or administration of a modulating agent.

In some instances, in final processing, a first insect species is combined with a second insect species whose nutritional profile provides a complementary benefit to the overall nutritional value of the food or feed product. For example, a species containing a high protein profile could be combined with a species containing a high omega 3/6 fatty acid profile. In this manner, insect protein meal may be custom
15 blended to suit the needs of humans or different species of animals.

II. Target Microorganisms

20 The microorganisms targeted by the modulating agent described herein may include any microorganism resident in or on the host, including, but not limited to, any bacteria and/or fungi described herein. Microorganisms resident in the host may include, for example, symbiotic (e.g., endosymbiotic microorganisms that provide beneficial nutrients or enzymes to the host), commensal, pathogenic, or parasitic microorganisms. A symbiotic microorganism (e.g., bacteria or fungi) may be an obligate
25 symbiont of the host or a facultative symbiont of the host. Microorganisms resident in the host may be acquired by any mode of transmission, including vertical, horizontal, or multiple origins of transmission.

i. Bacteria

Exemplary bacteria that may be targeted in accordance with the methods and compositions
30 provided herein, include, but are not limited to, *Xenorhabdus spp*, *Photorhabdus spp*, *Candidatus spp*, *Buchnera spp*, *Blattabacterium spp*, *Baumania spp*, *Wigglesworthia spp*, *Wolbachia spp*, *Rickettsia spp*, *Orientia spp*, *Sodalis spp*, *Burkholderia spp*, *Cupriavidus spp*, *Frankia spp*, *Snirrhizobium spp*, *Streptococcus spp*, *Wolinella spp*, *Xylella spp*, *Erwinia spp*, *Agrobacterium spp*, *Bacillus spp*, *Paenibacillus spp*, *Streptomyces spp*, *Micrococcus spp*, *Corynebacterium spp*, *Acetobacter spp*,
35 *Cyanobacteria spp*, *Salmonella spp*, *Rhodococcus spp*, *Pseudomonas spp*, *Lactobacillus spp*, *Enterococcus spp*, *Alcaligenes spp*, *Klebsiella spp*, *Paenibacillus spp*, *Arthrobacter spp*, *Corynebacterium spp*, *Brevibacterium spp*, *Thermus spp*, *Pseudomonas spp*, *Clostridium spp*, and *Escherichia spp*. Non-limiting examples of bacteria that may be targeted by the methods and compositions provided herein are shown in Table 1.

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Table 1: Examples of Target Bacteria and Host Insects

Primary endosymbiont	Host	Location	16S rRNA
Gamma proteobacteria			
<i>Carsonella ruddii</i>	Psyllids (Psylloidea)	bacteriocytes	TATCCAGCCACAGGTTCCCCTA CAGCTACCTTGTTACGACTTCA CCCCAGTTACAAATCATACCGTT GTAATAGTAAAATTACTTATGAT ACAATTTACTTCCATGGTGTGAC GGGCGGTGTGTACAAGGCTCG AGAACGTATTCACCGTAACATTC TGATTTACGATTACTAGCGATTTC CAACTTCATGAAATCGAGTTACA GATTTCAATCCGAACATAAGAATA TTTTTAAAGATTAGCATTATGTT GCCATATAGCATATAACTTTTTG TAATACTCATTGTAGCACGTGTG TAGCCCTACTTATAAGGGCCAT GATGACTTGACGTCGTCCTCAC CTTCCTCCAATTTATCATTGGCA GTTTCTTATTAGTTCTAATATATT TTTAGTAAAATAAGATAAGGGTT GCGCTCGTTATAGGACTTAACC CAACATTTCACAACACGAGCTG ACGACAGCCATGCAGCACCTGT CTCAAAGCTAAAAAAGCTTTATT ATTTCTAATAAATTCTTTGGATG TCAAAAGTAGGTAAGATTTTTCG TGTTGTATCGAATTAAACCACAT GCTCCACCGCTTGTGCGAGCCC CCGTCAATTCATTTGAGTTTTAA CCTTGCGGTCGTAATCCCCAGG CGGTCAACTTAACGCGTTAGCT TTTTCACTAAAAATATATACTTT TTTTCATAAACAAAATTACAATT ATAATATTTAATAAATAGTTGAC ATCGTTTACTGCATGGACTACC AGGGTATCTAATCCTGTTTGCTC CCCATGCTTTTCGTGTATTAGTGT CAGTATTAATAAGAAATACGCC TTCGCCACTAGTATTCTTTCAGA

			TATCTAAGCATTTCCTGCTACT CCTGAAATTCTAATTTCTTCTTTT ATACTCAAGTTTATAAGTATTAA TTTCAATATTAAATTACTTTAATA AATTTAAAAATTAATTTTTAAAAA CAACCTGCACACCCTTTACGCC CAATAATTCCGATTAACGCTTGC ACCCCTCGTATTACCGCGGCTG CTGGCACGAAGTTAGCCGGTGC TTCTTTTACAAATAACGTCAAAG ATAATATTTTTTTATTATAAAATC TCTTCTTACTTTGTTGAAAGTGT TTTACAACCCTAAGGCCTTCTTC ACACACGCGATATAGCTGGATC AAGCTTTGCTCATTGTCCAATA TCCCCCACTGCTGCCTTCGTA AAAGTTTGGGCGTGTCTCAGT CCCAATGTGGTTGTTTCATCCTCT AAGATCAACTACGAATCATAGTC TTGTTAAGCTTTTACTTTAACAA CTAACTAATTCGATATAAGCTCT TCTATTAGCGAACGACATTCTC GTTCTTTATCCATTAGGATACAT ATTGAATTACTATACATTTCTATA TACTTTTCTAATACTAATAGGTA GATTCTTATATATTACTCACCCG TTCGCTGCTAATTATTTTTTTAAT AATTCGCACAACCTGCATGTGTT AAGCTTATCGCTAGCGTTCAAT CTGAGCTATGATCAAACCTCA (SEQ ID NO: 1)
<i>Portiera aleyrodidarum</i> BT-B	whiteflies (Aleyrodoidea)	bacteriocytes	AAGAGTTTGATCATGGCTCAGA TTGAACGCTAGCGGCAGACATA ACACATGCAAGTCGAGCGGCAT CATACAGGTTGGCAAGCGGCG CACGGGTGAGTAATACATGTAA ATATACCTAAAAGTGGGAATA ACGTACGGAAACGTACGCTAAT ACCGCATAATTATTACGAGATAA

			AGCAGGGGCTTGATAAAAAAAAA TCAACCTTGCGCTTTTAGAAAAT TACATGCCGGATTAGCTAGTTG GTAGAGTAAAAGCCTACCAAGG TAACGATCCGTAGCTGGTCTGA GAGGATGATCAGCCACACTGGG ACTGAGAAAAGGCCCAGACTCC TACGGGAGGCAGCAGTGGGGA ATATTGGACAATGGGGGGAACC CTGATCCAGTCATGCCGCGTGT GTGAAGAAGGCCTTTGGGTTGT AAAGCACTTTCAGCGAAGAAGA AAAGTTAGAAAATAAAAAGTTAT AACTATGACGGTACTCGCAGAA GAAGCACCGGCTAACTCCGTGC CAGCAGCCGCGGTAAGACGGA GGGTGCAAGCGTTAATCAGAAT TACTGGGCGTAAAGGGCATGTA GGTGGTTTGTTAAGCTTTATGTG AAAGCCCTATGCTTAACATAGG AACGGAATAAAGAACTGACAAA CTAGAGTGCAGAAGAGGAAGGT AGAATTCCCGGTGTAGCGGTGA AATGCGTAGATATCTGGAGGAA TACCAGTTGCGAAGGCGACCTT CTGGGCTGACACTGACACTGAG ATGCGAAAGCGTGGGGAGCAA ACAGGATTAGATACCCTGGTAG TCCACGCTGTAAACGATATCAA CTAGCCGTTGGATTCTTAAAGA ATTTTGTGGCGTAGCTAACGCG ATAAGTTGATCGCCTGGGGAGT ACGGTCGCAAGGCTAAACTCA AATGAATTGACGGGGGCCCGCA CAAGCGGTGGAGCATGTGGTTT AATTCGATGCAACGCGCAAAAC CTTACCTACTCTTGACATCCAAA GTACTTTCCAGAGATGGAAGGG TGCCTTAGGGAACCTTGAGACA GGTGCTGCATGGCTGTCGTCAG
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			CTCGTGTTGTGAAATGTTGGGT TAAGTCCCGTAACGAGCGCAAC CCTTGTCTTAGTTGCCAACGC ATAAGGCGGGAACCTTAAGGAG ACTGCTGGTGATAAACCGGAGG AAGGTGGGGACGACGTCAAGT CATCATGGCCCTTAAGAGTAGG GCAACACACGTGCTACAATGGC AAAACAAAGGGTCGCAAAATG GTAACATGAAGCTAATCCCAAA AAAATTGTCTTAGTTCGGATTGG AGTCTGAAACTCGACTCCATAA AGTCGGAATCGCTAGTAATCGT GAATCAGAATGTCACGGTGAAT ACGTTCTCGGGCCTTGACACA CCGCCCGTCACACCATGGAAGT GAAATGCACCAGAAGTGGCAAG TTAAACCAAAAAACAGGAGAAC AGTCACTACGGTGTGGTTCATG ACTGGGGTGAAGTCGTAACAAG GTAGCTGTAGGGGAACCTGTGG CTGGATCACCTCCTTAA (SEQ ID NO: 2)
<i>Buchnera aphidicola str. APS (Acyrtosiphon pisum)</i>	Aphids (Aphidoidea)	bacteriocytes	AGAGTTTGATCATGGCTCAGAT TGAACGCTGGCGGCAAGCCTAA CACATGCAAGTCGAGCGGCAG CGAGAAGAGAGCTTGCTCTCTT TGTCGGCAAGCGGCAAACGGG TGAGTAATATCTGGGGATCTAC CCAAAGAGGGGGATAACTACT AGAAATGGTAGCTAATACCGCA TAATGTTGAAAACCAAAGTGG GGGACCTTTTGGCCTCATGCTT TTGGATGAACCCAGACGAGATT AGCTTGTTGGTAGAGTAATAGC CTACCAAGGCAACGATCTCTAG CTGGTCTGAGAGGATAACCAGC CCACTGGAAGTGAACACGGT CCAGACTCCTACGGGAGGCAG CAGTGGGGAATATTGCACAATG

			GGCGAAAGCCTGATGCAGCTAT GCCGCGTGTATGAAGAAGGCCT TAGGGTTGTAAAGTACTTTTCAG CGGGGAGGAAAAAATAAACT AATAATTTTATTTTCGTGACGTTA CCCGCAGAAGAAGCACCGGCT AACTCCGTGCCAGCAGCCGCG GTAATACGGAGGGTGCAAGCGT TAATCAGAATTACTGGGCGTAA AGAGCGCGTAGGTGGTTTTTTA AGTCAGGTGTGAAATCCCTAGG CTCAACCTAGGAAGTGCATTTG AACTGGAAAGTGTAGAGTTTCG TAGAGGGAGGTAGAATTCTAGG TGAGCGGTGAAATGCGTAGAT ATCTGGAGGAATACCCGTGGCG AAAGCGGCCTCCTAAACGAAAA CTGACACTGAGGCGCGAAAGC GTGGGGAGCAAACAGGATTAGA TACCCTGGTAGTCCATGCCGTA AACGATGTGCGACTTGGAGGTTG TTTCCAAGAGAAGTGACTTCCG AAGCTAACGCATTAAGTCGACC GCCTGGGGAGTACGGCCGCAA GGCTAAAGTCAAATGAATTGA CGGGGGCCCGCACAAGCGGTG GAGCATGTGGTTTAATTCGATG CAACGCGAAAAACCTTACCTGG TCTTGACATCCACAGAATTCTTT AGAAATAAAGAAGTGCCTTCGG GAGCTGTGAGACAGGTGCTGCA TGGCTGTGTCAGCTCGTGTTG TGAAATGTTGGGTTAAGTCCCG CAACGAGCGCAACCCTTATCCC CTGTTGCCAGCGGTTCCGGCCG GGAAGTCAAGAGGAGACTGCCG GTTATAAACCGGAGGAAGGTGG GGACGACGTCAAGTCATCATGG CCCTTACGACCAGGGCTACACA CGTGCTACAATGGTTTATACAAA
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			GAGAAGCAAATCTGCAAAGACA AGCAAACCTCATAAAGTAAATC GTAGTCCGGACTGGAGTCTGCA ACTCGACTCCACGAAGTCGGAA TCGCTAGTAATCGTGGATCAGA ATGCCACGGTGAATACGTTCCC GGGCCTTGTACACACCGCCCGT CACACCATGGGAGTGGGTTGCA AAAGAAGCAGGTATCCTAACCC TTTAAAAGGAAGGCGCTTACCA CTTTGTGATTCATGACTGGGGT GAAGTCGTAACAAGGTAACCGT AGGGGAACCTGCGGTTGGATCA CCTCCTT (SEQ ID NO: 3)
<i>Buchnera aphidicola str. Sg (Schizaphis graminum)</i>	Aphids (Aphidoidea)	bacteriocytes	AAACTGAAGAGTTTGATCATGG CTCAGATTGAACGCTGGCGGCA AGCCTAACACATGCAAGTCGAG CGGCAGCGAAAAGAAAGCTTGC TTTCTTGTGCGCGAGCGGCAAA CGGGTGAGTAATATCTGGGGAT CTGCCCCAAAGAGGGGGATAAC TACTAGAAATGGTAGCTAATACC GCATAAAGTTGAAAAACCAAAG TGGGGGACCTTTTTTAAAGGCC TCATGCTTTTGGATGAACCCAG ACGAGATTAGCTTGTGGTAAG GTAAAAGCTTACCAAGGCAACG ATCTCTAGCTGGTCTGAGAGGA TAACCAGCCACACTGGAAGTGA GACACGGTCCAGACTCCTACGG GAGGCAGCAGTGGGGAATATTG CACAATGGGCGAAAGCCTGATG CAGCTATGCCGCGTGTATGAAG AAGGCCTTAGGGTTGTAAAGTA CTTTCAGCGGGGAGGAAAAAT TAAACTAATAATTTTATTTTGTG ACGTTACCCGCAGAAGAAGCAC CGGCTAACTCCGTGCCAGCAGC CGCGGTAATACGGAGGGTGCG

			AGCGTTAATCAGAATTACTGGG CGTAAAGAGCACGTAGGTGGTT TTTTAAGTCAGATGTGAAATCCC TAGGCTTAACCTAGGAACTGCA TTTGAAACTGAAATGCTAGAGTA TCGTAGAGGGAGGTAGAATTCT AGGTGTAGCGGTGAAATGCGTA GATATCTGGAGGAATACCCGTG GCGAAAGCGGCCTCCTAAACGA ATACTGACACTGAGGTGCGAAA GCGTGGGGAGCAAACAGGATTA GATACCCTGGTAGTCCATGCCG TAAACGATGTCGACTTGGAGGT TGTTTCCAAGAGAAGTGAATTCT CGAAGCTAACGCGTTAAGTCGA CCGCCTGGGGAGTACGGCCGC AAGGCTAAAACTCAAATGAATTG ACGGGGGGCCCGCACAAGCGGT GGAGCATGTGGTTTAATTGAT GCAACGCGAAAAACCTTACCTG GTCTTGACATCCACAGAATTTTT TAGAAATAAAAAAGTGCCTTCG GGAAGTGTGAGACAGGTGCTGC ATGGCTGTGTCAGCTCGTGTT GTGAAATGTTGGGTTAAGTCCC GCAACGAGCGCAACCCTTATCC CCTGTTGCCAGCGGTTCCGCC GGGAACTCAGAGGAGACTGCC GGTTATAAACCGGAGGAAGGTG GGGACGACGTCAAGTCATCATG GCCCTTACGACCAGGGCTACAC ACGTGCTACAATGGTTTATACAA AGAGAAGCAAATCTGTAAAGAC AAGCAAACCTCATAAAGTAAATC GTAGTCCGGACTGGAGTCTGCA ACTCGACTCCACGAAGTCGGAA TCGCTAGTAATCGTGGATCAGA ATGCCACGGTGAATACGTTCCC GGGCCTTGTACACACCGCCCGT CACACCATGGGAGTGGGTTGCA
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			AAAGAAGCAGATTTCTAACCA CGAAAGTGGAAGGCGTCTACCA CTTTGTGATTCATGACTGGGGT GAAGTCGTAACAAGGTAACCGT AGGGGAACCTGCGGTTGGATCA CCTCCTTA (SEQ ID NO: 4)
<i>Buchnera aphidicola str.</i> <i>Bp (Baizongia pistaciae)</i>	Aphids (Aphidoidea)	bacteriocytes	ACTTAAAATTGAAGAGTTTGATC ATGGCTCAGATTGAACGCTGGC GGCAAGCTTAACACATGCAAGT CGAGCGGCATCGAAGAAAAGTT TACTTTTCTGGCGGCGAGCGGC AAACGGGTGAGTAACATCTGGG GATCTACCTAAAAGAGGGGGAC AACCATTGGAAACGATGGCTAA TACCGCATAATGTTTTTAAATAA ACCAAAGTAGGGGACTAAAATT TTAGCCTTATGCTTTTAGATGA ACCCAGACGAGATTAGCTTGAT GGTAAGGTAATGGCTTACCAAG GCGACGATCTCTAGCTGGTCTG AGAGGATAACCAGCCACACTGG AACTGAGATACGGTCCAGACTC CTACGGGAGGCAGCAGTGGGG AATATTGCACAATGGGCTAAAG CCTGATGCAGCTATGCCGCGTG TATGAAGAAGGCCTTAGGGTTG TAAAGTACTTTAGCGGGGAGG AAAGAATTATGTCTAATATACAT ATTTTGTGACGTTACCCGAAGA AGAAGCACCGGCTAACTCCGTG CCAGCAGCCGCGGTAATACGG AGGGTGCGAGCGTTAATCAGAA TACTGGGCGTAAAGAGCACGT AGGCGGTTTATTAAGTCAGATG TGAAATCCCTAGGCTTAACCTAG GAACTGCATTTGAACTAATAGA CTAGAGTCTCATAGAGGGAGGT AGAATTCTAGGTGTAGCGGTGA AATGCGTAGATATCTAGAGGAA

		TACCCGTGGCGAAAGCGACCTC CTAAATGAAACTGACGCTGAG GTGCGAAAGCGTGGGGAGCAA ACAGGATTAGATACCCTGGTAG TCCATGCTGTAAACGATGTGGA CTTGGAGGTTGTTTCCTAGAGA AGTGGCTTCCGAAGCTAACGCA TTAAGTCGACCGCCTGGGGAGT ACGGTCGCAAGGCTAAACTCA AATGAATTGACGGGGGCCCGCA CAAGCGGTGGAGCATGTGGTTT AATTCGATGCAACGCGAAGAAC CTTACCTGGTCTTGACATCCATA GAATTTTTTAGAGATAAAAGAGT GCCTTAGGGAACTATGAGACAG GTGCTGCATGGCTGTCGTCAGC TCGTGTTGTGAAATGTTGGGTT AAGTCCCGCAACGAGCGCAACC CCTATCCTTTGTTGCCATCAGGT TATGCTGGGAACTCAGAGGAGA CTGCCGTTATAAACCGGAGGA AGGTGGGGATGACGTCAAGTCA TCATGGCCCTTACGACCAGGGC TACACACGTGCTACAATGGCAT ATACAAAGAGATGCAACTCTGC GAAGATAAGCAAACCTCATAAA GTATGTCGTAGTCCGGAAGTGA GTCTGCAACTCGACTCCACGAA GTAGGAATCGCTAGTAATCGTG GATCAGAATGCCACGGTGAATA CGTTCCCGGGCCTTGTACACAC CGCCCGTCACACCATGGGAGT GGGTTGCAAAAGAAGCAGGTAG CTTAACCAGATTATTTATTGGA GGGCGCTTACCACTTTGTGATT CATGACTGGGGTGAAGTCGTAA CAAGGTAACCGTAGGGGAACCT GCGGTTGGATCACCTCCTTA (SEQ ID NO: 5)
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<i>Buchnera aphidicola</i> BCc	Aphids (Aphidoidea)	bacteriocytes	ATGAGATCATTAATATATAAAAA TCATGTTCCAATTAATAAATTAG GACAAAATTTTTACAGAATAAA GAAATTATTAATCAGATAATTAA TTAATAAATATTAATAAATAATGA TAATATTATTGAAATAGGATCAG GATTAGGAGCGTTAACTTTTCCT ATTTGTAGAATCATTAATAAAT GATAGTATTAGAAATTGATGAAG ATCTTGTGTTTTTTTAACTCAAA GTTTATTTATTAATAAATTACAAA TTATAATTGCTGATATTATAAAT TTGATTTTTGTTGTTTTTTCTT TACAGAAATATAAAAAATATAGG TTTATTGGTAATTTACCATATAAT ATTGCTACTATATTTTTTTTAAAA ACAATTAATTTCTTTATAATATA ATTGATATGCATTTTATGTTTCA AAAAGAAGTAGCAAAGAGATTA TTAGCTACTCCTGGTACTAAAGA ATATGGTAGATTAAGTATTATTG CACAATATTTTTATAAGATAGAA ACTGTTATTAATGTTAATAAATTT AATTTTTTCTACTCCTAAAGT AGATTCTACTTTTTTACGATTTA CTCCTAAATATTTAATAGTAAA TATAAAATAGATAAACATTTTTCT GTTTTAGAAATTAATTACTAGATT TTCTTTTCAACATAGAAGAAAAT TTTTAAATAATAATTTAATATCTT TATTTTCTACAAAAGAATTAATTT CTTTAGATATTGATCCATATTCA AGAGCAGAAAATGTTTCTTTAAT TCAATATTGTAAATTAATGAAAT ATTATTTGAAAAGAAAAATTTTAT GTTTAGATTAA (SEQ ID NO: 6)
<i>Buchnera aphidicola</i> (<i>Cinara tujaefilina</i>)	Aphids (Aphidoidea)	bacteriocytes	TTATCTTATTTACATATACGTA ATATTGCGCTGCGTGACGAGG ATTTTTTTGAATTTGAGATATATT

			TGGTTTAATACGTTTAATAAAAC GTATTTTTTTTTTATTTTCTTA TTTGCAATTCAGTAATAGGAAGT TTTTAGGTATATTTGGATAATT ACTGTAATTCTTAATAAAGTTTT TACAATCCTATCTTCAATAGAAT GAAAAC TAATAATAGCAATTTT GATCCGGAATGTAATATGTTAAT AATAATTTTAAATATTTTATGTAA TTCATTTATTTCTTGGTTAATATA TATTCGAAAAGCTTGAAATGTTT TCGTAGCTGGATGTTTAAATTTG TCATATTTTGGGATTGATTTTTT ATGATTTGAACTAACTCTAACGT GCTTGTTATGGTTTTTTTTTTAT TTGTAATATGATGGCTCGGGAT ATTTTTTTTGCATTTTTCTTCG CCAAAATTTTTATTACCTGTTC TATTGTTTTTGGTTTGTTTTTT TAACCATTGACTAACTGATATTC CAGATTTAGGGTTCATACGCAT ATCTAAAGGTCCATCATTCTAA ATGAAAATCCTCGGATACTAGA ATTTAACTGTATTGAAGAAATAC CTAAATCTAATAATTCCATCT ATTTATCTCTATTTTTTCTTTT TTAATATTTTTCAATATTAGAA AATTACCTAAAAATTTTAAAT CGCGAATCTTTATTTTTTTTCC GATTTTATAGATTGTGGGTCTT GATCAATACTATATAACTTTCCA TTAACCCTAATTCTTGAAGAAT TGCTTTTGAATGACCACCACCT CCAAATGTACAATCAACATATGT ACCGTCTTTTTTATTTTAAAGTA TTGTATGATTTCTTTGTAAAA CAGGTTTATGAATCAT (SEQ ID NO: 7) ATGAAAAGTATAAAACTTTTAA AAAACACTTCTCTGTGAAAAAT
<i>Buchnera aphidicola str. G002 (Myzus persicae)</i>	Aphids (Aphidoidea)	bacteriocytes	

			ATGGACAAAATTTTCTTATTAAT AAAGAGATCATAAAAAATATTGT TAAAAAATTAATCCAAATATAG AACAAACATTAGTAGAAATCGG ACCAGGATTAGCTGCATTAAC GAGCCCATATCTCAGTTATTA AGAGTTAATAGTTATTGAAATAG ACTGTAATCTATTATATTTTTTAA AAAACAACCATTTTATTCAAAA TTAATAGTTTTTTGTCAAGATGC TTTAACTTTAATTATACAAATTT ATTTTATAAAAAAATAAATTAAT TCGTATTTTGGTAATTTACCAT ATAATATCTCTACATCTTAATTA TTTTTTATTTCAACACATTAGA GTAATTCAAGATATGAATTTAT GCTTCAAAAAGAAGTTGCTGCA AGATTAATTGCATTACCTGGAAA TAAATATTACGGTCGTTTGAGCA TTATATCTCAATATTATTGTGATA TCAAAATTTTATTAAATGTTGCT CCTGAAGATTTTGGCCTATTCC GAGAGTTCATTCTATATTTGTAA ATTTAACACCTCATCATAATTCT CCTTATTTGTTTATGATATTAAT ATTTAAGCCTTATTACAAATAA GGCTTTCCAAAATAGAAGAAAA ATATTACGTCATAGTTTAAAAAA TTTATTTTCTGAAACAACTTTATT AAATTTAGATATTAATCCCAGAT TAAGAGCTGAAAATATTTCTGTT TTTCAAGTATTGTCAATTAGCTAA TTATTTGTATAAAAAAATTATAC TAAAAAAATTAA (SEQ ID NO: 8)
<i>Buchnera aphidicola str. Ak (Acyrthosiphon kondoi)</i>	Aphids (Aphidoidea)	bacteriocytes	ATTATAAAAAATTTTAAAAACAT TTTCTTTAAAAAGGTATGGACA AAATTTTCTTGTCATACAAAAA CTATTCAAAAGATAATTAATATA ATTAATCCAAACACCAACAAAC

			ATTAGTGGAAATTGGACCTGGA TTAGCTGCATTAACAAAACCAAT TTGTCAATTATTAGAAGAATTAA TTGTTATTGAAATAGATCCTAAT TTATTGTTTTTTATTAACAAAACGT TCATTTTATTCAAAATTAACAGTT TTTTATCAAGACGCTTTAAATTT CAATTATACAGATTTGTTTTATA AGAAAAATCAATTAATTCGTGTT TTTGGAACCTTGCCATATAATAT TTCTACATCTTTAATTATTTCTTT ATTCAATCATATTAAGTTATTC AAGATATGAATTTTATGTTACAG AAAGAGGTTGCTGAAAAGATTAA TTTCTATTCCTGGAAATAAATCT TATGGCCGTTTAAGCATTATTTCT TCAGTATTATTGTAAAATTAATA TATTATTAATGTTGTACCTGAA GATTTTCGACCTATACCGAAAGT GCATTCTGTTTTTATCAATTTAA CTCCTCATACCAATTCTCCATAT TTTGTTTATGATACAAATATCCT CAGTTCTATCACAAGAAATGCTT TTCAAAATAGAAGGAAAATTTTG CGTCATAGTTTAAAAAATTTATT TTCTGAAAAAGAACTAATTCAAT TAGAAATTAATCCAAATTTACGA GCTGAAAATATTTCTATCTTTCA GTATTGTCAATTAGCTGATTATT TATATAAAAAATTAATAATCTTG TAAAAATCAATTAA (SEQ ID NO: 9)
<i>Buchnera aphidicola</i> str. <i>Ua</i> (<i>Uroleucon</i> <i>ambrosiae</i>)	Aphids (Aphidoidea)	bacteriocytes	ATGATACTAAATAAATATAAAAA ATTTATTCCTTTAAAAAGATACG GACAAAATTTTCTTGAAATAGA GAAATAATCAAAATATTATCAA AATAATTAATCCTAAAAAACGC AAACATTATTAGAAATTGGACCG GGTTTAGGTGCGTTAACAAAAC CTATTTGTGAATTTTAAATGAA

			CTTATCGTCATTGAAATAGATCC TAATATATTATCTTTTTAAAGAA ATGTATATTTTTTGATAAATAAA AATATATTGTCATAATGCTTTAG ATTTTAATTATAAAAAATATATTCT ATAAAAAAGTCAATTAATTCGT ATTTTTGGAAATTTACCATATAA TATTTCTACATCTTTAATAATATA TTTATTTGGAATATTGATATTAT TCAAGATATGAATTTTATGTTAC AACAAGAAGTGGCTAAAAGATT AGTTGCTATTCTGGTGAAAAA CTTTATGGTCGTTTAAGTATTAT ATCTCAATATTATTGTAATATTAA AATATTATTACATATTCGACCTG AAAATTTTCAACCTATTCCTAAA GTTAATTCAATGTTTGTAATTT AACTCCGCATATTCATTCTCCTT ATTTTGTTTATGATATTAATTTAT TAACTAGTATTACAAAACATGCT TTTCAACATAGAAGAAAAATATT GCGTCATAGTTTAAGAAATTTTT TTTCTGAGCAAGATTTAATTCAT TTAGAAATTAATCCAAATTTAAG AGCTGAAAATGTTTCTATTATTC AATATTGTCAATTGGCTAATAAT TTATATAAAAAACATAAACAGTT TATTAATAATTAA (SEQ ID NO: 10)
<i>Buchnera aphidicola</i> (<i>Aphis glycines</i>)	Aphids (Aphidoidea)	bacteriocytes	ATGAAAAAGCATATTCCTATAAA AAAATTTAGTCAAAATTTCTTG TAGATTTGAGTGTGATTAATAAA ATAATTAATTTATTAATCCGCA GTTAAATGAAATATTGGTTGAAA TTGGACCGGGATTAGCTGCTAT CACTCGACCTATTTGTGATTTGA TAGATCATTTAATTGTGATTGAA ATTGATAAAATTTTATTAGATAG ATTAAACAGTTCTCATTTTATT CAAAATTAACAGTATATCATCAA

			GATGCTTTAGCATTGATTACAT AAAGTTATTTAATAAAAAAATA AATTAGTTCGAATTTTGGTAAT TTACCATATCATGTTTCTACGTC TTAATATTGCATTATTTAAAAG AATTAATATTATTAAGATATGA ATTTTATGCTACAAAAAGAAGTT GCTGAACGTTTAATTGCAACTC CAGGTAGTAAATTATATGGTCGT TTAAGTATTATTTCTCAATATTAT TGTAATATAAAAGTTTATTGCA TGTGTCTTCAAATGTTTTAAAC CAGTTCCTAAAGTAGAATCAATT TTTCTTAATTTGACACCTTATAC TGATTATTTCCCTTATTTTACTTA TAATGTAAACGTTCTTAGTTATA TTACAAATTTAGCTTTTCAAAAA AGAAGAAAAATATTACGTCATAG TTTAGGTAAAATATTTTCTGAAA AAGTTTTTATAAAATTAATATTA ATCCCAAATTAAGACCTGAGAAT ATTTCTATATTACAATATTGTCA GTTATCTAATTATATGATAGAAA ATAATATTCATCAGGAACATGTT TGTATTTAA (SEQ ID NO: 11)
<i>Annandia pinicola</i>	(Phylloxeroidea)	bacteriocytes	AGATTGAACGCTGGCGGCATGC CTTACACATGCAAGTGAACGG TAACAGGTCTTCGGACGCTGAC GAGTGGCGAACGGGTGAGTAAT ACATCGGAACGTGCCAGTCGT GGGGGATAACTACTCGAAAGAG TAGCTAATACCGCATACGATCT GAGGATGAAAGCGGGGGACCT TCGGGCCTCGCGCGATTGGAG CGGCCGATGGCAGATTAGGTAG TTGGTGGGATAAAAGCTTACCA AGCCGACGATCTGTAGCTGGTC TGAGAGGACGACCAGCCACACT GGAAGTGAATACGGTCCAGAC

		TCTTACGGGAGGCAGCAGTGG GGAATATTGCACAATGGGCGCA AGCCTGATGCAGCTATGTCGCG TGTATGAAGAAGACCTTAGGGT TGTAAGTACTTTTCGATAGCATA AGAAGATAATGAGACTAATAATT TTATTGTCTGACGTTAGCTATAG AAGAAGCACCGGCTAACTCCGT GCCAGCAGCCGCGGTAATACG GGGGGTGCTAGCGTTAATCGGA ATTACTGGGCGTAAAGAGCATG TAGGTGGTTTATTAAGTCAGATG TGAAATCCCTGGACTTAATCTAG GAACTGCATTTGAACTAATAG GCTAGAGTTTCGTAGAGGGAGG TAGAATTCTAGGTGTAGCGGTG AAATGCATAGATATCTAGAGGA ATATCAGTGGCGAAGGCGACCT TCTGGACGATAACTGACGCTAA AATGCGAAAGCATGGGTAGCAA ACAGGATTAGATACCCTGGTAG TCCATGCTGTAAACGATGTCTGA CTAAGAGGTTGGAGGTATAACT TTAATCTCTGTAGCTAACGCGT TAAGTCGACCGCCTGGGGAGTA CGGTCGCAAGGCTAAACTCAA ATGAATTGACGGGGGCTGCAC AAGCGGTGGAGCATGTGGTTTA ATTGATGCAACGCGTAAACC TTACCTGGTCTTGACATCCACA GAATTTTACAGAAATGTAGAAGT GCAATTTGAACTGTGAGACAGG TGCTGCATGGCTGTCGTCAGCT CGTGTTGTGAAATGTTGGGTTA AGTCCCGCAACGAGCGCAACC CTTGTCCTTTGTTACCATAAGAT TTAAGGAACTCAAAGGAGACTG CCGGTGATAAACTGGAGGAAGG CGGGGACGACGTCAAGTCATCA TGGCCCTTATGACCAGGGCTAC
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			ACACGTGCTACAATGGCATATA CAAAGAGATGCAATATTGCGAA ATAAAGCCAATCTTATAAAATAT GTCCTAGTTCGGACTGGAGTCT GCAACTCGACTCCACGAAGTCG GAATCGCTAGTAATCGTGGATC AGCATGCCACGGTGAATATGTT TCCAGGCCTTGTACACACCGCC CGTCACACCATGGAAGTGGATT GCAAAAGAAGTAAGAAAATTAA CCTTCTTAACAAGGAAATAACTT ACCACTTTGTGACTCATACTG GGGTGA (SEQ ID NO: 12)
<i>Moranella endobia</i>	(Coccoidea)	bacteriocytes	TCTTTTGGTAAGGAGGTGATC CAACCGCAGGTTCCCCTACGGT TACCTTGTTACGACTTCACCCCA GTCATGAATCACAAAGTGGTAA GCGCCCTCCTAAAAGGTTAGGC TACCTACTTCTTTTGAACCCAC TTCCATGGTGTGACGGGCGGTG TGTACAAGGCCCGGGAACGTAT TCACCGTGGCATTCTGATCCAC GATTACTAGCGATTCTACTTCA TGGAGTCGAGTTGCAGACTCCA ATCCGGACTACGACGCACTTTA TGAGGTCCGCTAACTCTCGCGA GCTTGCTTCTCTTTGTATGCGC CATTGTAGCACGTGTGTAGCCC TACTCGTAAGGGCCATGATGAC TTGACGTCATCCCCACCTTCCT CCGGTTTATCACCGGCAGTCTC CTTTGAGTTCCCGACCGAATCG CTGGCAAAAAAGGATAAGGGTT GCGCTCGTTGCGGGACTTAACC CAACATTTACAACACGAGCTG ACGACAGCCATGCAGCACCTGT CTCAGAGTTCCCGAAGGTACCA AAACATCTCTGCTAAGTTCTCTG GATGTCAAGAGTAGGTAAGGTT

			CTTCGCGTTGCATCGAATTAAA CCACATGCTCCACCGCTTGTGC GGGCCCCCGTCAATTCATTTGA GTTTTAACCTTGCGGCCGTACT CCCCAGGCGGTGCGATTTAACGC GTTAAC TACGAAAGCCACAGTT CAAGACCACAGCTTTCAAATCG ACATAGTTTACGGCGTGGACTA CCAGGGTATCTAATCCTGTTTG CTCCCCACGCTTTTGTACCTGA GCGTCAGTATTGTCAGGGGG CCGCCTTCGCCACTGGTATTCC TCCAGATATCTACACATTTACC GCTACACCTGGAATTCTACCCC CCTCTACGAGACTCTAGCCTAT CAGTTTCAAATGCAGTTCCTAG GTTAAGCCCAGGGATTTACAT CTGACTTAATAAACCGCCTACG TACTCTTTACGCCAGTAATTCC GATTAACGCTTGACCCCTCCGT ATTACCGCGGCTGCTGGCACG GAGTTAGCCGGTGCTTCTTCTG TAGGTAACGTCAATCAATAACC GTATTAAGGATATTGCCTTCCTC CCTACTGAAAGTGCTTTACAAC CCGAAGGCCTTCTTCACACACG CGGCATGGCTGCATCAGGGTTT CCCCATTGTGCAATATTCCCC ACTGCTGCCTCCCGTAGGAGTC TGGACCGTGTCTCAGTTCCAGT GTGGCTGGTCATCCTCTCAGAC CAGCTAGGGATCGTCGCCTAGG TAAGCTATTACCTCACCTACTAG CTAATCCCATCTGGGTTTCATCT GAAGGTGTGAGGCCAAAAGGTC CCCCACTTTGGTCTTACGACATT ATGCGGTATTAGCTACCGTTTC CAGCAGTTATCCCCCTCCATCA GGCAGATCCCCAGACTTTACTC ACCCGTTGCTGCTCGCCGGCA
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			AAAAAGTAACTTTTTTCCGTTG CCGCTCAACTTGCATGTGTTAG GCCTGCCGCCAGCGTTCAATCT GAGCCATGATCAAACCTCTTCAAT TAAA (SEQ ID NO: 13)
<i>Ishikawaella capsulata</i> <i>Mpkobe</i>	(Heteroptera)	bacteriocytes	AAATTGAAGAGTTTGATCATGG CTCAGATTGAACGCTAGCGGCA AGCTTAACACATGCAAGTCGAA CGGTAACAGAAAAAAGCTTGCT TTTTTGCTGACGAGTGGCGGAC GGGTGAGTAATGTCTGGGGATC TACCTAATGGCGGGGGATAACT ACTGGAAACGGTAGCTAATACC GCATAATGTTGTAAACCAAAGT GGGGGACCTTATGGCCTCACAC CATTAGATGAACCTAGATGGGA TTAGCTTGTAGGTGGGGTAAAG GCTCACCTAGGCAACGATCCCT AGCTGGTCTGAGAGGATGACCA GCCACACTGGAAGTGAATACG GTCCAGACTCCTACGGGAGGCA GCAGTGGGGAATCTTGACAAT GGGCGCAAGCCTGATGCAGCT ATGTCGCGTGTATGAAGAAGGC CTTAGGGTTGTAAAGTACTTTCA TCGGGGAAGAAGGATATGAGCC TAATATTCTCATATATTGACGTT ACCTGCAGAAGAAGCACCGGCT AACTCCGTGCCAGCAGCCGCG GTAACACGGAGGGTGCGAGCG TTAATCGGAATTACTGGGCGTA AAGAGCACGTAGGTGGTTTATT AAGTCATATGTGAAATCCCTGG GCTTAACCTAGGAACTGCATGT GAAACTGATAAACTAGAGTTTC GTAGAGGGAGGTGGAATTCCAG GTGTAGCGGTGAAATGCGTAGA TATCTGGAGGAATATCAGAGGC GAAGGCGACCTTCTGGACGAAA

			ACTGACACTCAGGTGCGAAAGC GTGGGGAGCAAACAGGATTAGA TACCCTGGTAGTCCACGCTGTA AACAATGTCGACTAAAAAAGTGT GAGCTTGACTTGTGGTTTTTGT GCTAACGCATTAAGTCGACCGC CTGGGGAGTACGGCCGCAAGG TAAAACTCAAATGAATTGACGG GGGTCCGCACAAGCGGTGGAG CATGTGGTTTAATTCGATGCAAC GCGAAAAACCTTACCTGGTCTT GACATCCAGCGAATTATATAGA AATATATAAGTGCCTTTCGGGG AACTCTGAGACGCTGCATGGCT GTCGTCAGCTCGTGTGTGAAA TGTTGGGTAAAGTCCCGCAACG AGCGCCCTTATCCTCTGTTGCC AGCGGCATGGCCGGGAAGTCA GAGGAGACTGCCAGTATTAAAC TGGAGGAAGGTGGGGATGACG TCAAGTCATCATGGCCCTTATG ACCAGGGCTACACACGTGCTAC AATGGTGTATACAAAGAGAAGC AATCTCGCAAGAGTAAGCAAAA CTCAAAAAGTACATCGTAGTTC GGATTAGAGTCTGCAACTCGAC TCTATGAAGTAGGAATCGCTAG TAATCGTGGATCAGAATGCCAC GGTGAATACGTTCTCTGGCCTT GTACACACCGCCCGTCACACCA TGGGAGTAAGTTGAAAAGAAG TAGGTAGCTTAACCTTTATAGGA GGGCGCTTACCACTTTGTGATT TATGACTGGGGTGAAGTCGTAA CAAGGTAAGTGTAGGGGAACCT GTGGTTGGATTACCTCCTTA (SEQ ID NO: 14)
<i>Baumannia cicadellincola</i>	sharpshooter leafhoppers (Cicadellinae)	bacteriocytes	TTCAATTGAAGAGTTTGATCATG GCTCAGATTGAACGCTGGCGGT AAGCTTAACACATGCAAGTCGA

		GCGGCATCGGAAAGTAAATTAA TTACTTTGCCGGCAAGCGGCGA ACGGGTGAGTAATATCTGGGGA TCTACCTTATGGAGAGGGATAA CTATTGGAAACGATAGCTAACA CCGCATAATGTCGTCAGACCAA AATGGGGGACCTAATTTAGGCC TCATGCCATAAGATGAACCCAG ATGAGATTAGCTAGTAGGTGAG ATAATAGCTCACCTAGGCAACG ATCTCTAGTTGGTCTGAGAGGA TGACCAGCCACACTGGAAGTGA GACACGGTCCAGACTCCTACGG GAGGCAGCAGTGGGGAATCTT GCACAATGGGGGAAACCCTGAT GCAGCTATACCGCGTGTGTGAA GAAGGCCTTCGGGTTGTAAAGC ACTTTCAGCGGGGAAGAAAATG AAGTTACTAATAATAATTGTCAA TTGACGTTACCCGCAAAAGAAG CACCGGCTAACTCCGTGCCAGC AGCCGCGGTAAGACGGAGGGT GCAAGCGTTAATCGGAATTACT GGGCGTAAAGCGTATGTAGGC GGTTTATTTAGTCAGGTGTGAAA GCCCTAGGCTTAACCTAGGAAT TGCATTTGAAACTGGTAAGCTA GAGTCTCGTAGAGGGGGGGAG AATTCCAGGTGTAGCGGTGAAA TGCGTAGAGATCTGGAAGAATA CCAGTGCGAAGGCGCCCCC TGGACGAAAAGTACGCTCAAG TACGAAAGCGTGGGAGCAAAC AGGATTAGATACCCTGGTAGTC CACGCTGTAAACGATGTCGATT TGAAGGTTGTAGCCTTGAGCTA TAGCTTTCGAAGCTAACGCATTA AATCGACCGCCTGGGGAGTAC GACCGCAAGGTTAAAGTCAAA TGAATTGACGGGGGCCCGCAC
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			AAGCGGTGGAGCATGTGGTTTA ATTGATACAACGCGAAAAACC TTACCTACTCTTGACATCCAGAG TATAAAGCAGAAAAGCTTTAGTG CCTTCGGGAACTCTGAGACAGG TGCTGCATGGCTGTCGTCAGCT CGTGTTGTGAAATGTTGGGTTA AGTCCCGCAACGAGCGCAACC CTTATCCTTTGTTGCCAACGATT AAGTCGGGAACTCAAAGGAGAC TGCCGGTGATAAACCGGAGGAA GGTGAGGATAACGTCAAGTCAT CATGGCCCTTACGAGTAGGGCT ACACACGTGCTACAATGGTGCA TACAAAGAGAAGCAATCTCGTA AGAGTTAGCAAACCTCATAAAG TGCATCGTAGTCCGGATTAGAG TCTGCAACTCGACTCTATGAAG TCGGAATCGCTAGTAATCGTGG ATCAGAATGCCACGGTGAATAC GTTCCCGGGCCTTGTACACACC GCCCCGCACACCATGGGAGTGT ATTGCAAAAGAAGTTAGTAGCTT AACTCATAATACGAGAGGGCGC TTACCACTTTGTGATTCATAACT GGGGTGAAGTCGTAACAAGGTA ACCGTAGGGGAACCTGCGGTT GGATCACCTCCTTACACTAAA (SEQ ID NO: 15)
<i>Sodalis like</i>	Rhopalus sapporensis	wider tissue tropism	ATTGAACGCTGGCGGCAGGCCT AACACATGCAAGTCGAGCGGCA GCGGGAAGAAGCTTGCTTCTTT GCCGGCGAGCGGCGGACGGGT GAGTAATGTCTGGGGATCTGCC CGATGGAGGGGGATAACTACTG GAAACGGTAGCTAATACCGCAT AACGTCGCAAGACCAAAGTGGG GGACCTTCGGGCCTCACACCAT CGGATGAACCCAGGTGGGATTA GCTAGTAGGTGGGGTAATGGCT

		CACCTAGGCGACGATCCCTAGC TGGTCTGAGAGGATGACCAGTC ACACTGGAAGTGAACACGGTC CAGACTCCTACGGGAGGCAGC AGTGGGGAATATTGCACAATGG GGGAAACCCTGATGCAGCCATG CCGCGTGTGTGAAGAAGGCCTT CGGGTTGTAAAGCACTTTCAGC GGGGAGGAAGGCGATGGCGTT AATAGCGCTATCGATTGACGTT ACCCGCAGAAGAAGCACCGGC TAACTCCGTGCCAGCAGCCGCG GTAATACGGAGGGTGCAGCG TTAATCGGAATTACTGGGCGTA AAGCGTACGCAGGCGGTCTGTT AAGTCAGATGTGAAATCCCCGG GCTCAACCTGGGAAGTGCATTT GAAACTGGCAGGCTAGAGTCTC GTAGAGGGGGGTAGAATTCCAG GTGTAGCGGTGAAATGCGTAGA GATCTGGAGGAATACCGGTGGC GAAGGCGGCCCCCTGGACGAA GACTGACGCTCAGGTACGAAAG CGTGGGGAGCAAACAGGATTAG ATACCCTGGTAGTCCACGCTGT AAACGATGTCGATTTGAAGGTT GTGGCCTTGAGCCGTGGCTTTC GGAGCTAACGTGTTAAATCGAC CGCCTGGGGAGTACGGCCGCA AGGTTAAACTCAAATGAATTGA CGGGGGCCCGCACAAAGCGGTG GAGCATGTGGTTTAATTCGATG CAACGCGAAGAACCTTACCTAC TCTTGACATCCAGAGAACTTGG CAGAGATGCTTTGGTGCCTTCG GGAAGTCTGAGACAGGTGCTGC ATGGCTGTCGTCAGCTCGTGTT GTGAAATGTTGGGTTAAGTCCC GCAACGAGCGCAACCCTTATCC TTTATTGCCAGCGATTCCGGTCG
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			GGAAGCTCAAAGGAGACTGCCG GTGATAAACCGGAGGAAGGTG GGGATGACGTCAAGTCATCATG GCCCTTACGAGTAGGGCTACAC ACGTGCTACAATGGCGCATACA AAGAGAAGCGATCTCGCGAGAG TCAGCGGACCTCATAAAGTGCG TCGTAGTCCGGATTGGAGTCTG CAACTCGACTCCATGAAGTCGG AATCGCTAGTAATCGTGATCA GAATGCCACGGTGAATACGTTT CCGGGCCTTGTACACACCGCCC GTCACACCATGGGAGTGGGTTG CAAAAGAAGTAGGTAGCTTAAC CTTCGGGAGGGCGCTTACCACT TTGTGATTCATGACTGGGGTG (SEQ ID NO: 16)
<i>Hartigia pinicola</i>	The pine bark adelgid	bacteriocytes	AGATTTAACGCTGGCGGCAGGC CTAACACATGCAAGTCGAGCGG TACCAGAAGAAGCTTGCTTCTT GCTGACGAGCGGCGGACGGGT GAGTAATGTATGGGATCTGCC CGACAGAGGGGGATAACTATTG GAAACGGTAGCTAATACCGCAT AATCTCTGAGGAGCAAAGCAGG GGAACCTCGGTCCTTGCGCTAT CGGATGAACCCATATGGGATTA GCTAGTAGGTGAGGTAATGGCT CCCCTAGGCAACGATCCCTAGC TGGTCTGAGAGGATGATCAGCC ACACTGGGACTGAGACACGGC CCAGACTCCTACGGGAGGCAG CAGTGGGGAATATTGCACAATG GGCGAAAGCCTGATGCAGCCAT GCCGCGTGTATGAAGAAGGCTT TAGGGTTGTAAAGTACTTTTCA CGAGAGGAAAACATTGATGCTA ATATCATCAATTATTGACGTTTC CGACAGAAGAAGCACCGGCTAA CTCCGTGCCAGCAGCCGCGGT

			AATACGGAGGGTGCAAGCGTTA ATCGGAATTACTGGGCGTAAAG CGCACGCAGGCGGTAAATTAAG TTAGATGTGAAAGCCCCGGGCT TAACCCAGGAATAGCATATAAAA CTGGTCAACTAGAGTATTGTAG AGGGGGGTAGAATTCCATGTGT AGCGGTGAAATGCGTAGAGATG TGGAGGAATACCA GTGGCGAAG GCGGCCCCCTGGACAAAACTG ACGCTCAAATGCGAAAGCGTGG GGAGCAAACAGGATTAGATACC CTGGTAGTCCATGCTGTAAACG ATGTCGATTTGGAGGTTGTTCC CTTGAGGAGTAGCTTCCGTAGC TAACGCGTTAAATCGACCGCCT GGGGGAGTACGACTGCAAGGT TAAAACTCAAATGAATTGACGG GGGCCCCGACAAGCGGTGGAG CATGTGGTTTAATTGATGCAAC GCGAAAAACCTTACCTACTCTT GACATCCAGATAATTTAGCAGA AATGCTTTAGTACCTTCGGGAA ATCTGAGACAGGTGCTGCATGG CTGTCGTCAGCTCGTGTTGTGA AATGTTGGGTAAAGTCCCGCAA CGAGCGCAACCCTTATCCTTTG TTGCCAGCGATTAGGTCGGGAA CTCAAAGGAGACTGCCGGTGAT AAACCGGAGGAAGGTGGGGAT GACGTCAAGTCATCATGGCCCT TACGAGTAGGGCTACACACGTG CTACAATGGCATATACAAAGGG AAGCAACCTCGCGAGAGCAAGC GAAACTCATAAATTATGTCGTAG TTCAGATTGGAGTCTGCAACTC GACTCCATGAAGTCGGAATCGC TAGTAATCGTAGATCAGAATGCT ACGGTGAATACGTTCCCGGGCC TTGTACACACCGCCCGTCACAC
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			CATGGGAGTGGGTTGCAAAAGA AGTAGGTAACCTTAACCTTATGGA AAGCGCTTACCACTTTGTGATTC ATAACTGGGGTG (SEQ ID NO: 17)
<i>Wigglesworthia glossinidia</i>	tsetse fly (Diptera: Glossinidae)	bacteriocytes	
Beta proteobacteria			
<i>Tremblaya phenacola</i>	Phenacoccus avenae (TPPAVE).	bacteriomes	AGGTAATCCAGCCACACCTTCC AGTACGGCTACCTTGTTACGAC TTCACCCAGTCACAACCCTTA CCTTCGGAAGTGCCTCCTCAC AACTCAAACCACCAACACTTTT AAATCAGGTTGAGAGAGGTTAG GCCTGTTACTTCTGGCAAGAAT TATTTCCATGGTGTGACGGGCG GTGTGTACAAGACCCGAGAACA TATTCACCGTGGCATGCTGATC CACGATTACTAGCAATTCCAAC TCATGCACTCGAGTTTCAGAGT ACAATCCGAAGTGAAGCCGGCT TTGTGAGATTAGCTCCCTTTTGC AAGTTGGCAACTCTTTGGTCCG GCCATTGTATGATGTGTGAAGC CCCACCCATAAAGGCCATGAGG ACTTGACGTCATCCCCACCTTC CTCCAACCTTATCGCTGGCAGTC TCTTTAAGGTAAGTACTAATCC AGTAGCAATTAAGACAGGGGT TGCGCTCGTTACAGGACTTAAC CCAACATCTCACGACACGAGCT GACGACAGCCATGCAGCACCTG TGCACTAATTCTCTTTCAAGCAC TCCCGCTTCTCAACAGGATCTT AGCCATATCAAAGGTAGGTAAG GTTTTTCGCGTTGCATCGAATTA ATCCACATCATCCACTGCTTGT GCGGGTCCCCGTCAATTCCTTT

		GAGTTTTAACCTTGCGGCCGTA CTCCCCAGGCGGTGACTTGTG CGTTAGCTGCACCACTGAAAAG GAAAAGTGCCCAATGGTTAGTC AACATCGTTTAGGGCATGGACT ACCAGGGTATCTAATCCTGTTT GCTCCCCATGCTTTAGTGTCTG AGCGTCAGTAACGAACCAGGAG GCTGCCTACGCTTTCGGTATTC CTCCACATCTCTACACATTTAC TGCTACATGCGGAATTCTACCT CCCCCTCTCGTACTCCAGCCTG CCAGTAACTGCCGCATTCTGAG GTTAAGCCTCAGCCTTTCACAG CAATCTTAACAGGCAGCCTGCA CACCCCTTACGCCCAATAAATCT GATTAACGCTCGCACCCCTACGT ATTACCGCGGCTGCTGGCACGT AGTTTGCCGGTGCTTATTCTTTC GGTACAGTCACACCACCAAATT GTTAGTTGGGTGGCTTTCCTTTC CGAACAAAAGTGCTTTACAACC CAAAGGCCTTCTTCACACACGC GGCATTGCTGGATCAGGCTTCC GCCCATTTGTCCAAGATTCCTCA CTGCTGCCTTCCTCAGAAGTCT GGGCCGTGTCTCAGTCCCAGTG TGGCTGGCCGTCTCTCAGACC AGCTACCGATCATTGCCTTGGG AAGCCATTACCTTCCAACAAG CTAATCAGACATCAGCCAATCT CAGAGCGCAAGGCAATTGGTCC CCTGCTTTCATTCTGCTTGGTAG AGAACTTTATGCGGTATTAATTA GGCTTTCACCTAGCTGTCCCCC ACTCTGAGGCATGTTCTGATGC ATTACTACCCGTTTGCCACTTG CCACCAAGCCTAAGCCCGTGTT GCCGTTGACTTG CATGTGTAA
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			GGCATGCCGCTAGCGTTCAATC TGAGCCAGGATCAAACCTCT (SEQ ID NO: 18)
<i>Tremblaya princeps</i>	citrus mealybug <i>Planococcus citri</i>	bacteriomes	AGAGTTTGATCCTGGCTCAGAT TGAACGCTAGCGGCATGCATTA CACATGCAAGTCGTACGGCAGC ACGGGCTTAGGCCTGGTGGCG AGTGGCGAACGGGTGAGTAAC GCCTCGGAACGTGCCTTGTAGT GGGGGATAGCCTGGCGAAAGC CAGATTAATACCGCATGAAGCC GCACAGCATGCGCGGTGAAAGT GGGGGATTCTAGCCTCACGCTA CTGGATCGGCCGGGGTCTGATT AGCTAGTTGGCGGGGTAATGGC CCACCAAGGCTTAGATCAGTAG CTGGTCTGAGAGGACGATCAGC CACACTGGGACTGAGACACGG CCCAGACTCCTACGGGAGGCA GCAGTGGGGAATCTTGGACAAT GGGCGCAAGCCTGATCCAGCA ATGCCGCGTGTGTGAAGAAGGC CTTCGGGTCGTAAAGCACTTTT GTTCTGGGATGAAGGGGGGCGT GCAAACACCATGCCCTCTTGAC GATACCGAAAGAATAAGCACCG GCTAACTACGTGCCAGCAGCCG CGGTAATACGTAGGGTGCGAGC GTTAATCGGAATCACTGGGCGT AAAGGGTGCGCGGGTGGTTTG CCAAGACCCCTGTAAAATCCTA CGGCCCAACCGTAGTGCTGCG GAGGTTACTGGTAAGCTTGAGT ATGGCAGAGGGGGGTAGAATTC CAGGTGTAGCGGTGAAATGCGT AGATATCTGGAGGAATACCGAA GGCGAAGGCAACCCCTGGGC CATCACTGACACTGAGGCACGA AAGCGTGGGGAGCAAACAGGA TTAGATACCCTGGTAGTCCACG

			CCCTAAACCATGTCGACTAGTT GTCGGGGGGAGCCCTTTTTCCT CGGTGACGAAGCTAACGCATGA AGTCGACCGCCTGGGGAGTAC GACCGCAAGGTTAAAACTCAAA GGAATTGACGGGGACCCGCAC AAGCGGTGGATGATGTGGATTA ATTGATGCAACGCGAAAAACC TTACCTACCCTTGACATGGCGG AGATTCTGCCGAGAGGCGGAA GTGCTCGAAAGAGAATCCGTGC ACAGGTGCTGCATGGCTGTCGT CAGCTCGTGTGTCGTGAGATGTTG GGTTAAGTCCCATAACGAGCGC AACCCCGTCTTTAGTTGCTAC CACTGGGGCACTCTATAGAGAC TGCCGGTGATAAACCGGAGGAA GGTGGGGACGACGTCAAGTCAT CATGGCCTTTATGGGTAGGGCT TCACACGTCATACAATGGCTGG AGCAAAGGGTCGCCAACTCGAG AGAGGGAGCTAATCCCACAAAC CCAGCCCCAGTTCGGATTGCAC TCTGCAACTCGAGTGCATGAAG TCGGAATCGCTAGTAATCGTGG ATCAGCATGCCACGGTGAATAC GTTCTCGGGTCTTGACACACC GCCCGTCACACCATGGGAGTAA GCCGCATCAGAAGCAGCCTCCC TAACCCTATGCTGGGAAGGAGG CTGCGAAGGTGGGGTCTATGAC TGGGGTGAAGTCGTAACAAGGT AGCCGTACCGGAAGGTGCGGC TGGATTACCT (SEQ ID NO: 19)
Vidania		bacteriomes	
<i>Nasuia deltocephalinicola</i>	pestiferous insect host, Macrosteles quadripunctulatu	bacteriomes	AGTTTAATCCTGGCTCAGATTTA ACGCTTGCGACATGCCTAACAC ATGCAAGTTGAACGTTGAAAATA

	s (Hemiptera: Cicadellidae)	TTTCAAAGTAGCGTATAGGTGA GTATAACATTTAAACATACCTTA AAGTTCGGAATACCCCGATGAA AATCGGTATAATACCGTATAAAA GTATTTAAGAATTAAAGCGGGG AAAACCTCGTGCTATAAGATTGT TAAATGCCTGATTAGTTTGTGG TTTTTAAGGTAAAAGCTTACCAA GACTTTGATCAGTAGCTATTCTG TGAGGATGTATAGCCACATTGG GATTGAAATAATGCCCAAACCT CTACGGAGGGCAGCAGTGGGG AATATTGGACAATGAGCGAAAG CTTGATCCAGCAATGTCGCGTG TGCGATTAAGGGAAACTGTAAA GCACTTTTTTTTAAGAATAAGAA ATTTTAATTAATAATTAATTTT TGAATGTATTAAGAATAAGTA CCGACTAATCACGTGCCAGCAG TCGCGGTAATACGTGGGGTGC GAGCGTTAATCGGATTATTGG GCGTAAAGTGATTTCAGGCTGC TTAAAAAGATTTATATTAATATT TAAATTAATTTAAAAAATGTATA AATTACTATTAAGCTAGAGTTTA GTATAAGAAAAAGAATTTTATG TGTAGCAGTGAAATGCGTTGAT ATATAAGGAACGCCGAAAGCG AAAGCATTTTTCTGTAATAGAAC TGACGCTTATATACGAAAGCGT GGGTAGCAAACAGGATTAGATA CCCTGGTAGTCCACGCCCTAAA CTATGTCAATTAAGTATTAGAAT TTTTTTAGTGGTGTAGCTAACG CGTTAAATTGACCGCCTGGGTA TTACGATCGCAAGATTAAACTC AAAGGAATTGACGGGGACCAGC ACAAGCGGTGGATGATGTGGAT TAATTCGATGATACGCGAAAAA CCTTACCTGCCCTTGACATGGT
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			TAGAATTTTATTGAAAAATAAAA GTGCTTGAAAAAGAGCTAACAC ACAGGTGCTGCATGGCTGTCGT CAGCTCGTGTCGTGAGATGTTG GGTTAAGTCCCGCAACGAGCGC AACCCCTACTCTTAGTTGCTAAT TAAAGAACTTTAAGAGAACAGCT AACAATAAGTTTAGAGGAAGGA GGGGATGACTTCAAGTCCTCAT GGCCCTTATGGGCAGGGCTTCA CACGTCATACAATGGTTAATACA AAAAGTTGCAATATCGTAAGATT GAGCTAATCTTTAAATTAATCT TAGTTCGGATTGTACTCTGCAA CTCGAGTACATGAAGTTGGAAT CGCTAGTAATCGCGGATCAGCA TGCCGCGGTGAATAGTTTAACT GGTCTTGACACACCGCCCGTC ACACCATGGAAATAAATCTTGTT TTAAATGAAGTAATATATTTATC AAAACAGGTTTTGTAACCGGGG TGAAGTCGTAACA (SEQ ID NO: 20)
<i>Zinderia insecticola</i> CARI	spittlebug <i>Clastoptera</i> <i>arizonana</i>	bacteriocytes	ATATAAATAAGAGTTTGATCCTG GCTCAGATTGAACGCTAGCGGT ATGCTTTACACATGCAAGTGA ACGACAATATTAAGCTTGCTTT AATATAAAGTGGCGAACGGGTG AGTAATATATCAAAACGTACCTT AAAGTGGGGGATAACTAATTGA AAAATTAGATAATACCGCATATT AATCTTAGGATGAAAATAGGAAT AATATCTTATGCTTTTAGATCGG TTGATATCTGATTAGCTAGTTGG TAGGGTAAATGCTTACCAAGGC AATGATCAGTAGCTGGTTTTAG CGAATGATCAGCCACACTGGAA CTGAGACACGGTCCAGACTTCT ACGGAAGGCAGCAGTGGGGAA TATTGGACAATGGGAGAAATCC

			TGATCCAGCAATACCGCGTGAG TGATGAAGGCCTTAGGGTCGTA AAACTCTTTTGTAGGAAAGAAA TAATTTTAAATAATATTTAAAATT GATGACGGTACCTAAAGAATAA GCACCGGCTAACTACGTGCCAG CAGCCGCGGTAATACGTAGGGT GCAAGCGTTAATCGGAATTATT GGGCGTAAAGAGTGCGTAGGC TGTTATATAAGATAGATGTGAAA TACTTAAGCTTAACTTAAGAACT GCATTTATTACTGTTTAACTAGA GTTTATTAGAGAGAAGTGGAATT TTATGTGTAGCAGTGAAATGCG TAGATATATAAAGGAATATCGAT GGCGAAGGCAGCTTCTTGGAAT AATACTGACGCTGAGGCACGAA AGCGTGGGGAGCAAACAGGATT AGATACCCTGGTAGTCCACGCC CTAAACTATGTCTACTAGTTATT AAATTAAAAATAAAATTTAGTAA CGTAGCTAACGCATTAAGTAGA CCGCCTGGGGAGTACGATCGC AAGATTAAAACTCAAAGGAATTG ACGGGGACCCGCACAAGCGGT GGATGATGTGGATTAATTCGAT GCAACACGAAAAACCTTACCTA CTCTTGACATGTTTGGAATTTTA AAGAAATTTAAAAGTGCTTGAAA AAGAACC AAAACACAGGTGCTG CATGGCTGTCGTCAGCTCGTGT CGTGAGATGTTGGGTTAAGTCC CGCAACGAGCGCAACCCTTGTT ATTATTTGCTAATAAAAAAGAACT TTAATAAGACTGCCAATGACAAA TTGGAGGAAGGTGGGGATGAC GTCAAGTCCTCATGGCCCTTAT GAGTAGGGCTTCACACGTCATA CAATGATATATACAATGGGTAG CAAATTTGTGAAAATGAGCCAAT
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			CCTTAAAGTATATCTTAGTTCGG ATTGTAGTCTGCAACTCGACTA CATGAAGTTGGAATCGCTAGTA ATCGCGGATCAGCATGCCGCG GTGAATACGTTCTCGGGTCTTG TACACACCGCCCGTCACACCAT GGAAGTGATTTTTACCAGAAATT ATTTGTTTAACCTTTATTGGA AAAATAATTAAGGTAGAATTCAT GACTGGGGTGAAGTCGTAACAA GGTAGCAGTATCGGAAGGTGC GGCTGGATTACATTTTAAAT (SEQ ID NO: 21)
<i>Proffella armatura</i>	<i>Diaphorina citri</i> , the Asian citrus psyllid	bacteriomes	
Alpha proteobacteria			
Hodgkinia	Cicada <i>Diceroprocta</i> <i>semicincta</i>	bacteriome	AATGCTGGCGGCAGGCCTAACA CATGCAAGTCGAGCGGACAACG TTCAAACGTTGTTAGCGGCGAA CGGGTGAGTAATACGTGAGAAT CTACCCATCCCAACGTGATAAC ATAGTCAACACCATGTCAATAAC GTATGATTCCTGCAACAGGTAA AGATTTTATCGGGGATGGATGA GCTCACGCTAGATTAGCTAGTT GGTGAGATAAAAGCCCACCAAG GCCAAGATCTATAGCTGGTCTG GAAGGATGGACAGCCACATTGG GACTGAGACAAGGCCCAACCCT CTAAGGAGGGCAGCAGTGAGG AATATTGGACAATGGGCGTAAG CCTGATCCAGCCATGCCGCATG AGTGATTGAAGGTCCAACGGAC TGTAAACTCTTTTCTCCAGAGA TCATAAATGATAGTATCTGGTGA TATAAGCTCCGGCCAACTTCGT GCCAGCAGCCGCGGTAATACG AGGGGAGCGAGTATTGTTCCGT

		TTTATTGGGCGTAAAGGGTGTC CAGGTTGCTAAGTAAGTTAACA ACAAAATCTTGAGATTCAACCTC ATAACGTTCCGTTAATACTACTA AGCTCGAGCTTGGATAGAGACA AACGGAATTCCGAGTGTAGAGG TGAAATTCGTTGATACTTGGAG GAACACCAGAGGCGAAGGCGG TTTGTACATACCAAGCTGACACT GAAGACACGAAAGCATGGGGA GCAAACAGGATTAGATACCCTG GTAGTCCATGCCCTAAACGTTG AGTGCTAACAGTTCGATCAAGC CACATGCTATGATCCAGGATTG TACAGCTAACGCGTTAAGCACT CCGCCTGGGTATTACGACCGCA AGGTTAAAACTCAAAGGAATTG ACGGAGACCCGCACAAGCGGT GGAGCATGTGGTTTAATTGAA GCTACACGAAGAACCTTACCAG CCCTTGACATACCATGGCCAAC CATCCTGGAAACAGGATGTTGT TCAAGTTAAACCCTTGAAATGCC AGGAACAGGTGCTGCATGGCTG TTGTCAGTTCGTGTCGTGAGAT GTATGGTTAAGTCCCAAAACGA ACACAACCCTCACCCATAGTTG CCATAAACACAATTGGGTTCTCT ATGGGTACTGCTAACGTAAGTT AGAGGAAGGTGAGGACCACAA CAAGTCATCATGGCCCTTATGG GCTGGGCCACACACATGCTACA ATGGTGGTTACAAAGAGCCGCA ACGTTGTGAGACCGAGCAAATC TCCAAAGACCATCTCAGTCCGG ATTGTACTCTGCAACCCGAGTA CATGAAGTAGGAATCGCTAGTA ATCGTGGATCAGCATGCCACGG TGAATACGTTCTCGGGTCTTGT ACACGCCGCCCGTCACACCATG
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			GGAGCTTCGCTCCGATCGAAGT CAAGTTACCCTTGACCACATCTT GGCAAGTGACCGA (SEQ ID NO: 22)
<i>Wolbachia sp. wPip</i>	Mosquito <i>Culex</i> <i>quinquefasciatus</i>	bacteriome	AAATTTGAGAGTTTGATCCTGG CTCAGAATGAACGCTGGCGGCA GGCCTAACACATGCAAGTCGAA CGGAGTTATATTGTAGCTTGCTA TGGTATAACTTAGTGGCAGACG GGTGAGTAATGTATAGGAATCT ACCTAGTAGTACGGAATAATTGT TGGAAACGACAACATAACCGT ATACGCCCTACGGGGGAAAAAT TTATTGCTATTAGATGAGCCTAT ATTAGATTAGCTAGTTGGTGGG GTAATAGCCTACCAAGGTAATG ATCTATAGCTGATCTGAGAGGA TGATCAGCCACACTGGAAGTGA GATACGGTCCAGACTCCTACGG GAGGCAGCAGTGGGGAATATTG GACAATGGGCGAAAGCCTGATC CAGCCATGCCGCATGAGTGAAG AAGGCCCTTTGGGTTGTAAAGCT CTTTTAGTGAGGAAGATAATGA CGGTACTCACAGAAGAAGTCCT GGCTAACTCCGTGCCAGCAGCC GCGGTAATACGGAGAGGGCTA GCGTTATTCGGAATTATTGGGC GTAAAGGGCGCGTAGGCTGGTT AATAAGTTAAAAGTGAAATCCCG AGGCTTAACCTTGGAATTGCTTT TAAACTATTAATCTAGAGATTG AAAGAGGATAGAGGAATTCCTG ATGTAGAGGTAAAATTCGTAAAT ATTAGGAGGAACACCAAGTGCGG AAGGCGTCTATCTGGTTCAAAT CTGACGCTGAAGCGCGAAGGC GTGGGGAGCAAACAGGATTAGA TACCCTGGTAGTCCACGCTGTA AACGATGAATGTTAAATATGGG

			GAGTTTACTTTCTGTATTACAGC TAACGCGTTAAACATTCCGCCT GGGACTACGGTCGCAAGATTA AAACTCAAAGGAATTGACGGGG ACCCGCACAAGCGGTGGAGCA TGTGGTTTAATTGATGCAACG CGAAAAACCTTACCACTTCTTGA CATGAAAATCATACCTATTGAA GGGATAGGGTCGGTTCGGCCG GATTTTACACAAGTGTTGCATG GCTGTCGTCAGCTCGTGTCTGTG AGATGTTGGGTAAAGTCCCGCA ACGAGCGCAACCCTCATCCTTA GTTGCCATCAGGTAATGCTGAG TACTTTAAGGAACTGCCAGTG ATAAGCTGGAGGAAGGTGGGG ATGATGTCAAGTCATCATGGCC TTTATGGAGTGGGCTACACACG TGCTACAATGGTGTCTACAATG GGCTGCAAGGTGCGCAAGCCT AAGCTAATCCCTAAAAGACATCT CAGTTCGGATTGTA CTCTGCAA CTCGAGTACATGAAGTTGGAAT CGCTAGTAATCGTGGATCAGCA TGCCACGGTGAATACGTTCTCG GGTCTTGTACACACTGCCCGTC ACGCCATGGGAATTGGTTTCAC TCGAAGCTAATGGCCTAACCGC AAGGAAGGAGTTATTTAAAGTG GGATCAGTGACTGGGGTGAAGT CGTAACAAGGTAGCAGTAGGGG AATCTGCAGCTGGATTACCTCC TTA (SEQ ID NO: 23)
Bacteroidetes			
<i>Uzinura diaspidicola</i>	armoured scale insects	bacteriocytes	AAAGGAGATATTCCAACCACAC CTTCCGGTACGGTTACCTTGTT ACGACTTAGCCCTAGTCATCAA GTTTACCTTAGGCAGACCACTG

		AAGGATTACTGACTTCAGGTAC CCCCGACTCCCATGGCTTGACG GGCGGTGTGTACAAGGTTTCGAG AACATATTCACCGCGCCATTGC TGATGCGCGATTACTAGCGATT CCTGCTTCATAGAGTCGAATTG CAGACTCCAATCCGAACTGAGA CTGGTTTTAGAGATTAGCTCCT GATCACCCAGTGGCTGCCCTTT GTAACCAGCCATTGTAGCACGT GTGTAGCCCAAGGCATAGAGGC CATGATGATTTGACATCATCCCC ACCTTCCTCACAGTTTACACCG GCAGTTTTGTTAGAGTCCCCGG CTTTACCCGATGGCAACTAACA ATAGGGGTTGCGCTCGTTATAG GACTTAACCAAACACTTCACAG CACGAACTGAAGACAACCATGC AGCACCTTGTAATACGTCTGATA GACTAAGCTGTTTCCAGCTTATT CGTAATACATTTAAGCCTTGGTA AGGTTCTCGCGTATCATCGAA TTAAACCACATGCTCCACCGCT TGTGCGAACCCCGTCAATTCC TTTGAGTTTCAATCTTGCGACTG TACTTCCCAGGTGGATCACTTAT CGCTTTTCGCTAAGCCACTGAAT ATCGTTTTTCCAATAGCTAGTGA TCATCGTTTAGGGCGTGGAATA CCAGGGTATCTAATCCTGTTTG CTCCCCACGCTTTCGTGCACTG AGCGTCAGTAAAGATTTAGCAA CCTGCCTTCGCTATCGGTGTTT TGTATGATATCTATGCATTTAC CGCTACACCATACATTCCAGAT GCTCCAATCTTACTCAAGTTTAC CAGTATCAATAGCAATTTTACAG TTAAGCTGTAAGCTTTCCTACT GACTTAATAAACAGCCTACACA CCCTTTAAACCCAATAAATCCGA
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			ATAACGCTTGTGTCATCCGTATT GCCGCGGCTGCTGGCACGGAA TTAGCCGACACTTATTCGTATAG TACCTTCAATCTCCTATCACGTA AGATATTTTATTTCTATACAAAA GCAGTTTACAACCTAAAAGACC TTCATCCTGCACGCGACGTAGC TGGTTCAGAGTTTCCTCCATTGA CCAATATTCCTCACTGCTGCCT CCCGTAGGAGTCTGGTCCGTGT CTCAGTACCAGTGTGGAGGTAC ACCCTCTTAGGCCCCCTACTGA TCATAGTCTTGGTAGAGCCATTA CCTCACCAACTAACTAATCAAAC GCAGGCTCATCTTTGCCACCT AAGTTTTAATAAAGGCTCCATGC AGAAACTTTATATTATGGGGGAT TAATCAGAATTTCTTCTGGCTAT ACCCCAGCAAAAGGTAGATTGC ATACGTGTTACTCACCCATTG CCGGTCGCCGACAAATTAATAA TTTTTCGATGCCCCCTCGACTTG CATGTGTTAAGCTCGCCGCTAG CGTTAATTCTGAGCCAGGATCA AACTCTTCGTTGTAG (SEQ ID NO: 24)
<i>Sulcia muelleri</i>	Blue-Green Sharpshooter and several other leafhopper species	bacteriocytes	CTCAGGATAAACGCTAGCGGAG GGCTTAACACATGCAAGTCGAG GGGCAGCAAAAATAATTATTTTT GGCGACCGGCAAACGGGTGAG TAATACATACGTAACCTTCCTTA TGCTGAGGAATAGCCTGAGGAA ACTTGATTAATACCTCATAATA CAATTTTTTAGAAAGAAAAATTG TTAAAGTTTTATTATGGCATAAG ATAGGCGTATGTCCAATTAGTTA GTTGGTAAGGTAATGGCTTACC AAGACGATGATTGGTAGGGGGC CTGAGAGGGGCGTTCCCCCAC ATTGGTACTGAGACACGGACCA

			AACTTCTACGGAAGGCTGCAGT GAGGAATATTGGTCAATGGAGG AAACTCTGAACCAGCCACTCCG CGTGCAGGATGAAAGAAAGCCT TATTGGTTGTAACTGCTTTTGT ATATGAATAAAAAATTCTAATTAT AGAAATAATTGAAGGTAATATAC GAATAAGTATCGACTAACTCTGT GCCAGCAGTCGCGGTAAGACA GAGGATACAAGCGTTATCCGGA TTTATTGGGTTTAAAGGGTGCG TAGGCGGTTTTTAAAGTCAGTA GTGAAATCTTAAAGCTTAACTTT AAAAGTGCTATTGATACTGAAAA ACTAGAGTAAGGTTGGAGTAAC TGGAATGTGTGGTGTAGCGGTG AAATGCATAGATATCACACAGAA CACCGATAGCGAAAGCAAGTTA CTAACCTATACTGACGCTGAG TCACGAAAGCATGGGGAGCAAA CAGGATTAGATACCCTGGTAGT CCATGCCGTAAACGATGATCAC TAACTATTGGGTTTTATACGTTG TAATTCAGTGGTGAAGCGAAAG TGTTAAGTGATCCACCTGAGGA GTACGACCGCAAGGTTGAACT CAAAGGAATTGACGGGGGCCC GCACAATCGGTGGAGCATGTGG TTTAATTCGATGATACACGAGGA ACCTTACCAAGACTTAAATGTAC TACGAATAAATTGGAACAATTT AGTCAAGCGACGGAGTACAAGG TGCTGCATGGTTGTCGTCAGCT CGTGCCGTGAGGTGTAAGGTTA AGTCCTTTAAACGAGCGCAACC CTTATTATTAGTTGCCATCGAGT AATGTCAGGGGACTCTAATAAG ACTGCCGGCGCAAGCCGAGAG GAAGGTGGGGATGACGTCAAAT CATCACGGCCCTTACGTCTTGG
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			GCCACACACGTGCTACAATGAT CGGTACAAAAGGGAGCGACTG GGTGACCAGGAGCAAATCCAGA AAGCCGATCTAAGTTCCGATTG GAGTCTGAAACTCGACTCCATG AAGCTGGAATCGCTAGTAATCG TGCATCAGCCATGGCACGGTGA ATATGTTCCCGGGCCTTGTACA CACCGCCCGTCAAGCCATGGAA GTTGGAAGTACCTAAAGTTGGT TCGCTACCTAAGGTAAGTCTAAT AACTGGGGCTAAGTCGTAACAA GGTA (SEQ ID NO: 25)
Yeast like			
<i>Symbiotaphrina buchneri</i> voucher JCM9740	Anobiid beetles <i>Stegobium</i> <i>paniceum</i>	mycetome between the foregut and midgut	AGATTAAGCCATGCAAGTCTAA GTATAAGNAATCTATACNGTGAA ACTGCGAATGGCTCATTAAATC AGTTATCGTTTATTTGATAGTAC CTTACTACATGGATAACCGTGG TAATTCTAGAGCTAATACATGCT AAAAACCCCGACTTCGGAAGGG GTGTATTTATTAGATAAAAAACC AATGCCCTTCGGGGCTCCTTGG TGATTCATGATAACTTAACGAAT CGCATGGCCTTGCGCCGGCGA TGGTTCATTCAAATTTCTGCCCT ATCAACTTTTCGATGGTAGGATA GTGGCCTACCATGGTTTAAACG GGTAACGGGGAATTAGGGTTTCG ATTCCGGAGAGGGAGCCTGAG AAACGGCTACCACATCCAAGGA AGGCAGCAGGCGCGCAAATTAC CCAATCCCGACACGGGGAGGT AGTGACAATAAATACTGATACAG GGCTCTTTTGGGTCTTGTAATTG GAATGAGTACAATTTAAATCCCT TAACGAGGAACAATTGGAGGGC AAGTCTGGTGCCAGCAGCCGC

			GGTAATTCCAGCTCCAATAGCG TATATTAAAGTTGTTGCAGTTAA AAAGCTCGTAGTTGAACCTTGG GCCTGGCTGGCCGGTCCGCCT AACCGCGTGTACTGGTCCGGCC GGGCCTTTCTTCTGGGGAGCC GCATGCCCTTCACTGGGTGTGT CGGGGAACCAGGACTTTTACTT TGAAAAAATTAGAGTGTTCAAAG CAGGCCTATGCTCGAATACATT AGCATGGAATAATAGAATAGGA CGTGCGGTTCTATTTTGTTGGTT TCTAGGACCGCCGTAATGATTA ATAGGGATAGTCGGGGGCATCA GTATTCAATTGTCAGAGGTGAA ATTCTTGGATTTATTGAAGACTA ACTACTGCGAAAGCATTGCGCA AGGATGTTTTTATTAATCAGTGA ACGAAAGTTAGGGGATCGAAGA CGATCAGATACCGTCGTAGTCT TAACCATAAACTATGCCGACTA GGGATCGGGCGATGTTATTATT TTGACTCGCTCGGCACCTTACG AGAAATCAAAGTCTTTGGGTTCT GGGGGGAGTATGGTCGCAAGG CTGAAACTTAAAGAAATTGACG GAAGGGCACCACCAGGAGTGG AGCCTGCGGCTTAATTTGACTC AACACGGGGAAACTCACCAGGT CCAGACACATTAAGGATTGACA GATTGAGAGCTCTTTCTTGATTA TGTGGGTGGTGGTGCATGGCC GTTCTTAGTTGGTGGAGTGATTT GTCTGCTTAATTGCGATAACGA ACGAGACCTTAACCTGCTAAAT AGCCCGGTCCGCTTTGGCGGG CCGCTGGCTTCTTAGAGGGACT ATCGGCTCAAGCCGATGGAAGT TTGAGGCAATAACAGGTCTGTG ATGCCCTTAGATGTTCTGGGCC
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			GCACGCGCGCTACACTGACAGA GCCAACGAGTAAATCACCTTGG CCGGAAGGTCTGGGTAATCTTG TTAAACTCTGTCTGCTGGGGA TAGAGCATTGCAATTATTGCTCT TCAACGAGGAATTCCTAGTAAG CGCAAGTCATCAGCTTGCGCTG ATTACGTCCCTGCCCTTTGTACA CACCGCCCGTCGCTACTACCGA TTGAATGGCTCAGTGAGGCCTT CGGACTGGCACAGGGACGTTG GCAACGACGACCCAGTGCCGG AAAGTTGGTCAAACCTTGGTCATT TAGAGGAAGTAAAAGTCGTAAC AAGGTTTCCGTAGGTGAACCTG CGGAAGGATCATT (SEQ ID NO: 26)
<i>Symbiotaphrina kochii</i> voucher CBS 589.63	Anobiid beetles <i>Lasioderma</i> <i>serricorne</i>	mycetome	TACCTGGTTGATTCTGCCAGTA GTCATATGCTTGTCTCAAAGATT AAGCCATGCAAGTCTAAGTATA AGCAATCTATACGGTGAAACTG CGAATGGCTCATTAAATCAGTTA TCGTTTATTTGATAGTACCTTAC TACATGGATAACCGTGGTAATT CTAGAGCTAATACATGCTAAAAA CCTCGACTTCGGAAGGGGTGTA TTTATTAGATAAAAAACCAATGC CCTTCGGGGCTCCTTGGTGATT CATGATAACTTAACGAATCGCAT GGCCTTGCGCCGGCGATGGTT CATTCAAATTTCTGCCCTATCAA CTTTCGATGGTAGGATAGTGGC CTACCATGGTTTCAACGGGTAA CGGGGAATTAGGGTTCGATTCC GGAGAGGGAGCCTGAGAAACG GCTACCACATCCAAGGAAGGCA GCAGGCGCGCAAATTACCCAAT CCCGACACGGGGAGGTAGTGA CAATAAATACTGATACAGGGCT CTTTTGGGTCTTGTAATTGGAAT

		GAGTACAATTTAAATCCCTTAAC GAGGAACAATTGGAGGGCAAGT CTGGTGCCAGCAGCCGCGGTA ATTCCAGCTCCAATAGCGTATAT TAAAGTTGTTGCAGTTAAAAAGC TCGTAGTTGAACCTTGGGCCTG GCTGGCCGGTCCGCCTAACCG CGTGTACTGGTCCGGCCGGGC CTTTCCTTCTGGGGAGCCGCAT GCCCTTCACTGGGTGTGTCGGG GAACCAGGACTTTTACTTTGAAA AAATTAGAGTGTTCAAAGCAGG CCTATGCTCGAATACATTAGCAT GGAATAATAGAATAGGACGTGT GGTTCTATTTTGTGGTTTCTAG GACCGCCGTAATGATTAATAGG GATAGTCGGGGGCATCAGTATT CAATTGTCAGAGGTGAAATTCTT GGATTTATTGAAGACTAACTACT GCGAAAGCATTGCGCAAGGATG TTTTCATTAATCAGTGAACGAAA GTTAGGGGATCGAAGACGATCA GATACCGTCGTAGTCTTAACCA TAACTATGCCGACTAGGGATC GGGCGATGTTATTATTTGACTC GCTCGGCACCTTACGAGAAATC AAAGTCTTTGGGTTCTGGGGGG AGTATGGTCGCAAGGCTGAAAC TTAAAGAAATTGACGGAAGGGC ACCACCAGGAGTGGAGCCTGC GGCTTAATTTGACTCAACACGG GGAAACTCACCAGGTCCAGACA CATTAAAGGATTGACAGATTGAG AGCTCTTCTTGATTATGTGGGT GGTGGTGCATGGCCGTTCTTAG TTGGTGGAGTGATTTGTCTGCT TAATTGCGATAACGAACGAGAC CTTAACCTGCTAAATAGCCCGG TCCGCTTTGGCGGGCCGCTGG CTTCTTAGAGGGACTATCGGCT
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			CAAGCCGATGGAAGTTTGAGGC AATAACAGGTCTGTGATGCCCT TAGATGTTCTGGGCCGCACGCG CGCTACACTGACAGAGCCAACG AGTACATCACCTTGGCCGGAAG GTCTGGGTAATCTTGTTAAACTC TGTCGTGCTGGGGATAGAGCAT TGCAATTATTGCTCTTCAACGAG GAATTCCTAGTAAGCGCAAGTC ATCAGCTTGCGCTGATTACGTC CCTGCCCTTTGTACACACCGCC CGTCGCTACTACCGATTGAATG GCTCAGTGAGGCCTTCGGACTG GCACAGGGACGTTGGCAACGA CGACCCAGTGCCGGAAGTTTCG TCAAACCTGGTCATTTAGAGGAA GNNNAAGTCGTAACAAGGTTTC CGTAGGTGAACCTGCGGAAGG ATCATTA (SEQ ID NO: 27)
Primary extracellular symbiont	Host	location	16 rRNA
fenitrothion-degrading bacteria			
<i>Burkholderia</i> sp. <i>SFA1</i>	<i>Riptortus pedestris</i>	Gut	AGTTTGATCCTGGCTCAGATTG AACGCTGGCGGCATGCCTTACA CATGCAAGTCGAACGGCAGCAC GGGGGCAACCCTGGTGGCGAG TGGCGAACGGGTGAGTAATACA TCGGAACGTGTCCTGTAGTGGG GGATAGCCCGGCGAAAGCCGG ATTAATACCGCATACGACCTAA GGGAGAAAGCGGGGGATCTTC GGACCTCGCGCTATAGGGGCG GCCGATGGCAGATTAGCTAGTT GGTGGGGTAAAGGCCTACCAA GGCGACGATCTGTAGCTGGTCT GAGAGGACGACCAGCCACACT GGGACTGAGACACGGCCAGA

		CTCCTACGGGAGGCAGCAGTG GGGAATTTTGGACAATGGGGGC AACCCTGATCCAGCAATGCCGC GTGTGTGAAGAAGGCTTCGGGT TGTAAGCACTTTTGTCCGGAA AGAAAACCTTCGTCCCTAATATG GATGGAGGATGACGGTACCGG AAGAATAAGCACCGGCTAACTA CGTGCCAGCAGCCGCGGTAATA CGTAGGGTGCGAGCGTTAATCG GAATTACTGGGCGTAAAGCGTG CGCAGGCGGTCTGTTAAGACCG ATGTGAAATCCCCGGGCTTAAC CTGGGAACTGCATTGGTGA CTG GCAGGCTTTGAGTGTGGCAGAG GGGGGTAGAATTCCACGTGTAG CAGTGAAATGCGTAGAGATGTG GAGGAATACCGATGGCGAAGG CAGCCCCCTGGGCCAACTACTG ACGCTCATGCACGAAAGCGTGG GGAGCAAACAGGATTAGATACC CTGGTAGTCCACGCCCTAAACG ATGTCAACTAGTTGTTGGGGAT TCATTTCCCTTAGTAACGTAGCTA ACGCGTGAAGTTGACCGCCTGG GGAGTACGGTCGCAAGATTA AA ACTCAAAGGAATTGACGGGGAC CCGCACAAGCGGTGGATGATGT GGATTAATTGATGCAACGCGA AAAACCTTACCTACCCTTGACAT GGTCGGAACCCTGCTGAAAGGT GGGGGTGCTCGAAAGAGAACC GGCGCACAGGTGCTGCATGGC TGTCGTCAGCTCGTGTCTGAG ATGTTGGGTAAAGTCCCGCAAC GAGCGCAACCCTTGTCCTTAGT TGCTACGCAAGAGCACTCTAAG GAGACTGCCGGTGACAAACCG GAGGAAGGTGGGGATGACGTC AAGTCCTCATGGCCCTTATGGG
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			TAGGGCTTCACACGTCATACAA TGGTCGGAACAGAGGGTTGCCA AGCCGCGAGGTGGAGCCAATC CCAGAAAACCGATCGTAGTCCG GATCGCAGTCTGCAACTCGACT GCGTGAAGCTGGAATCGCTAGT AATCGCGGATCAGCATGCCGCG GTGAATACGTTCCCGGGTCTTG TACACACCGCCCGTCACACCAT GGGAGTGGGTTTCACCAGAAGT AGGTAGCCTAACCGCAAGGAG GGCGCTTACCACGGTGGGATTC ATGACTGGGGTGAAGTCGTAAC AAGGTAGC (SEQ ID NO: 28)
<i>Burkholderia</i> sp. KM-A	<i>Riptortus pedestris</i>	Gut	GCAACCCTGGTGGCGAGTGGC GAACGGGTGAGTAATACATCGG AACGTGTCCTGTAGTGGGGGAT AGCCCGGCGAAAGCCGGATTAA TACCGCATACGATCTACGGAAG AAAGCGGGGGATCCTTCGGGA CCTCGCGCTATAGGGGCGGCC GATGGCAGATTAGCTAGTTGGT GGGGTAAAGGCCTACCAAGGC GACGATCTGTAGCTGGTCTGAG AGGACGACCAGCCCACTGGG ACTGAGACACGGCCCAGACTCC TACGGGAGGCAGCAGTGGGGA ATTTTGGACAATGGGGGCAACC CTGATCCAGCAATGCCGCGTGT GTGAAGAAGGCCTTCGGGTTGT AAAGCACTTTTGTCCGGAAAGA AAACGTCTTGTTAATACCTGA GGCGGATGACGGTACCGGAAG AATAAGCACCGGCTAACTACGT GCCAGCAGCCGCGGTAATACGT AGGGTGCGAGCGTTAATCGGAA TACTGGGCGTAAAGCGTGCGC AGGCGGTCTGTTAAGACCGATG TGAAATCCCCGGGCTTAACCTG

		GGAAGTGCATTGGTGAAGTGGCA GGCTTTGAGTGTGGCAGAGGG GGGTAGAATTCCACGTGTAGCA GTGAAATGCGTAGAGATGTGGA GGAATACCGATGGCGAAGGCA GCCCCCTGGGCCAACACTGAC GCTCATGCACGAAAGCGTGGG GAGCAAACAGGATTAGATACCC TGGTAGTCCACGCCCTAAACGA TGTCAACTAGTTGTTGGGGATT CATTTCTTAGTAACGTAGCTAA CGCGTGAAGTTGACCGCCTGG GGAGTACGGTCGCAAGATTAAG ACTCAAAGGAATTGACGGGGAC CCGCACAAGCGGTGGATGATGT GGATTAATTGATGCAACGCGA AAACCTTACCTACCTTGACAT GGTCGGAAGTCTGCTGAGAGGT GGACGTGCTCGAAAGAGAACC GGCGCACAGGTGCTGCATGGC TGTCGTCAGCTCGTGTCTGAG ATGTTGGGTAAAGTCCCGCAAC GAGCGCAACCCTTGCTCTAGT TGCTACGCAAGAGCACTCTAAG GAGACTGCCGGTGACAAACCG GAGGAAGGTGGGGATGACGTC AAGTCCTCATGGCCCTTATGGG TAGGGCTTCACACGTCATACAA TGGTCGGAACAGAGGGTTGCCA AGCCGCGAGGTGGAGCCAATC CCAGAAAACCGATCGTAGTCCG GATCGCAGTCTGCAACTCGACT GCGTGAAGCTGGAATCGCTAGT AATCGCGGATCAGCATGCCGCG GTGAATACGTTCCCGGGTCTTG TACACACCGCCCGTCACACCAT GGGAGTGGGTTTACCAGAAGT AGGTAGCCTAACCGCAAGGAG GGCGCTTACCACGGTGGGATTG ATGACTGGGGTGAAGT
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			(SEQ ID NO: 29)
Burkholderia sp. KM-G	Riptortus pedestris	Gut	GCAACCCTGGTGGCGAGTGGC GAACGGGTGAGTAATACATCGG AACGTGTCCTGTAGTGGGGAT AGCCCGGCGAAAGCCGGATTAA TACCGCATACGACCTAAGGGAG AAAGCGGGGGATCTTCGGACCT CGCGCTATAGGGGCGCCGAT GGCAGATTAGCTAGTTGGTGGG GTAAAGGCCTACCAAGGCGACG ATCTGTAGCTGGTCTGAGAGGA CGACCAGCCACACTGGGACTGA GACACGGCCCAGACTCCTACG GGAGGCAGCAGTGGGGAATTTT GGACAATGGGGGCAACCCTGAT CCAGCAATGCCGCGTGTGTGAA GAAGGCCTTCGGGTTGTAAAGC ACTTTTGTCCGAAAGAAACTT CGAGGTTAATAACCTTGGAGGA TGACGGTACCGGAAGAATAAGC ACCGGCTAACTACGTGCCAGCA GCCGCGTAATACGTAGGGTG CGAGCGTTAATCGGAATTACTG GGCGTAAAGCGTGCGCAGGCG GTCTGTTAAGACCGATGTGAAA TCCCGGGCTTAACCTGGGAAC TGCATTGGTGA CTGGCAGGCTT TGAGTGTGGCAGAGGGGGTA GAATTCCACGTGTAGCAGTGAA ATGCGTAGAGATGTGGAGGAAT ACCGATGGCGAAGGCAGCCCC CTGGGCCAACACTGACGCTCAT GCACGAAAGCGTGGGGAGCAA ACAGGATTAGATACCCTGGTAG TCCACGCCCTAAACGATGTCAA CTAGTTGTTGGGGATTCAATTC TTAGTAACGTAGCTAACGCGTG AAGTTGACCGCTGGGGAGTAC GGTCGCAAGATTAAACTCAA GGAATTGACGGGGACCCGCAC

			AAGCGGTGGATGATGTGGATTA ATTGATGCAACGCGAAAAACC TTACCTACCCTTGACATGGTCG GAAGTCTGCTGAGAGGTGGAC GTGCTCGAAAGAGAACCGGCG CACAGGTGCTGCATGGCTGTCTG TCAGCTCGTGTCTGTGAGATGTT GGGTAAAGTCCCGCAACGAGC GCAACCCTTGCTCTTAGTTGCT ACGCAAGAGCACTCTAAGGAGA CTGCCGGTGACAAACCGGAGG AAGGTGGGGATGACGTCAAGTC CTCATGGCCCTTATGGGTAGGG CTTCACACGTCATACAATGGTC GGAACAGAGGGTTGCCAAGCC GCGAGGTGGAGCCAATCCCAG AAAACCGATCGTAGTCCGGATC GCAGTCTGCAACTCGACTGCGT GAAGCTGGAATCGCTAGTAATC GCGGATCAGCATGCCGCGGTG AATACGTTCCCGGGTCTTGAC ACACCGCCCGTCACACCATGGG AGTGGGTTTCACCAGAAGTAGG TAGCCTAACCTGCAAAGGAGGG CGCTTACCACG (SEQ ID NO: 30)
Bees			
<i>Snodgrassella alvi</i>	Honeybee (<i>Apis mellifera</i>) and <i>Bombus</i> spp.	Ileum	GAGAGTTTGATCCTGGCTCAGA TTGAACGCTGGCGGCATGCCTT ACACATGCAAGTCGAACGGCAG CACGGAGAGCTTGCTCTCTGGT GGCGAGTGGCGAACGGGTGAG TAATGCATCGGAACGTACCGAG TAATGGGGGATAACTGTCCGAA AGGATGGCTAATACCGCATACG CCCTGAGGGGGAAAGCGGGGG ATCGAAAGACCTCGCGTTATTT GAGCGGCCGATGTTGGATTAGC TAGTTGGTGGGGTAAAGGCCTA

		CCAAGGCGACGATCCATAGCG GGTCTGAGAGGATGATCCGCCA CATTGGGACTGAGACACGGCCC AAACTCCTACGGGAGGCAGCAG TGGGGAATTTTGGACAATGGGG GGAACCCTGATCCAGCCATGCC GCGTGTCTGAAGAAGGCCTTCG GGTTGTAAAGGACTTTTGTTAG GGAAGAAAAGCCGGGTGTTAAT ACCATCTGGTGCTGACGGTACC TAAAGAATAAGCACCGGCTAAC TACGTGCCAGCAGCCGCGGTAA TACGTAGGGTGCGAGCGTTAAT CGGAATTACTGGGCGTAAAGCG AGCGCAGACGGTTAATTAAGTC AGATGTGAAATCCCCGAGCTCA ACTTGGGACGTGCATTTGAAAC TGGTAACTAGAGTGTGTCAGA GGGAGGTAGAATTCCACGTGTA GCAGTGAAATGCGTAGAGATGT GGAGGAATACCGATGGCGAAG GCAGCCTCCTGGGATAACACTG ACGTTTCATGCTCGAAAGCGTGG GTAGCAAACAGGATTAGATACC CTGGTAGTCCACGCCCTAAACG ATGACAATTAGCTGTTGGGACA CTAGATGTCTTAGTAGCGAAGC TAACGCGTGAAATTGTCCGCCT GGGGAGTACGGTCGCAAGATTA AAACTCAAAGGAATTGACGGGG ACCCGCACAAGCGGTGGATGAT GTGGATTAATTCGATGCAACGC GAAGAACCTTACCTGGTCTTGA CATGTACGGAATCTCTTAGAGA TAGGAGAGTGCCTTCGGAACC GTAACACAGGTGCTGCATGGCT GTCGTCAGCTCGTGTCTGAGA TGTTGGGTTAAGTCCCGCAACG AGCGCAACCCTTGTCAATAGTT GCCATCATTAAGTTGGGCACTC
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			TAATGAGACTGCCGGTGACAAA CCGGAGGAAGGTGGGGATGAC GTCAAGTCCTCATGGCCCTTAT GACCAGGGCTTCACACGTCATA CAATGGTCGGTACAGAGGGTAG CGAAGCCGCGAGGTGAAGCCA ATCTCAGAAAGCCGATCGTAGT CCGGATTGCACTCTGCAACTCG AGTGCATGAAGTCGGAATCGCT AGTAATCGCAGGTCAGCATACT GCGGTGAATACGTTCCCGGGTC TTGTACACACCGCCCGTCACAC CATGGGAGTGGGGGATACCAG AATTGGGTAGACTAACCGCAAG GAGGTCGCTTAACACGGTATGC TTCATGACTGGGGTGAAGTCGT AACAAGGTAGCCGTAG (SEQ ID NO: 33)
<i>Gilliamella apicola</i>	honeybee (<i>Apis mellifera</i>) and <i>Bombus</i> spp.	Ileum	TTAAATTGAAGAGTTTGATCATG GCTCAGATTGAACGCTGGCGGC AGGCTTAACACATGCAAGTCGA ACGGTAACATGAGTGCTTGACAC TTGATGACGAGTGGCGGACGG GTGAGTAAAGTATGGGGATCTG CCGAATGGAGGGGGACAACAG TTGGAAACGACTGCTAATACCG CATAAAGTTGAGAGACCAAAGC ATGGGACCTTCGGGCCATGCG CCATTTGATGAACCCATATGGG ATTAGCTAGTTGGTAGGGTAAT GGCTTACCAAGGCGACGATCTC TAGCTGGTCTGAGAGGATGACC AGCCACACTGGAAGTGAACAC GGTCCAGACTCCTACGGGAGG CAGCAGTGGGGAATATTGCACA ATGGGGGAAACCCTGATGCAGC CATGCCGCGTGTATGAAGAAGG CCTTCGGGTTGTAAAGTACTTTC GGTGATGAGGAAGGTGGTGTAT CTAATAGGTGCATCAATTGACG

		TTAATTACAGAAGAAGCACCGG CTAACTCCGTGCCAGCAGCCGC GGTAATACGGAGGGTGCGAGC GTTAATCGGAATGACTGGGCGT AAAGGGCATGTAGGCGGATAAT TAAGTTAGGTGTGAAAGCCCTG GGCTCAACCTAGGAATTGCACT TAAACTGGTTAACTAGAGTATT GTAGAGGAAGGTAGAATTCCAC GTGTAGCGGTGAAATGCGTAGA GATGTGGAGGAATACCGGTGG CGAAGGCGGCCTTCTGGACAG ATACTGACGCTGAGATGCGAAA GCGTGGGGAGCAAACAGGATTA GATACCCTGGTAGTCCACGCTG TAAACGATGTCGATTTGGAGTTT GTTGCCTAGAGTGATGGGCTCC GAAGCTAACGCGATAAATCGAC CGCCTGGGGAGTACGGCCGCA AGGTTAAACTCAAATGAATTGA CGGGGGCCCGCACAAGCGGTG GAGCATGTGGTTTAATTCGATG CAACGCGAAGAACCTTACCTGG TCTTGACATCCACAGAATCTTGC AGAGATGCGGGAGTGCCTTCG GGAAGTGTGAGACAGGTGCTGC ATGGCTGTCTCAGCTCGTGTT GTGAAATGTTGGGTTAAGTCCC GCAACGAGCGCAACCCTTATCC TTTGTTGCCATCGGTTAGGCCG GGAAGTCAAAGGAGACTGCCGT TGATAAAGCGGAGGAAGGTGG GGACGACGTCAAGTCATCATGG CCCTTACGACCAGGGCTACACA CGTGCTACAATGGCGTATACAA AGGGAGGCGACCTCGCGAGAG CAAGCGGACCTCATAAAGTACG TCTAAGTCCGGATTGGAGTCTG CAACTCGACTCCATGAAGTCGG AATCGCTAGTAATCGTGAATCA
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			GAATGTCACGGTGAATACGTTCCCGGGCCTTGTACACACCGCCC GTCACACCATGGGAGTGGGTTGCACCAGAAGTAGATAGCTTAAC CTTCGGGAGGGCGTTTACCACGGTGTGGTCCATGACTGGGGTGA AGTCGTAACAAGGTAACCGTAGGGGAACCTGCGGTTGGATCACC TCCTTAC (SEQ ID NO: 34)
<i>Bartonella apis</i>	honeybee (<i>Apis mellifera</i>)	Gut	AAGCCAAAATCAAATTTTCAACTTGAGAGTTTGATCCTGGCTCAG AACGAACGCTGGCGGCAGGCTTAACACATGCAAGTCGAACGCA CTTTTCGGAGTGAGTGGCAGACGGGTGAGTAACGCGTGGGAAT CTACCTATTTCTACGGAATAACGCAGAGAAATTTGTGCTAATACC GTATACGTCCTTCGGGAGAAAAGATTATCGGAGATAGATGAGCC CGCGTTGGATTAGCTAGTTGGTGAGGTAATGGCCACCAAGGC GACGATCCATAGCTGGTCTGAGAGGATGACCAGCCACATTGGGA CTGAGACACGGCCCAGACTCCTACGGGAGGCAGCAGTGGGGAA TATTGGACAATGGGCGCAAGCCTGATCCAGCCATGCCGCGTGAG TGATGAAGGCCCTAGGGTTGTAAAGCTCTTTCACCGGTGAAGAT AATGACGGTAACCGGAGAAGAAAGCCCCGGCTAACTTCGTGCCAG CAGCCGCGGTAATACGAAGGGGGCTAGCGTTGTTTCGGATTAC TGGGCGTAAAGCGCACGTAGGCGGATATTTAAGTCAGGGGTGA AATCCCGGGGCTCAACCCCGGAAGTGCCTTTGATACTGGATATC TTGAGTATGGAAGAGGTAAGTGAATTCCGAGTGTAGAGGTGAA

			ATTCGTAGATATTCGGAGGAAC ACCA GTGGCGAAGGCGGCTTA CTGGTCCATTACTGACGCTGAG GTGCGAAAGCGTGGGGAGCAA ACAGGATTAGATACCCTGGTAG TCCACGCTGTAAACGATGAATG TTAGCCGTTGGACAGTTTACTG TTCGGTGGCGCAGCTAACGCAT TAAACATTCCGCCTGGGGAGTA CGGTCGCAAGATTAAAACTCAA AGGAATTGACGGGGGCCCCGCA CAAGCGGTGGAGCATGTGGTTT AATTCGAAGCAACGCGCAGAAC CTTACCAGCCCTTGACATCCCG ATCGCGGATGGTGGAGACACC GTCTTTCAGTTCGGCTGGATCG GTGACAGGTGCTGCATGGCTGT CGTCAGCTCGTGTCTGAGATG TTGGGTAAAGTCCCGCAACGAG CGCAACCCTCGCCCTTAGTTGC CATCATTTAGTTGGGCACTCTAA GGGGA CTGCCGGTGATAAGCC GAGAGGAAGGTGGGGATGACG TCAAGTCCTCATGGCCCTTACG GGCTGGGCTACACACGTGCTAC AATGGTGGTGACAGTGGGCAG CGAGACCGCGAGGTGAGCTA ATCTCCAAAAGCCATCTCAGTTC GGATTGCACTCTGCAACTCGAG TGCATGAAGTTGGAATCGCTAG TAATCGTGGATCAGCATGCCAC GGTGAATACGTTCCCGGGCCTT GTACACACCGCCCGTCACACCA TGGGAGTTGGTTTTACCCGAAG GTGCTGTGCTAACCGCAAGGAG GCAGGCAACCACGGTAGGGTC AGCGACTGGGGTGAAGTCGTAA CAAGGTAGCCGTAGGGGAACCT GCGGCTGGATCACCTCCTTTCT AAGGAAGATGAAGAATTGGAA
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[illegible]

			CATGTGGTTTAATTCTGAAGCAA CGCGCAGAACCTTACCAGGGCT TGCATGGGGAGGCTGTATTCAG AGATGGATATTTCTTCGGACCT CCCGCACAGGTGCTGCATGGCT GTCGTCAGCTCGTGTCTGAGA TGTTGGGTAAAGTCCCGCAACG AGCGCAACCCCTTGCTTTAGTT GCCATCACGTCTGGGTGGGCA CTCTAGAGAGACTGCCGGTGAC AAGCCGGAGGAAGGTGGGGAT GACGTCAAGTCCTCATGGCCCT TATGTCCTGGGCTACACACGTG CTACAATGGCGGTGACAGAGG GATGCTACATGGTGACATGGTG CTGATCTCAAAAACCGTCTCA GTTCCGATTGTACTCTGCAACT CGAGTGCATGAAGGTGGAATCG CTAGTAATCGCGGATCAGCATG CCGCGGTGAATACGTTCCCGG GCCTTGACACACCGCCCGTCA CACCATGGGAGTTGGTTTGACC TTAAGCCGGTGAGCGAACCGCA AGGAACGCAGCCGACCACCGG TTCGGGTTGAGCGACTGGGGG A (SEQ ID NO: 36)
<i>Lactobacillus kunkeei</i>	honeybee (<i>Apis mellifera</i>)	Gut	TTCCTTAGAAAGGAGGTGATCC AGCCGCAGGTTCTCCTACGGCT ACCTTGTTACGACTTCACCCTAA TCATCTGTCCACCTTAGACGA CTAGCTCCTAAAAGGTTACCCC ATCGTCTTTGGGTGTTACAACT CTCATGGTGTGACGGGCGGTGT GTACAAGGCCCGGGAACGTATT CACCGTGGCATGCTGATCCACG ATTACTAGTGATTCCAATTCTAT GCAGGCGAGTTGCAGCCTGCA ATCCGAACTGAGAATGGCTTTA AGAGATTAGCTTGACCTCGCGG

		TTTCGCGACTCGTTGTACCATC CATTGTAGCACGTGTGTAGCCC AGCTCATAAGGGGCATGATGAT TTGACGTCGTCCCCACCTTCCT CCGGTTTATCACCGGCAGTCTC ACTAGAGTGCCCAACTAAATGC TGGCAACTAATAATAAGGGTTG CGCTCGTTGCGGGACTTAACCC AACATCTCACGACACGAGCTGA CGACAACCATGCACCACCTGTC ATTCTGTCCCCGAAGGGAACGC CCAATCTCTTGGGTTGGCAGAA GATGTCAAGAGCTGGTAAGGTT CTTCGCGTAGCATCGAATTA CCACATGCTCCACCACTTGTGC GGGCCCCCGTCAATTCCTTTGA GTTTCAACCTTGCGGTCGTA CCCCAGGCGGAATACTTAATGC GTTAGCTGCGGCACTGAAGGG CGGAAACCTCCAACACCTAGT ATTCATCGTTTACGGCATGGAC TACCAGGGTATCTAATCCTGTTC GCTACCCATGCTTTGAGCCTC AGCGTCAGTAACAGACCAGAAA GCCGCCCTTCGCCACTGGTGTT TTCCATATATCTACGCATTTAC CGCTACACATGGAGTTCCACTT TCCTCTTCTGTAAGTTTGT TAGTTTCCACTGCACTTCCTCAG TTGAGCTGAGGGCTTTCACAGC AGACTTACAAAACCGCCTGCGC TCGCTTACGCCAATAAATCC GGACAACGCTTGCCACCTACGT ATTACCGCGGCTGCTGGCACGT AGTTAGCCGTGGCTTTCTGGTT AAATACCGTCAAAGTGTTAACA GTTACTCTAACACTTGTTCTTCT TTAACAACAGAGTTTACGATCC GAAAACCTTCATCACTCACGCG GCGTTGCTCCATCAGACTTTTCG
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			TCCATTGTGGAAGATTCCCTACT GCTGCCTCCCGTAGGAGTCTGG GCCGTGTCTCAGTCCCAATGTG GCCGATTACCCTCTCAGGTCGG CTACGTATCATCGTCTTGGTGG GCTTTTATCTCACCAACTA ATACGGCGCGGGTCCATCCCAA AGTGATAGCAAAGCCATCTTTC AAGTTGGAACCATGCGGTCCA ACTAATTATGCGGTATTAGCACT TGTTTCAAATGTTATCCCCCGC TTCGGGGCAGGTTACCCACGTG TACTCACCAGTTCGCCACTCG CTCCGAATCCAAAAATCATTAT GCAAGCATAAAATCAATTTGGG AGAACTCGTTCGACTTGCGTGT ATTAGGCACGCCGCCAGCGTTC GTCCTGAGCCAGGATCAAATC TCATCTTAA (SEQ ID NO: 37)
<i>Lactobacillus Firm-4</i>	honeybee (<i>Apis mellifera</i>)	Gut	ACGAACGCTGGCGGCGTGCCT AATACATGCAAGTCGAGCGCGG GAAGTCAGGGAAGCCTTCGGGT GGAAGTGGTGGAACGAGCGGC GGATGGGTGAGTAACACGTAGG TAACCTGCCCTAAAGCGGGGGA TACCATCTGGAACAGGTGCTA ATACCGCATAAACCCAGCAGTC ACATGAGTGCTGGTTGAAAGAC GGCTTCGGCTGTCACTTTAGGA TGGACCTGCGGCGTATTAGCTA GTTGGTGGAGTAACGGTTCACC AAGGCAATGATACGTAGCCGAC CTGAGAGGGTAATCGGCCACAT TGGGACTGAGACACGGCCCAAA CTCCTACGGGAGGCAGCAGTA GGGAATCTTCCACAATGGACGC AAGTCTGATGGAGCAACGCCGC GTGGATGAAGAAGGTCTTCGGA TCGTAAAATCCTGTTGTTGAAGA

			AGAACGGTTGTGAGAGTAACTG CTCATAACGTGACGGTAATCAA CCAGAAAGTCACGGCTAACTAC GTGCCAGCAGCCGCGGTAATAC GTAGGTGGCAAGCGTTGTCCG GATTTATTGGGCGTAAAGGGAG CGCAGGCGGTCTTTTAAGTCTG AATGTGAAAGCCCTCAGCTTAA CTGAGGAAGAGCATCGGAAACT GAGAGACTTGAGTGCAGAAGAG GAGAGTGGAATCCATGTGTAG CGGTGAAATGCGTAGATATATG GAAGAACACCAAGTGGCGAAGG CGGCTCTCTGGTCTGTTACTGA CGCTGAGGCTCGAAAGCATGG GTAGCGAACAGGATTAGATACC CTGGTAGTCCATGCCGTAAACG ATGAGTGCTAAGTGTTGGGAGG TTCCGCCTCTCAGTGCTGCAG CTAACGCATTAAGCACTCCGCC TGGGGAGTACGACCGCAAGGTT GAAACTCAAAGGAATTGACGGG GGCCCGCACAAAGCGGTGGAGC ATGTGGTTTAATTGAAGCAAC GCGAAGAACCCTTACCAGGTCTT GACATCTCCTGCAAGCCTAAGA GATTAGGGGTTCCCTTCGGGGA CAGGAAGACAGGTGGTGCATG GTTGTCGTCAGCTCGTGTCTG AGATGTTGGGTTAAGTCCCGCA ACGAGCGCAACCCTTGTTACTA GTTGCCAGCATTAAAGTTGGGCA CTCTAGTGAGACTGCCGGTGAC AAACCGGAGGAAGGTGGGGAC GACGTCAAATCATCATGCCCT TATGACCTGGGCTACACACGTG CTACAATGGATGGTACAATGAG AAGCGAACTCGCGAGGGGAAG CTGATCTCTGAAAACCATTCTCA GTTCCGATTGCAGGCTGCAACT
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			CGCCTGCATGAAGCTGGAATCG CTAGTAATCGCGGATCAGCATG CCGCGGTGAATACGTTCCCGG GCCTTGTACACACCGCCC (SEQ ID NO: 38)
Silk worm			
Enterococcus	<i>Bombyx mori</i>	Gut	AGGTGATCCAGCCGCACCTTCC GATACGGCTACCTTGTTACGAC TTCACCCCAATCATCTATCCAC CTTAGGCGGCTGGCTCCAAAA GGTTACCTCACCGACTTCGGGT GTTACAACTCTCGTGGTGTGA CGGGCGGTGTGTACAAGGCC GGGAACGTATTCACCGCGGCGT GCTGATCCGCGATTACTAGCGA TTCCGGCTTCATGCAGGCGAGT TGCAGCCTGCAATCCGAACTGA GAGAAGCTTTAAGAGATTTGCA TGACCTCGCGGTCTAGCGACTC GTTGTACTTCCCATTGTAGCAC GTGTGTAGCCCAGGTCATAAGG GGCATGATGATTTGACGTCATC CCCACCTTCTCCGGTTTGTCA CCGGCAGTCTCGCTAGAGTGCC CAACTAAATGATGGCAACTAAC AATAAGGGTTGCGCTCGTTGCG GGACTTAACCCAACATCTCACG ACACGAGCTGACGACAACCATG CACCACCTGTCACTTTGTCCCC GAAGGGAAAGCTCTATCTCTAG AGTGGTCAAAGGATGTCAAGAC CTGGTAAGGTTCTTCGCGTTGC TTCGAATTAACCACATGCTCCA CCGCTTGTGCGGGCCCCCGTC AATTCCTTTGAGTTTCAACCTTG CGGTGCTACTCCCAGGCGGA GTGCTTAATGCGTTTGCTGCAG CACTGAAGGGCGGAAACCCTCC AACACTTAGCACTCATCGTTTAC

		GGCGTGGACTACCAGGGTATCT AATCCTGTTTGCTCCCCACGCT TTCGAGCCTCAGCGTCAGTTAC AGACCAGAGAGCCGCCTTCGC CACTGGTGTTCTCCATATATCT ACGCATTTACCGCTACACATG GAATTCCTCTCCTCTTCTGCA CTCAAGTCTCCCAGTTTCCAAT GACCCTCCCCGGTTGAGCCGG GGGCTTTCACATCAGACTTAAG AAACCGCCTGCGCTCGCTTTAC GCCCAATAAATCCGGACAACGC TTGCCACCTACGTATTACGCG GCTGCTGGCACGTAGTTAGCCG TGGCTTCTGGTTAGATACCGT CAGGGGACGTTCACTTAAC GTCCTTGTTCTTCTCAACAACA GAGTTTTACGATCCGAAAACCTT CTTCACTCACGGCGGCTTGCTC GGTCAGACTTTTGTCCATTGCC GAAGATTCCCTACTGCTGCCTC CCGTAGGAGTCTGGGCCGTGT CTCAGTCCCAGTGTGGCCGATC ACCCTCTCAGGTCGGCTATGCA TCGTGGCCTTGGTGAGCCGTTA CCTCACCAACTAGCTAATGCAC CGCGGGTCCATCCATCAGCGAC ACCCGAAAGCGCCTTCACTCT TATGCCATGCGGCATAAACTGT TATGCGGTATTAGCACCTGTTTC CAAGTGTTATCCCCCTCTGATG GGTAGGTTACCCACGTGTTACT CACCCGTCCGCCACTCCTCTTT CCAATTGAGTGCAAGCACTCGG GAGGAAAGAAGCGTTCTGACTTG CATGTATTAGGCACGCCGCCAG CGTTCGTCCTGAGCCAGGATCA AACTCT (SEQ ID NO: 39)
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<i>Delftia</i>	<i>Bombyx mori</i>	Gut	CAGAAAGGAGGTGATCCAGCC GCACCTTCCGATACGGCTACCT TGTTACGACTTCACCCCAGTCA CGAACCCCGCCGTGGTAAGCG CCCTCCTTGCGGTTAGGCTACC TACTTCTGGCGAGACCCGCTCC CATGGTGTGACGGGCGGTGTG TACAAGACCCGGAACGTATT ACCGCGGCATGCTGATCCGCG ATTACTAGCGATTCCGACTTCAC GCAGTCGAGTTGCAGACTGCGA TCCGGACTACGACTGGTTTTAT GGGATTAGCTCCCCCTCGCGG GTTGGCAACCCTCTGTACCAGC CATTGTATGACGTGTGTAGCCC CACCTATAAGGGCCATGAGGAC TTGACGTCATCCCCACCTTCCT CCGGTTTGTACCGGCAGTCTC ATTAGAGTGCTCAACTGAATGTA GCAACTAATGACAAGGGTTGCG CTCGTTGCGGGACTTAACCCAA CATCTCACGACACGAGCTGACG ACAGCCATGCAGCACCTGTGTG CAGGTTCTCTTTGAGCACGAA TCCATCTCTGGAACTTCCTGC CATGTCAAAGGTGGGTAAGGTT TTTCGCGTTGCATCGAATTAAAC CACATCATCCACCGCTTGTGCG GGTCCCCGTCAATTCCTTTGAG TTTCAACCTTGCGGCCGTACTC CCCAGGCGGTCAACTCACGCG TTAGCTTCGTTACTGAGAAAAC AATTCCCAACAACCAGTTGACAT CGTTTAGGGCGTGGACTACCAG GGTATCTAATCCTGTTTGCTCCC CACGCTTTCGTGCATGAGCGTC AGTACAGGTCCAGGGGATTGCC TTCGCCATCGGTGTTCTCCGC ATATCTACGCATTTCACTGCTAC ACGCGGAATTCCATCCCCCTCT
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			ACCGTACTCTAGCCATGCAGTC ACAAATGCAGTTCCCAGGTTGA GCCCCGGGATTTCACATCTGTC TTACATAACCGCCTGCGCACGC TTTACGCCCAGTAATTCCGATTA ACGCTCGCACCCCTACGTATTAC CGCGGCTGCTGGCACGTAGTTA GCCGGTGCTTATTCTTACGGTA CCGTCATGGGCCCCCTGTATTA GAAGGAGCTTTTTCGTTCCGTA CAAAAGCAGTTTACAACCCGAA GGCCTTCATCCTGCACGCGGCA TTGCTGGATCAGGCTTTCGCCC ATTGTCCAAAATTCCCCACTGCT GCCTCCCGTAGGAGTCTGGGC CGTGTCTCAGTCCCAGTGTGGC TGGTCGTCTCTCAGACCAGCT ACAGATCGTCGGCTTGGTAAGC TTTTATCCCACCAACTACCTAAT CTGCCATCGGCCGCTCCAATCG CGCGAGGCCCGAAGGGCCCCC GCTTTCATCCTCAGATCGTATG CGGTATTAGCTACTCTTTCGAGT AGTTATCCCCACGACTGGGCA CGTTCCGATGTATTACTACCC GTTCGCCACTCGTCAGCGTCCG AAGACCTGTTACCGTTGACTT GCATGTGTAAGGCATGCCGCCA GCGTTCAATCTGAGCCAGGATC AAACTCTACAGTTCGATCT (SEQ ID NO: 40)
<i>Pelomonas</i>	<i>Bombyx mori</i>	Gut	ATCCTGGCTCAGATTGAACGCT GGCGGCATGCCTTACACATGCA AGTCGAACGGTAACAGGTTAAG CTGACGAGTGGCGAACGGGTG AGTAATATATCGGAACGTGCCC AGTCGTGGGGGATAACTGCTCG AAAGAGCAGCTAATACCGCATA CGACCTGAGGGTGAAAGCGGG GGATCGCAAGACCTCGCNGAT

		TGGAGCGGCCGATATCAGATTA GGTAGTTGGTGGGGTAAAGGC CCACCAAGCCAACGATCTGTAG CTGGTCTGAGAGGACGACCAG CCACACTGGGACTGAGACACG GCCCAGACTCCTACGGGAGGC AGCAGTGGGGAATTTGGACAA TGGGCGCAAGCCTGATCCAGC CATGCCGCGTGC GGGAAGAAG GCCTTCGGGTTGTAAACCGCTT TTGTCAGGGAAGAAAAGTTCT GGTTAATACCTGGGACTCATGA CGGTACCTGAAGAATAAGCACC GGCTAACTACGTGCCAGCAGCC GCGGTAATACGTAGGGTGCAAG CGTTAATCGGAATTACTGGGCG TAAAGCGTGCGCAGGCGGTTAT GCAAGACAGAGGTGAAATCCCC GGGCTCAACCTGGGAACTGCCT TTGTGACTGCATAGCTAGAGTA CGGTAGAGGGGGATGGAATTC CGCGTGTAGCAGTGAAATGCGT AGATATGCGGAGGAACACCGAT GGCGAAGGCAATCCCCTGGAC CTGTACTGACGCTCATGCACGA AAGCGTGGGAGCAAACAGGA TTAGATACCCTGGTAGTCCACG CCCTAAACGATGTCAACTGGTT GTTGGGAGGGTTTCTTCTCAGT AACGTANNTAACGCGTGAAGTT GACCGCCTGGGGAGTACGGCC GCAAGGTTGAAACTCAAAGGAA TTGACGGGGACCCGCACAAGC GGTGGATGATGTGGTTTAATTC GATGCAACGCGAAAAACCTTAC CTACCCTTGACATGCCAGGAAT CCTGAAGAGATTTGGGAGTGCT CGAAAGAGAACCTGGACACAGG TGCTGCATGGCCGTGTCAGCT CGTGTCGTGAGATGTTGGGTTA
--	--	--

			AGTCCCGCAACGAGCGCAACC CTTGTCATTAGTTGCTACGAAAG GGCACTCTAATGAGACTGCCGG TGACAAACCGGAGGAAGGTGG GGATGACGTCAGGTCATCATGG CCCTTATGGGTAGGGCTACACA CGTCATACAATGGCCGGGACAG AGGGCTGCCAACCCGCGAGGG GGAGCTAATCCCAGAAACCCGG TCGTAGTCCGGATCGTAGTCTG CAACTCGACTGCGTGAAGTCGG AATCGCTAGTAATCGCGGATCA GCTTGCCGCGGTGAATACGTTT CCGGGTCTTGTACACACCGCCC GTCACACCATGGGAGCGGGTTC TGCCAGAAGTAGTTAGCCTAAC CGCAAGGAGGGCGATTACCAC GGCAGGGTTCGTGACTGGGGT GAAGTCGTAACAAGGTAGCCGT ATCGGAAGGTGCGGCTGGATCA C (SEQ ID NO: 41)
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Any number of bacterial species may be targeted by the compositions or methods described herein. For example, in some instances, the modulating agent may target a single bacterial species. In some instances, the modulating agent may target at least about any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 500, or more distinct bacterial species. In some instances, the modulating agent may target any one of about 1 to about 5, about 5 to about 10, about 10 to about 20, about 20 to about 50, about 50 to about 100, about 100 to about 200, about 200 to about 500, about 10 to about 50, about 5 to about 20, or about 10 to about 100 distinct bacterial species. In some instances, the modulating agent may target at least about any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, or more phyla, classes, orders, families, or genera of bacteria.

In some instances, the modulating agent may increase a population of one or more bacteria (e.g., symbiotic bacteria) by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more in the host in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may reduce the population of one or more bacteria (e.g., pathogenic or parasitic bacteria) by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in the host in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may eradicate the population of a bacterium (e.g., a pathogenic or parasitic bacteria) in the host. In some instances, the modulating agent may increase the level of one or more symbiotic bacteria by at least about any of 10%, 20%, 30%, 40%, 50%,

60%, 70%, 80%, 90% or more in the host and/or decreases the level of one or more pathogenic bacteria by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in the host in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the modulating agent may alter the bacterial diversity and/or bacterial composition of the host. In some instances, the modulating agent may increase the bacterial diversity in the host relative to a starting diversity by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may decrease the bacterial diversity in the host relative to a starting diversity by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the modulating agent may alter the function, activity, growth, and/or division of one or more bacterial cells. For example, the modulating agent may alter the expression of one or genes in the bacteria. In some instances, the modulating agent may alter the function of one or more proteins in the bacteria. In some instances, the modulating agent may alter the function of one or more cellular structures (e.g., the cell wall, the outer or inner membrane) in the bacteria. In some instances, the modulating agent may kill (e.g., lyse) the bacteria.

The target bacterium may reside in one or more parts of the insect. Further, the target bacteria may be intracellular or extracellular. In some instances, the bacteria reside in or on one or more parts of the host gut, including, e.g., the foregut, midgut, and/or hindgut. In some instances, the bacteria reside as an intracellular bacteria within a cell of the host insect. In some instances, the bacteria reside in a bacteriocyte of the host insect.

Changes to the populations of bacteria in the host may be determined by any methods known in the art, such as microarray, polymerase chain reaction (PCR), real-time PCR, flow cytometry, fluorescence microscopy, transmission electron microscopy, fluorescence *in situ* hybridization (e.g., FISH), spectrophotometry, matrix-assisted laser desorption ionization-mass spectrometry (MALDI-MS), and DNA sequencing. In some instances, a sample of the host treated with a modulating agent is sequenced (e.g., by metagenomics sequencing of 16S rRNA or rDNA) to determine the microbiome of the host after delivery or administration of the modulating agent. In some instances, a sample of a host that did not receive the modulating agent is also sequenced to provide a reference.

ii. Fungi

Exemplary fungi that may be targeted in accordance with the methods and compositions provided herein, include, but are not limited to *Amylostereum areolatum*, *Epichloe spp*, *Pichia pinus*, *Hansenula capsulate*, *Daldinia decipien*, *Ceratocytis spp*, *Ophiostoma spp*, and *Attamyces bromatificus*. Non-limiting examples of yeast and yeast-like symbionts found in insects include *Candida*, *Metschnikowia*, *Debaromyces*, *Scheffersomyces shehatae* and *Scheffersomyces stipites*, *Starmerella*, *Pichia*, *Trichosporon*, *Cryptococcus*, *Pseudozyma*, and yeast-like symbionts from the subphylum *Pezizomycotina* (e.g., *Symbiotaphrina buchneri* and *Symbiotaphrina kochii*). Non-limiting examples of yeast that may be targeted by the methods and compositions herein are listed in Table 2.

Table 2

Insect Species	Order: Family	Yeast Location (Species)
<i>Stegobium paniceum</i>	Coleoptera: Anobiidae	Mycetomes
(= <i>Sitodrepa panicea</i>)		(<i>Saccharomyces</i>)
		Cecae (<i>Torulopsis buchnerii</i>)
		Mycetome between foregut and midgut
		Mycetomes (<i>Symbiotaphrina buchnerii</i>)
		Mycetomes and digestive tube (<i>Torulopsis buchnerii</i>)
		Gut cecae (<i>Symbiotaphrina buchnerii</i>)
<i>Lasioderma serricorne</i>	Coleoptera: Anobiidae	Mycetome between foregut and midgut
		(<i>Symbiotaphrina kochii</i>)
<i>Ernobius abietis</i>	Coleoptera: Anobiidae	Mycetomes (<i>Torulopsis karawaiewii</i>)
		(<i>Candida karawaiewii</i>)
<i>Ernobius mollis</i>	Coleoptera: Anobiidae	Mycetomes (<i>Torulopsis ernobii</i>)
		(<i>Candida ernobii</i>)
<i>Hemicoelus gibbicollis</i>	Coleoptera: Anobiidae	Larval mycetomes
<i>Xestobium plumbeum</i>	Coleoptera: Anobiidae	Mycetomes (<i>Torulopsis xestobii</i>)
		(<i>Candida xestobii</i>)
<i>Criocephalus rusticus</i>	Coleoptera: Cerambycidae	Mycetomes
<i>Phoracantha semipunctata</i>	Coleoptera: Cerambycidae	Alimentary canal (<i>Candida guilliermondii</i> , <i>C. tenuis</i>)
		Cecae around midgut (<i>Candida guilliermondii</i>)
<i>Harpium inquisitor</i>	Coleoptera: Cerambycidae	Mycetomes (<i>Candida rhagii</i>)
<i>Harpium mordax</i> <i>H. sycophanta</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida tenuis</i>)
<i>Gaurotes virginea</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida rhagii</i>)
<i>Leptura rubra</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida tenuis</i>)
		Cecae around midgut (<i>Candida parapsilosis</i>)
<i>Leptura maculicornis</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida parapsilosis</i>)

<i>L. cerambyciformis</i>		
<i>Leptura sanguinolenta</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida</i> sp.)
<i>Rhagium bifasciatum</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida tenuis</i>)
<i>Rhagium inquisitor</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida guilliermondii</i>)
<i>Rhagium mordax</i>	Coleoptera: Cerambycidae	Cecae around midgut (<i>Candida</i>)
<i>Carpophilus hemipterus</i>	Coleoptera: Nitidulidae	Intestinal tract (10 yeast species)
<i>Odontotaenius disjunctus</i>	Coleoptera: Passalidae	Hindgut (<i>Enteroramus dimorphus</i>)
<i>Odontotaenius disjunctus</i>	Coleoptera: Passalidae	Gut (<i>Pichia stipitis</i> , <i>P. segobiensis</i> , <i>Candida shehatae</i>)
<i>Verres sternbergianus</i>		(<i>C. ergatensis</i>)
<i>Scarabaeus semipunctatus</i>	Coleoptera: Scarabaeidae	Digestive tract (10 yeast species)
<i>Chironitis furcifer</i>		
<i>Unknown species</i>	Coleoptera: Scarabaeidae	Guts (<i>Trichosporon cutaneum</i>)
<i>Dendroctonus and Ips spp.</i>	Coleoptera: Scolytidae	Alimentary canal (13 yeast species)
<i>Dendroctonus frontalis</i>	Coleoptera: Scolytidae	Midgut (<i>Candida</i> sp.)
<i>Ips sexdentatus</i>	Coleoptera: Scolytidae	Digestive tract (<i>Pichia bovis</i> , <i>P. rhodanensis</i>)
		<i>Hansenula holstii</i> (<i>Candida rhagii</i>)
		Digestive tract
		(<i>Candida pulcherina</i>)
<i>Ips typographus</i>	Coleoptera: Scolytidae	Alimentary canal
		Alimentary tracts (<i>Hansenula capsulata</i> , <i>Candida parapsilosis</i>)
		Guts and beetle homogenates (<i>Hansenula holstii</i> , <i>H. capsulata</i> , <i>Candida diddensii</i> , <i>C. mohshtana</i> , <i>C. nitratophila</i> , <i>Cryptococcus albidus</i> , <i>C. laurentii</i>)
<i>Trypodendron lineatum</i>	Coleoptera: Scolytidae	Not specified

<i>Xyloterinus politus</i>	Coleoptera: Scolytidae	Head, thorax, abdomen (<i>Candida</i> , <i>Pichia</i> , <i>Saccharomycopsis</i>)
<i>Periplaneta americana</i>	Dictyoptera: Blattidae	Hemocoel (<i>Candida</i> sp. nov.)
<i>Blatta orientalis</i>	Dictyoptera: Blattidae	Intestinal tract (<i>Kluyveromyces blattae</i>)
<i>Blatella germanica</i>	Dictyoptera: Blattellidae	Hemocoel
<i>Cryptocercus punctulatus</i>	Dictyoptera: Cryptocercidae	Hindgut (1 yeast species)
<i>Philophylla heraclei</i>	Diptera: Tephritidae	Hemocoel
<i>Aedes</i> (4 species)	Diptera: Culicidae	Internal microflora (9 yeast genera)
<i>Drosophila pseudoobscura</i>	Diptera: Drosophilidae	Alimentary canal (24 yeast species)
<i>Drosophila</i> (5 spp.)	Diptera: Drosophilidae	Crop (42 yeast species)
<i>Drosophila melanogaster</i>	Diptera: Drosophilidae	Crop (8 yeast species)
<i>Drosophila</i> (4 spp.)	Diptera: Drosophilidae	Crop (7 yeast species)
<i>Drosophila</i> (6 spp.)	Diptera: Drosophilidae	Larval gut (17 yeast species)
<i>Drosophila</i> (20 spp.)	Diptera: Drosophilidae	Crop (20 yeast species)
<i>Drosophila</i> (8 species groups)	Diptera: Drosophilidae	Crop (<i>Kloeckera</i> , <i>Candida</i> , <i>Kluyveromyces</i>)
<i>Drosophila serido</i>	Diptera: Drosophilidae	Crop (18 yeast species)
<i>Drosophila</i> (6 spp.)	Diptera: Drosophilidae	Intestinal epithelium (<i>Coccidiascus legeri</i>)
<i>Protaxymia melanoptera</i>	Diptera	Unknown (<i>Candida</i> , <i>Cryptococcus</i> , <i>Sporobolomyces</i>)
<i>Astegopteryx styraci</i>	Homoptera: Aphididae	Hemocoel and fat body
<i>Tuberaphis</i> sp.	Homoptera: Aphididae	Tissue sections
<i>Hamiltonaphis styraci</i>		
<i>Glyphinaphis bambusae</i>		
<i>Cerataphis</i> sp.		
<i>Hamiltonaphis styraci</i>	Homoptera: Aphididae	Abdominal hemocoel
<i>Cofana unimaculata</i>	Homoptera: Cicadellidae	Fat body

<i>Leofa unicolor</i>	Homoptera: Cicadellidae	Fat body
<i>Lecaniines, etc.</i>	Homoptera: Coccoidea d	Hemolymph, fatty tissue, etc.
<i>Lecanium sp.</i>	Homoptera: Coccidae	Hemolymph, adipose tissue
<i>Ceroplastes (4 sp.)</i>	Homoptera: Coccidae	Blood smears
<i>Laodelphax striatellus</i>	Homoptera: Delphacidae	Fat body
		Eggs
		Eggs (<i>Candida</i>)
<i>Nilaparvata lugens</i>	Homoptera: Delphacidae	Fat body
		Eggs (2 unidentified yeast species)
		Eggs, nymphs (<i>Candida</i>)
		Eggs (7 unidentified yeast species)
		Eggs (<i>Candida</i>)
<i>Nisia nervosa</i>	Homoptera: Delphacidae	Fat body
<i>Nisia grandiceps</i>		
<i>Perkinsiella spp.</i>		
<i>Sardia rostrata</i>		
<i>Sogatella furcifera</i>		
<i>Sogatodes orizicola</i>	Homoptera: Delphacidae	Fat body
<i>Amrasca devastans</i>	Homoptera: Jassidae	Eggs, mycetomes, hemolymph
<i>Tachardina lobata</i>	Homoptera: Kerriidae	Blood smears (<i>Torulopsis</i>)
<i>Laccifer (=Lakshadia) sp.</i>	Homoptera: Kerriidae	Blood smears (<i>Torula variabilis</i>)
<i>Comperia merceti</i>	Hymenoptera: Encyrtidae	Hemolymph, gut, poison gland
<i>Solenopsis invicta</i>	Hymenoptera: Formicidae	Hemolymph (<i>Myrmecomyces annellisae</i>)
<i>S. quinquecupis</i>		
<i>Solenopsis invicta</i>	Hymenoptera: Formicidae	Fourth instar larvae (<i>Candida parapsilosis</i> , <i>Yarrowia lipolytica</i>)
		Gut and hemolymph (<i>Candida parapsilosis</i> , <i>C. lipolytica</i> , <i>C.</i>

		<i>guillermoidii</i> , <i>C. rugosa</i> , <i>Debaryomyces hansenii</i>)
<i>Apis mellifera</i>	Hymenoptera: Apidae	Digestive tracts (<i>Torulopsis</i> sp.)
		Intestinal tract (<i>Torulopsis apicola</i>)
		Digestive tracts (8 yeast species)
		Intestinal contents (12 yeast species)
		Intestinal contents (7 yeast species)
		Intestines (14 yeast species)
		Intestinal tract (<i>Pichia melissophila</i>)
		Intestinal tracts (7 yeast species)
		Alimentary canal (<i>Hansenula silvicola</i>)
		Crop and gut (13 yeast species)
<i>Apis mellifera</i>	Hymenoptera: Apidae	Midguts (9 yeast genera)
<i>Anthophora occidentalis</i>	Hymenoptera:Anthophoridae	
<i>Nomia melanderi</i>	Hymenoptera:Halictidae	
<i>Halictus rubicundus</i>	Hymenoptera:Halictidae	
<i>Megachile rotundata</i>	Hymenoptera:Megachilidae	

Any number of fungal species may be targeted by the compositions or methods described herein. For example, in some instances, the modulating agent may target a single fungal species. In some instances, the modulating agent may target at least about any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 500, or more distinct fungal species. In some instances, the modulating agent may target any one of about 1 to about 5, about 5 to about 10, about 10 to about 20, about 20 to about 50, about 50 to about 100, about 100 to about 200, about 200 to about 500, about 10 to about 50, about 5 to about 20, or about 10 to about 100 distinct fungal species. In some instances, the modulating agent may target at least about any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, or more phyla, classes, orders, families, or genera of fungi.

In some instances, the modulating agent may increase a population of one or more fungi (e.g., symbiotic fungi) by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more in the host in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may reduce the population of one or more fungi (e.g., pathogenic or parasitic fungi) by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more in the host in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may eradicate the population of a fungi (e.g., a pathogenic or parasitic fungi) in the host. In some instances, the modulating agent may increase the level of one or more symbiotic fungi by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more in the host and/or may decrease the level of one or more pathogenic fungi by at least about any of 10%,

20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more in the host in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the modulating agent may alter the fungal diversity and/or fungal composition of the host. In some instances, the modulating agent may increase the fungal diversity in the host relative to a starting diversity by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in comparison to a host organism to which the modulating agent has not been administered. In some instances, the modulating agent may decrease the fungal diversity in the host relative to a starting diversity by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more in comparison to a host organism to which the modulating agent has not been administered.

In some instances, the modulating agent may alter the function, activity, growth, and/or division of one or more fungi. For example, the modulating agent may alter the expression of one or more genes in the fungus. In some instances, the modulating agent may alter the function of one or more proteins in the fungus. In some instances, the modulating agent may alter the function of one or more cellular components in the fungus. In some instances, the modulating agent may kill the fungus.

Further, the target fungus may reside in one or more parts of the insect. In some instances, the fungus resides in or on one or more parts of the insect gut, including, e.g., the foregut, midgut, and/or hindgut. In some instances, the fungus lives extracellularly in the hemolymph, fat bodies or in specialized structures in the host.

Changes to the population of fungi in the host may be determined by any methods known in the art, such as microarray, polymerase chain reaction (PCR), real-time PCR, flow cytometry, fluorescence microscopy, transmission electron microscopy, fluorescence *in situ* hybridization (e.g., FISH), spectrophotometry, matrix-assisted laser desorption ionization-mass spectrometry (MALDI-MS), and DNA sequencing. In some instances, a sample of the host treated with a modulating agent is sequenced (e.g., by metagenomics sequencing) to determine the microbiome of the host after delivery or administration of the modulating agent. In some instances, a sample of a host that did not receive the modulating agent is also sequenced to provide a reference.

III. Modulating Agents

The modulating agent of the methods and compositions provided herein may include a phage, a polypeptide, a small molecule, an antibiotic, a secondary metabolite, a bacterium, a fungus, or any combination thereof.

i. Phage

The modulating agent described herein may include a phage (e.g., a lytic phage or a non-lytic phage). In some instances, an effective concentration of any phage described herein may altering a level, activity, or metabolism of one or more microorganisms (as described herein) resident in a host described herein, the alteration resulting in an increase in the host's fitness. In some instances, the modulating agent includes at least one phage selected from the order *Tectiviridae*, *Myoviridae*, *Siphoviridae*, *Podoviridae*, *Caudovirales*, *Lipothrixviridae*, *Rudiviridae*, or *Ligamenvirales*. In some instances, the composition includes at least one phage selected from the family *Myoviridae*, *Siphoviridae*,

Podoviridae, *Lipothrixviridae*, *Rudiviridae*, *Ampullaviridae*, *Bicaudaviridae*, *Clavaviridae*, *Corticoviridae*, *Cystoviridae*, *Fuselloviridae*, *Gluboloviridae*, *Guttaviridae*, *Inoviridae*, *Leviviridae*, *Microviridae*, *Plasmaviridae*, and *Tectiviridae*. Further non-limiting examples of phages useful in the methods and compositions are listed in Table 3.

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Table 3: Examples of Phage and Targeted Bacteria

Phage and Accession #	Target bacteria	Target host
SA1(NC_027991), phiP68 (NC_004679)	<i>Staphylococcus</i> sp.	<i>Apidae</i> family
WO (AB036666.1)	<i>Wolbachia</i> sp.	<i>Aedes aegypti</i> ; <i>Drosophila melanogaster</i> ; <i>Plasmodium</i> sp.; <i>Teleogryllus taiwanemma</i> ; <i>Bombyx mori</i>
KL1 (NC_018278), BcepNazgul (NC_005091) PhiE125 (NC_003309)	<i>Burkholderia</i> sp.	<i>Riptortus</i> sp.; <i>Pyrrhocoris apterus</i> .
Fern (NC_028851), Xenia (NC_028837), HB10c2 (NC_028758)	<i>Paenibacillus</i> larvae	bumble bees: <i>Bombus</i> sp.; honey bees: <i>A. mellifera</i>
CP2 (NC_020205), XP10 (NC_004902), XP15 (NC_007024), phiL7 (NC_012742)	<i>Xanthomonas</i> sp.	<i>Plebeina denoiti</i> ; <i>Apidae</i> family; <i>Apis mellifera</i> ; <i>Drosophilidae</i> family; and <i>Chloropidae</i> family
PP1 (NC_019542), PM1 (NC_023865)	<i>Pectobacterium carotovorum</i> subsp. <i>carotovorum</i>	<i>Apidae</i> family
ΦRSA1 (NC_009382), ΦRSB1 (NC_011201), ΦRSL1 (NC_010811), RSM1 (NC_008574)	<i>Ralstonia solanacearum</i>	<i>Bombyx mori</i>
SF1(NC_028807)	<i>Streptomyces scabies</i>	<i>Philantus</i> sp.; <i>Trachypus</i> sp
ECML-4 (NC_025446), ECML-117 (NC_025441), ECML-134 (NC_025449)	<i>Escherichia coli</i>	<i>Apidae</i> family; <i>Varroa destructor</i>
SSP5(JX274646.1), SSP6 (NC_004831), SFP10 (NC_016073), F18SE (NC_028698)	<i>Salmonella</i> sp.	<i>Drosophilidae</i> family
γ (NC_001416), Bcp1 (NC_024137)	<i>Bacillus</i> sp.	Gypsy moth; <i>Lymantria dispar</i> ; <i>Varroa destructor</i>

Phi1 (NC_009821)	<i>Enterococcus</i> <i>sp.</i>	<i>Schistocerca gregaria</i>
ΦKMV (NC_005045), ΦEL(AJ697969.1), ΦKZ (NC_004629)	<i>Pseudomonas</i> <i>sp.</i>	<i>Lymantria dispar</i> ; <i>Apidae</i> family
A2 (NC_004112), phig1e (NC_004305)	<i>Lactobacilli sp.</i>	<i>Apidae</i> family; <i>Drosophila</i> family; <i>Varroa destructor</i>
KLPN1 (NC_028760)	<i>Klebsiella sp</i>	<i>C. capitata</i>
vB_AbaM_Acibel004 (NC_025462), vB_AbaP_Acibel007 (NC_025457)	<i>Acinetobacter</i> <i>sp.</i>	<i>Schistocerca gregaria</i>

In some instances, a modulating agent includes a lytic phage. Thus, after delivery of the lytic phage to a bacterial cell resident in the host, the phage causes lysis in the target bacterial cell. In some instances, the lytic phage targets and kills a bacterium resident in a host insect to increase the fitness of the host. Alternatively or additionally, the phage of the modulating agent may be a non-lytic phage (also referred to as lysogenic or temperate phage). Thus, after delivery of the non-lytic phage to a bacterial cell resident in the host, the bacterial cell may remain viable and able to stably maintain expression of genes encoded in the phage genome. In some instances, a non-lytic phage is used to alter gene expression in a bacterium resident in a host insect to increase the fitness of the host. In some instances, the modulating agent includes a mixture of lytic and non-lytic phage.

The modulating agent described herein may include phage with either a narrow or broad bacterial target range. In some instances, the phage has a narrow bacterial target range. In some instances, the phage is a promiscuous phage with a large bacterial target range. For example, the promiscuous phage may target at least about any of 5, 10, 20, 30, 40, 50, or more bacterium resident in the host. A phage with a narrow bacterial target range may target a specific bacterial strain in the host without affecting another, e.g., non-targeted, bacterium in the host. For example, the phage may target no more than about any of 50, 40, 30, 20, 10, 8, 6, 4, 2, or 1 bacterium resident in the host.

The compositions described herein may include any number of phage, such as at least about any one of 1, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, or more phage. In some instances, the composition includes phage from one or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, or more phage) families, one or more orders (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, or more phage), or one or more species (e.g., 1, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, or more phage). Compositions including one or more phage are also referred herein as "phage cocktails." Phage cocktails are useful because they allow for targeting of a wider host range of bacteria. Furthermore, they allow for each bacterial strain (i.e. subspecies) to be targeted by multiple orthogonal phages, thereby preventing or significantly delaying the onset of resistance. In some instances, a cocktail includes multiple phages targeting one bacterial species. In some instances, a cocktail includes multiple phages targeting multiple bacterial species. In some instances, a one-phage "cocktail" includes a single promiscuous phage (i.e. a phage with a large host range) targeting many strains within a species.

Suitable concentrations of the phage in the modulating agent described herein depends on factors such as efficacy, survival rate, transmissibility of the phage, number of distinct phage, and/or lysis

types in the compositions, formulation, and methods of application of the composition. In some instances, the phage is in a liquid or a solid formulation. In some instances, the concentration of each phage in any of the compositions described herein is at least about any of 10^2 , 10^3 , 10^4 , 10^5 , 10^6 , 10^7 , 10^8 , 10^9 , 10^{10} or more pfu/ml. In some instances, the concentration of each phage in any of the compositions described herein is no more than about any of 10^2 , 10^3 , 10^4 , 10^5 , 10^6 , 10^7 , 10^8 , 10^9 pfu/ml. In some instances, the concentration of each phage in the composition is any of about 10^2 to about 10^3 , about 10^3 to about 10^4 , about 10^4 to about 10^5 , about 10^5 to about 10^6 , about 10^7 to about 10^8 , about 10^8 to about 10^9 , about 10^2 to about 10^4 , about 10^4 to about 10^6 , about 10^6 to about 10^9 , or about 10^3 to about 10^8 pfu/ml. In some instances, wherein the composition includes at least two types of phages, the concentration of each type of the phages may be the same or different. For example, in some instances, the concentration of one phage in the cocktail is about 10^8 pfu/ml and the concentration of a second phage in the cocktail is about 10^6 pfu/ml.

A modulating agent including a phage as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of phage concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of phage concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of phage concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

As illustrated by Example 7 and 9, phages can be used as a modulating agents by eliminating bacterial pathogens such as *Serratia marcescens*, *Erwinia carotovora*, and *Pseudomonas entomophila* from insect hosts, such as crickets.

ii. Polypeptides

Numerous polypeptides (e.g., a bacteriocin, R-type bacteriocin, nodule C-rich peptide, antimicrobial peptide, lysin, or bacteriocyte regulatory peptide) may be used in the compositions and methods described herein. In some instances, an effective concentration of any peptide or polypeptide described herein may alter a level, activity, or metabolism of one or more microorganisms (as described herein) resident in a host, the alteration resulting in an increase in the host's fitness. Polypeptides included herein may include naturally occurring polypeptides or recombinantly produced variants. For example, the polypeptide may be a functionally active variant of any of the polypeptides described herein with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a polypeptide described herein or a naturally occurring polypeptide.

A modulating agent comprising a polypeptide as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of

one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

(a) *Bacteriocins*

- 5 The modulating agent described herein may include a bacteriocin. In some instances, the bacteriocin is naturally produced by Gram-positive bacteria, such as *Pseudomonas*, *Streptomyces*, *Bacillus*, *Staphylococcus*, or lactic acid bacteria (LAB, such as *Lactococcus lactis*). In some instances, the bacteriocin is naturally produced by Gram-negative bacteria, such as *Hafnia alvei*, *Citrobacter freundii*, *Klebsiella oxytoca*, *Klebsiella pneumonia*, *Enterobacter cloacae*, *Serratia plymthicum*,
10 *Xanthomonas campestris*, *Erwinia carotovora*, *Ralstonia solanacearum*, or *Escherichia coli*. Exemplary bacteriocins include, but are not limited to, Class I-IV LAB antibiotics (such as lantibiotics), colicins, microcins, and pyocins. Non-limiting examples of bacteriocins are listed in Table 4.

Table 4: Examples of Bacteriocins

Class	Name	Producer	Targets	Sequence
Class I	nisin	<i>Lactococcus lactis</i>	Active on Gram-positive bacteria: <i>Enterococcus</i> - <i>Lactobacillus</i> - <i>Lactococcus</i> - <i>Leuconostoc</i> – <i>Listeria</i> - <i>clostridium</i>	ITSISLCTPGCKT GALMGCNMKTA TCHCSIHVSK (SEQ ID NO: 42)
	epidermin	<i>Staphylococcus epidermis</i>	Gram-positive bacteria	IASKFICTPGCA KTGSFNSYCC (SEQ ID NO: 43)
Class II				
Class II a	pediocin PA-1	<i>Pediococcus acidilactici</i>	<i>Pediococci</i> - <i>Lactobacilli</i> - <i>Leuconostoc</i> - <i>Brochothrix</i> <i>thermosphacta</i> - <i>propionibacteria</i> - <i>Bacilli</i> - <i>Enterococci</i> - <i>Staphylococci</i> - <i>Listeria clostridia</i> - <i>Listeria</i> <i>monocytogenes</i> - <i>Listeria</i> <i>innocua</i>	KYYGNGVTCG KHSCSVDWGK ATTCTINNGAMA WATGGHQGNH KC (SEQ ID NO: 44)
Class II b	Enterocin P	<i>Enterococcus faecium</i>	<i>Lactobacillus sakei</i> - <i>Enterococcus faecium</i>	ATRSYGNGVYC NNSKCWVNWG EAKENIAGIVISG WASGLAGMGH (SEQ ID NO: 45)

Class II c	lactococci n G	<i>Streptococcus lactis</i>	Gram-positive bacteria	GTWDDIGQGIG RVAYWVGKAM GNMSDVNQAS RINRKKKH (SEQ ID NO: 46)
Class II d	Lactacin-F	<i>Lactobacillus johnsonii</i>	<i>Lactobacilli - Enterococcus faecalis</i>	NRWGDTVLSAA SGAGTGKACK SFGPWGMAICG VGGAAIGGYFG YTHN (SEQ ID NO: 47)
Class III				
Class III a	Enterocin AS-48	<i>Enterococcus faecalis</i>	Broad spectrum: Gram positive and Gram negative bacteria.	MAKEFGIPAAVA GTVLNVEAGG WVTIVSILTAV GSGGLSLLAAA GRESIKAYLKKE IKKKGKRAVIAW (SEQ ID NO: 48)
Class III b	aureocin A70	<i>Staphylococcus aureus</i>	Broad spectrum: Gram positive and Gram negative bacteria.	MSWLNFLKYIAK YGKKAWSAAWK YKGKVLEWLVN GPTLEWVWQKL KKIAGL (SEQ ID NO: 49)
Class IV	Garvicin A	<i>Lactococcus garvieae</i>	Broad spectrum: Gram positive and Gram negative bacteria.	IGGALGNALNGL GTWANMMNGG GFVNQWQVYA NKGKINQYRPY (SEQ ID NO: 50)
Unclassified	Colicin V	<i>Escherichia coli</i>	Active against <i>Escherichia coli</i> (also closely related bacteria) - Enterobacteriaceae	MRTLTLNELDS VSGGASGRDIA MAIGTLGQFV AGGIGAAAGGV AGGAIYDYAST HKPNPAMSPSG LGGTIKQKPEGI PSEAWNYAAGR LCNWSPNNLSD VCL (SEQ ID NO: 51)

In some instances, the bacteriocin is a colicin, a pyocin, or a microcin produced by Gram-negative bacteria. In some instances, the bacteriocin is a colicin. The colicin may be a group A colicin (e.g., uses the Tol system to penetrate the outer membrane of a target bacterium) or a group B colicin (e.g., uses the Ton system to penetrate the outer membrane of a target bacterium). In some instances, the bacteriocin is a microcin. The microcin may be a class I microcin (e.g., < 5 kDa, has post-translational modifications) or a class II microcin (e.g., 5-10 kDa, with or without post-translational modifications). In some instances, the class II microcin is a class IIa microcin (e.g., requires more than one genes to synthesize and assemble functional peptides) or a class IIb microcin (e.g., linear peptides with or without post-translational modifications at C-terminus). In some instances, the bacteriocin is a pyocin. In some instances, the pyocin is an R-pyocin, F-pyocin, or S-pyocin.

In some instances, the bacteriocin is a class I, class II, class III, or class IV bacteriocin produced by Gram-positive bacteria. In some instances, the modulating agent includes a Class I bacteriocin (e.g., lanthionine-containing antibiotics (lantibiotics) produced by a Gram-positive bacteria). The class I bacteriocins or lantibiotic may be a low molecular weight peptide (e.g., less than about 5 kDa) and may possess post-translationally modified amino acid residues (e.g., lanthionine, β -methylanthionine, or dehydrated amino acids).

In some instances, the bacteriocin is a Class II bacteriocin (e.g., non-lantibiotics produced by Gram-positive bacteria). Many are positively charged, non-lanthionine-containing peptides, which unlike lantibiotics, do not undergo extensive post-translational modification. The Class II bacteriocin may belong to one of the following subclasses: "pediocin-like" bacteriocins (e.g., pediocin PA-1 and carnobacteriocin X (Class IIa)); two-peptide bacteriocins (e.g., lactacin F and ABP-118 (Class IIb)); circular bacteriocins (e.g., carnocyclin A and enterocin AS-48 (Class IIc)); or unmodified, linear, non-pediocin-like bacteriocins (e.g., epidermicin NI01 and lactococcin A (Class IId)).

In some instances, the bacteriocin is a Class III bacteriocin (e.g., produced by Gram-positive bacteria). Class III bacteriocins may have a molecular weight greater than 10 kDa and may be heat unstable proteins. The Class III bacteriocins can be further subdivided into Group IIIA and Group IIIB bacteriocins. The Group IIIA bacteriocins include bacteriolytic enzymes which kill sensitive strains by lysis of the cell wall, such as Enterolysin A. Group IIIB bacteriocins include non-lytic proteins, such as Caseicin 80, Helveticin J, and lactacin B.

In some instances, the bacteriocin is a Class IV bacteriocin (e.g., produced by Gram-positive bacteria). Class IV bacteriocins are a group of complex proteins, associated with other lipid or carbohydrate moieties, which appear to be required for activity. They are relatively hydrophobic and heat stable. Examples of Class IV bacteriocins leuconocin S, lactocin 27, and lactocin S.

In some instances, the bacteriocin is an R-type bacteriocin. R-type bacteriocins are contractile bacteriocidal protein complexes. Some R-type bacteriocins have a contractile phage-tail-like structure. The C-terminal region of the phage tail fiber protein determines target-binding specificity. They may attach to target cells through a receptor-binding protein, e.g., a tail fiber. Attachment is followed by sheath contraction and insertion of the core through the envelope of the target bacterium. The core penetration results in a rapid depolarization of the cell membrane potential and prompt cell death. Contact with a single R-type bacteriocin particle can result in cell death. An R-type bacteriocin, for

example, may be thermolabile, mild acid resistant, trypsin resistant, sedimentable by centrifugation, resolvable by electron microscopy, or a combination thereof. Other R-type bacteriocins may be complex molecules including multiple proteins, polypeptides, or subunits, and may resemble a tail structure of bacteriophages of the myoviridae family. In naturally occurring R-type bacteriocins, the subunit structures
 5 may be encoded by a bacterial genome, such as that of *C. difficile* or *P. aeruginosa* and form R-type bacteriocins to serve as natural defenses against other bacteria. In some instances, the R-type bacteriocin is a pyocin. In some instances, the pyocin is an R-pyocin, F-pyocin, or S-pyocin.

In some instances, the bacteriocin is a functionally active variant of the bacteriocins described herein. In some instances, the variant of the bacteriocin has at least 70%, 71%, 72%, 73%, 74%, 75%,
 10 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a bacteriocin described herein or a naturally occurring bacteriocin.

In some instances, the bacteriocin may be bioengineered, according to standard methods, to modulate their bioactivity, e.g., increase or decrease or regulate, or to specify their target
 15 microorganisms. In other instances, the bacteriocin is produced by the translational machinery (e.g. a ribosome, etc.) of a microbial cell. In some instances, the bacteriocin is chemically synthesized. Some bacteriocins can be derived from a polypeptide precursor. The polypeptide precursor can undergo cleavage (e.g., processing by a protease) to yield the polypeptide of the bacteriocin itself. As such, in some instances, the bacteriocin is produced from a precursor polypeptide. In some other instances, the
 20 bacteriocin includes a polypeptide that has undergone post-translational modifications, for example, cleavage, or the addition of one or more functional groups.

The bacteriocins described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of bacteriocins, such as at least about any one of 1 bacteriocin, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, or
 25 more bacteriocins. Suitable concentrations of each bacteriocin in the compositions described herein depends on factors such as efficacy, stability of the bacteriocin, number of distinct bacteriocin types in the compositions, formulation, and methods of application of the composition. In some instances, each bacteriocin in a liquid composition is from about 0.01 ng/ml to about 100 mg/mL. In some instances, each bacteriocin in a solid composition is from about 0.01 ng/g to about 100 mg/g. In some instances, wherein
 30 the composition includes at least two types of bacteriocins, the concentration of each type of the bacteriocins may be the same or different. In some instances, the bacteriocin is provided in a composition including a bacterial cell that secretes the bacteriocin. In some instances, the bacteriocin is provided in a composition including a polypeptide (e.g., a polypeptide isolated from a bacterial cell).

Bacteriocins may neutralize (e.g., kill) at least one microorganism other than the individual
 35 bacterial cell in which the polypeptide is made, including cells clonally related to the bacterial cell and other microbial cells. As such, a bacterial cell may exert cytotoxic or growth-inhibiting effects on a plurality of microbial organisms by secreting bacteriocins. In some instances, the bacteriocin targets and kills one or more species of bacteria resident in the host via cytoplasmic membrane pore formation, cell wall interference (e.g., peptidoglycanase activity), or nuclease activity (e.g., DNase activity, 16S rRNase
 40 activity, or tRNase activity).

In some instances, the bacteriocin has a neutralizing activity. Neutralizing activity of bacteriocins may include, but is not limited to, arrest of microbial reproduction, or cytotoxicity. Some bacteriocins have cytotoxic activity, and thus can kill microbial organisms, for example bacteria, yeast, algae, and the like. Some bacteriocins can inhibit the reproduction of microbial organisms, for example bacteria, yeast, algae, and the like, for example by arresting the cell cycle.

In some instances, the bacteriocin has killing activity. The killing mechanism of bacteriocins is specific to each group of bacteriocins. In some instances, the bacteriocin has narrow-spectrum bioactivity. Bacteriocins are known for their very high potency against their target strains. Some bacteriocin activity is limited to strains that are closely related to the bacteriocin producer strain (narrow-spectrum bioactivity). In some instances, the bacteriocin has broad-spectrum bioactivity against a wide range of genera.

In some instances, bacteriocins interact with a receptor molecule or a docking molecule on the target bacterial cell membrane. For example, nisin is extremely potent against its target bacterial strains, showing antimicrobial activity even at a single-digit nanomolar concentration. The nisin molecule has been shown to bind to lipid II, which is the main transporter of peptidoglycan subunits from the cytoplasm to the cell wall.

In some instances, the bacteriocin has anti-fungal activity. A number of bacteriocins with anti-yeast or anti-fungal activity have been identified. For example, bacteriocins from *Bacillus* have been shown to have neutralizing activity against some yeast strains (see, for example, Adetunji and Olaoye, *Malaysian Journal of Microbiology* 9:130-13, 2013). In another example, an *Enterococcus faecalis* peptide has been shown to have neutralizing activity against *Candida* species (see, for example, Shekh and Roy, *BMC Microbiology* 12:132, 2012). In another example, bacteriocins from *Pseudomonas* have been shown to have neutralizing activity against fungi, such as *Curvularia lunata*, *Fusarium species*, *Helminthosporium species*, and *Biopolaris species* (see, for example, Shalani and Srivastava, *The Internet Journal of Microbiology* Volume 5 Number 2, 2008). In another example, botrycidin AJ1316 and alirin B1 from *B. subtilis* have been shown to have antifungal activities.

A modulating agent including a bacteriocin as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of bacteriocin concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of bacteriocin concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of bacteriocin concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

(b) Lysins

The modulating agent described herein may include a lysin (e.g., also known as a murein hydrolase or peptidoglycan autolysin). Any lysin suitable for inhibiting a bacterium resident in the host may be used. In some instances, the lysin is one that can be naturally produced by a bacterial cell. In some instances, the lysin is one that can be naturally produced by a bacteriophage. In some instances, the lysin is obtained from a phage that inhibits a bacterium resident in the host. In some instances, the

lysins is engineered based on a naturally occurring lysin. In some instances, the lysin is engineered to be secreted by a host bacterium, for example, by introducing a signal peptide to the lysin. In some instances, the lysin is used in combination with a phage holin. In some instances, a lysin is expressed by a recombinant bacterium host that is not sensitive to the lysin. In some instances, the lysin is used to inhibit a Gram-positive or Gram-negative bacterium resident in the host.

The lysin may be any class of lysin and may have one or more substrate specificities. For example, the lysin may be a glycosidase, an endopeptidase, a carboxypeptidase, or a combination thereof. In some instances, the lysin cleaves the β -1-4 glycosidic bond in the sugar moiety of the cell wall, the amide bond connecting the sugar and peptide moieties of the bacterial cell wall, and/or the peptide bonds between the peptide moieties of the cell wall. The lysin may belong to one or more specific lysin groups, depending on the cleavage site within the peptidoglycan. In some instances, the lysin is a *N*-acetyl- β -D-muramidase (e.g., lysozyme), lytic transglycosylase, *N*-acetyl- β -D-glucosaminidase, *N*-acetylmuramyl-L-alanine amidase, L,D-endopeptidase, D,D-endopeptidase, D,D-carboxypeptidase, L,D-carboxypeptidase, or L,D-transpeptidase. Non-limiting examples of lysins and their activities are listed in Table 5.

Table 5: Examples of Lysins

Target Bacteria	Producer	Lysins	Activity	Sequence
<i>S. pneumoniae</i>	Cp1	Cpl-1	Muramidase	MVKKNDLFVDVSSHNG YDITGILEQMGTNTNIIKI SESTTYLNPCLSAQVEQ SNPIGFYHFARFGGDVA EAEREAQFFLDNVPMQ VKYLVLDYEDDPSGDA QANTNACLRFMQMIAD AGYKPIYYSYKPFTHDN VDYQQILAQFPNSLWIA GYGLNDGTANFEYFPS MDGIRWWQYSSNPFDK NIVLLDDEEDDKPKTAG TWKQDSKGWWFRRNN GSFPYNKWEKIGGVWY YFDSKGYCLTSEWLKD NEKWYYLKDNGAMATG WVLVGSEWYYMDDSG AMVTGWVKYKNNWYY MTNERGNMVSNEFIKS GKGWYFMNTNGELADN PSFTKEPDGLITVA (SEQ ID NO: 52)

<i>S. pneumoniae</i>	Dp-1	Pal	Amidase	MGVDIEKGVAVWMQARK GRVSYSMDFRDGPDSY DCSSSMYYALRSAGAS SAGWAVNTEYMHAWLI ENGYELISENAPWDAKR GDIFIWGRKGASAGAG GHTGMFIDSDNIIHCNYA YDGISVNDHDERWYYA GQPYYYVYRLTNANAQ PAEKKLGWQKDATGFW YARANGTYPKDEFEYIE ENKSWFYFDDQGYMLA EKWLKHTDGNWYWFD RDGYMATSWKRIGESW YYFNRDGSMVTGWIKY YDNWYYCDATNGDMKS NAFIRYNDGWYLLLPDG RLADKPQFTVEPDGLIT AKV (SEQ ID NO: 53)
<i>S. pyogenes</i>	C1	C1	Amidase	N/A
<i>B. anthracis</i>	γ	PlyG	Amidase	MEIQKKLVDPSKYGTKC PYTMKPKYITVHNTYND APAENEVSYMISNNNEV SFHIAVDDKKAIQGIPLE RNAWACGDGNGSGNR QSI SVEICYSKSGGDRY YKAEDNAVDVVRQLMS MYNIPIENVRTHQSWSG KYCPRMLAEGRWGAF IQKVKNNGNVATTSPKQ NIIQSGAFSPYETPDVM GALTSLKMTADFILQSD GLTYFISKPTSDAQLKA MKEYLDRKGWWYEVK (SEQ ID NO: 54)
<i>B. anthracis</i>	Ames prophage	PlyPH	Amidase	N/A
<i>E. faecalis</i> and <i>E. faecium</i>	Phi1	PlyV12	Amidase	N/A

<i>S. aureus</i>	ΦMR11	MV-L	Endopeptidase and amidase	MQAKLTKEFIEWLKTS EGKQFNVDLWYGFQCF DYANAGWKVLFGLLLK GLGAKDIPFANNFDGLA TVYQNTPDFLAQPGDM VVFSGSNYGAGYGHVAW VIEATLDYIIVYEQNWLG GGWTDRIEQPGWGWE KVTRRQHAYDFPMWFI RPNFKSETAPRSIQSPT QASKKETAKPQPKAVEL KIIKDVVKG YDLPKRGG NPKGIVIHNDAGSKGAT AEAYRNLVNAPLSRLE AGIAHSYVSGNTVWQAL DESQVGWHTANQLGNK YYYGIEVCQSMGADNA TFLKNEQATFQECARLL KKWGLPANRNTIRLHNE FTSTSCPHRSSVLHTGF DPVTRGLLPEDKQLQLK DYFIKQIRVYMDGKIPVA TVSNESSASSNTVKPVA SAWKRNKYGTYYMEEN ARFTNGNQIPITVRKIGP FLSCP VAYQFQPGGYC DYTEVMLQDGHVWVG Y TWEGQRYLPIRTWNG SAPPNQILGDLWGEIS (SEQ ID NO: 55)
<i>S. pyogenes</i>	C1	PlyC	Amidase	N/A
<i>S. agalactiae</i>	B30	GBS lysin	Muramidase and endopeptidase	MVINIEQAIWMA SRKG KVTYSMDYRNGPSSYD CSSSVYFALRSAGASDN GWAVNTEYEHDWLIKN GYVLIAENTNWN AQRG DIFIWGKRGASAGAFGH TGMFVDPDNIIHCNYGY NSITVNNHDEIWGYNGQ PYVYAYRYS GKQSN AK

				VDNKSVVSKFEKELDVN TPLSNSNMPYYEATISE DYYVESKPDVNSTDKEL LVAGTRVRVYEKVKGW ARIGAPQSNQWVEDAY LIDATDM (SEQ ID NO: 56)
<i>S. aureus</i>	P68	Lys16	Endopeptidase	N/A
<i>S. aureus</i>	K	LysK	Amidase and endopeptidase	MAKTQAEINKRLDAYAK GTVDSPYRVKKATSYDP SFGVMEAGADADGYY HAQCQDLITDYVLWLT NKVRTWGNADQIKQS YGTGFKIHENKPSTVPK KGWIAVFTSGSYEQWG HIGIVYDGGNTSTFTILE QNWNGYANKKPTKRVD NYYGLTHFIEIPVKAGTT VKKETAKKSASKTPAPK KKATLKVSKNHINYTMD KRGKKPEGMVIHNDAG RSSGQQYENSLANAGY ARYANGIAHYGSEGYV WEAIDAKNQIAWHTGD GTGANSNGNFRFAGIEVC QSMSASDAQFLKNEQA VFQFTAEEKFKEWGLTPN RKTVRLHMEFVPTACPH RSMVLHTGFNPVTQGR PSQAIMNKLKDYFIKQIK NYMDKGTSSSTVVKDG KTSSASTPATRPVTGS WKKNQYGTWYKPENAT FVNGNQPIVTRIGSPFLN APVGGNLPAGATIVYDE VCIQAGHIWIGYNAYNG NRVYCPVRTCQGVPPN QIPGVAWGVPK (SEQ ID NO: 57)
<i>L. monocytogenes</i>	A118	Ply118	Amidase	MTSYYYSRSLANVNKLA DNTKAAARKLLDWSES

				NGIEVLIYETIRTKEQQA ANVNSGASQTMRSYHL VGQALDFVMAKGKTVD WGAYRSDKGKKFVAKA KSLGFEWGGDWSGFV DNPHLQFNKYGYGTD FGKGASTSNSSKPSADT NTNSLGLVDYMNLNKLD SSFANRKKLATSYGIKN YSGTATQNTTLLAKLKA GKPHTPASKNTYYTENP RKVKTLVQCDLYKSVDF TTKNQTTGGTFPPGTVFT ISGMGKTKGGTPRLKTK SGYYLTANTKFVKKI (SEQ ID NO: 58)
<i>L. monocytogenes</i>	A511	Ply511	Amidase	MVKYTVENKIIAGLPKGG LKGANFVIAHETANSKS TIDNEVSymTRNWKNAF VTHFVGGGGRRVQVAN VNYVSWGAGQYANSYS YAQVELCRTSNATTFKK DYEVCQLLVDLAKKAG IPITLDSGSKTSDKGIKS HKWVADKLGGTTHQDP YAYLSSWGISKAQFASD LAKVSGGGNTGTAPAK PSTPAPKPSTPSTNLDK LGLVDYMNNAKKMDSSY SNRDKLAKQYGIANYSG TASQNTTLLSKIKGGAP KPSTPAPKPSTSTAKKIY FPPNKGWNSVYPTNKA PVKANAIGAINPTKFGGL TYTIQKDRGNGVYEIQT DQFGRVQVYGAPSTGA VIKK (SEQ ID NO: 59)
<i>L. monocytogenes</i>	A500	Ply500	Endopeptidase	MALTEAWLIEKANRKLN AGGMYKITSKTRNVIK KMAKEGIYLCVAQGYRS

				TAEQNALYAQGRTKPG AIVTNAKGGQSNHNYG VAVDLCLYTNDGKDVIW ESTTSRWKKVVAAMKA EGFKWGGDWKSFKDY PHFELCDAVSGEKIPAA TQNTNTNSNRYEGKVID SAPLLPKMDFKSSPFRM YKVGTEFLVYDHNQYW YKTYIDDKLYMYKSFC DVVAKKDAKGRIKVRK SAKDLRIPVWNNIKLNS GKIKWYAPNVKLAWYN YRRGYLELWYPNDGWY YTAEYFLK (SEQ ID NO: 60)
<i>S. pneumoniae</i>	ΦDp-1	Pal, S	Endopeptidase and amidase	N/A
<i>S. agalactiae</i>	LambdaSa1 prophage	LambdaSa1	Glycosidase	MVINIEQAIWMSARKG KVTYSMDYRNGPSSYD CSSSVYFALRSAGASDN GWAVNTEYEHDWLIKN GYVLIAENTNWNQARG DIFIWGKRGASAGAFGH TGMFVDPDNIHCNNGY NSITVNNHDEIWGYNGQ PYVYAYRYARKQSNK VDNQSVVSKFEKELDVN TPLSNSNMPYYEATISE DYYVESKPDVNSTDKE LVAGTRVRVYEKVKGW ARIGAPQSNQWVEDAY LIDATDM (SEQ ID NO: 61)
<i>S. agalactiae</i>	LambdaSa2 prophage	LambdaSa2	Glycosidase and endopeptidase	MEINTEIAIWMASARQG KVSYSMDYRDGPNSYD CSSSVYYALRSAGASSA GWAVNTEYMHDLIKN GYELIAENVWNAVRG DIAIWGMRGHSSGAGG HVVMFIDPENIIHCNWA

				NNGITVNNYNQTAAASG WMYCYVYRLKSGASTQ GKSLDTLVKETLAGNYG NGEARKAVLGNQYEAV MSVINGKTTTNQKTVDQ LVQEVIAGKHGNGEARK KSLGSQYDAVQKRVTEL LKKQPSEPFKAQEVNKP TETKTSQTELTGQATAT KEEGDLSFNGLTILKKAVL DKILGNCKKHDILPSYAL TILHYEGLWGTSAVGKA DNNWGGMTWTGQGNR PSGVTVTQGSARPSNE GGHYMHYASVDDFLTD WFYLLRAGGSYKVSGA KTFSEAIKGMFKVGGAV YDYAASGFDSYIVGASS RLKAIEAENGSLDKFDK ATDIGDGSKDKIDITIEGI EVTINGITYELTKKPV (SEQ ID NO: 62)
<i>S. uberis</i>	(ATCC700407) prophage	Ply700	Amidase	MTDSIQEMRKLQSIPVR YDMGDRYGNDADRDG RIEMDCSSAVSKALGIS MTNNTETLQQALPAIGY GKIHDVAVDGTDFDMQAY DVIIWAPRDGSSSLGAF GHVLIATSPPTAIHCNYG SDGITENDYNYWEING RPREIVFRKGVTTQTQAT VTSQFERELDVNARLTV SDKPYYEATLSEYYVE AGPRIDSQDKELIKAGT RVRVYEKLNWWSRINH PESAQWVEDSYLV DAT EM (SEQ ID NO: 63)
<i>S. suis</i>	SMP	LySMP	Glycosidase and endopeptidase	N/A

<i>B. anthracis</i>	Bcp1	PlyB	Muramidase	N/A
<i>S. aureus</i>	Phi11 and Phi12	Phi11 lysin	Amidase and endopeptidase	MQAKLTKEFIEWLKTS EGKQFNVDLWYGFQCF DYANAGWKVLFGLLLK GLGAKDIPFANNFDGLA TVYQNTPDFLAQPGDM VVFSGSNYGAGYGHVAW VIEATLDYIIVYEQNWLG GGWTDGIEQPGWGWE KVTRRQHAYDFPMWFI RPNFKSETAPRSVQSPT QAPKKETAKPQPKAVEL KIIKD VVKGYDLPKRGS NPKGIVIHNDAGSKGAT AEAYRNLVNAPLSRLE AGIAHSYVSGNTVWQAL DESQVGWHTANQIGNK YYYGIEVCQSMGADNA TFLKNEQATFQECARLL KKWGLPANRNTIRLHNE FTSTSCPHRSSVLHTGF DPVTRGLLPEDKRLQLK DYFIKQIRAYMDGKIPVA TVSNESSASSNTVKPVA SAWKRNKYGTYYMEES ARFTNGNQPITVRKVGP FLSCPVG YQFQPGGYC DYTEVMLQDGHVWVG Y TWEGQRY YLP IRTWNG SAPPNQILGDLWGEIS (SEQ ID NO: 64)
<i>S. aureus</i>	ΦH5	LysH5	Amidase and endopeptidase	MQAKLTKEFIEWLKTS EGKQYNADGWYGFQC FDYANAGWKALFGLLLK GVGAKDIPFANNFDGLA TVYQNTPDFLAQPGDM VVFSGSNYGAGYGHVAW VIEATLDYIIVYEQNWLG GGWTDGVQQPGSGWE KVTRRQHAYDFPMWFI

				RPNFKSETAPRSVQSPT QASKKETAKPQPKAVEL KIIKDVVKG YDLPKRG S NPNFIVIHNDAGSKGAT AEAYRNLGNAPLSRLE AGIAHSYVSGNTVWQAL DESQVGWHTANQIGNK YGYGIEVCQSMGADNA TFLKNEQATFQECARLL KKWGLPANRNTIRLHNE FTSTSCPHRSSVLHTGF DPVTRGLLPEDKRLQLK DYFIKQIRAYMDGKIPVA TVSNDSSASSNTVKPVA SAWKRNKYGTYYMEES ARFTNGNQPIVRKVGP FLSCPVG YQFQPGGYC DYTEVMLQDGHVWVG Y TWEGQRYLPIRTWNG SAPPNQILGDLWGEIS (SEQ ID NO: 65)
<i>S. warneri</i>	ΦWMY	LysWMY	Amidase and endopeptidase	MKTAKAQAKSWINSKIGK GIDWDGMYGYQCMDE AVDYIHHVTDGKVTMW GNAIDAPKNNFQGLCTV YTNTPEFRPAYGDVIVW SYGTFATYGHIAIVNPD PYGDLQYITVLEQNWN NGIYKTEFATIRTHDYT GVSHFIRPKFADEVKET AKTVNKL SVQKKIVTPK NSVERIKNYVKTSYIN GEHYELYNRGHKPKGV VIHNTAGTASATQEGQR LTNMTFQQLANGVAHV YIDKNTIYETLPEDRIAW HVAQQYGNTEFYGIEVC GSRNTDKEQFLANEQV AFQEAARRLKSWGMRA NRNTVRLHHTFSSTEC P

				DMSMLLHTGYSMKNGK PTQDITNKCADYFMKQI NAYIDGKQPTSTVVGSS SSNKLKAKNKDKSTGW NTNEYGTLWKKEHATFT CGVRQGIVTRTTGPFTS CPQAGVLYYGQSVNYD TVCKQDGYVWISWTTS DGYDVWMPIRTWDRST DKVSEIWGTIS (SEQ ID NO: 66)
<i>Streptococci (GBS)</i>	ΦNCTC 11261	PlyGBS	Muramidase and endopeptidase	MATYQEYKSRSGNAY DIDGSFGAQCWDGYAD YCKYLGLPYANCTNTGY ARDIWEQRHENGILNYF DEVEVMQAGDVAIFMV VDGVTPYSHVAIFDSDA GGGYGWFLGQNQGGA NGAYNIVKIPYSATYPTA FRPKVFKNVAVTGNIG LNKGDYFIDVSAYQQAD LTTTCQQAGTTKTIKVS ESIAWLSDRHQQQANT SDPIGYYHFGRFGGDSA LAQREADLFLSNLPSKK VSYLVIDYEDSASADKQ ANTNAVIAFMDKIASAG YKPIYYSYKPFTLNNIDY QKIIAKYPNSIWIAGYPD YEV RTEPLWEFFPSMD GVRWWQFTSVGVAGG LDKNIVLLADDSSKMDIP KVDKPQELTFYQKLATN TKLDNSNVPYYEATLST DYYVESKPNASSADKEF IKAGTRVRVYEKVNGW SRINHPESAQWVEDSYL VNATDM (SEQ ID NO: 67)
<i>C. perfringens</i>	Φ3626	Ply3626	Amidase	N/A
<i>C. difficile</i>	ΦCD27	CD27 lysin	Amidase	N/A

<i>E. faecalis</i>	Φ1	PlyV12	Amidase	N/A
<i>A. naeslundii</i>	ΦAv-1-	Av-1 lysin	Putative amidase/mura midase	N/A
<i>L. gasseri</i>	ΦgaY	LysgaY	Muramidase	N/A
<i>S. aureus</i>	ΦSA4	LysSA4	Amidase and endopeptidase	N/A
<i>S. haemolyticus</i>	ΦSH2	SH2	Amidase and endopeptidase	N/A
<i>B. thuringiensis</i>	ΦBtCS33	PlyBt33	Amidase	N/A
<i>L. monocytogenes</i>	ΦP40	PlyP40	Amidase	N/A
<i>L. monocytogenes</i>	ΦFWLLm3	LysZ5	Amidase	MVKYTVENKIIAGLPK GK LKGANFVIAHETANSKS TIDNEVS YMTRNWQNA FVTHFVGGGGRRVQVA NVNYVSWGAGQYANSY SYAQVELCRTSNATTFK KDYEVYCQLLDLAKKA GIPITLD SGSKTSDKGIK SHKWVADKLGGTTHQD PYAYLSSWGISKAQFAS DLAKVSGGGNTGTAPA KPSTPSTNLDKGLVDY MNAKKMDSSYSNRAKL AKQYGIANYSGTASQNT TLLSKIKGGAPKPSTPAP KPSTSTAKKIYFPPNKG NWSVYPTNKAPVKANAI GAINPTKFGGLTYTIQKD RGNGVYEIQTDQFGRV QVYGAPSTGAVIKK (SEQ ID NO: 68)
<i>B. cereus</i>	ΦBPS13	LysBPS13	Amidase	MAKREKYIFDVEAEVGK AAKSIKSLEAELSKLQKL NKEIDATGGDRTEKEML ATLKAAKEVNAEYQKM QRILKDLSKYSGKVS RK EFNDSKVINNAKTSVQGG GKVTD SFGQMLKNMER QINSV NKQFDNHRKAM

				VDRGQQYTPHLKTNRK DSQGNSNPSMMGRNK STTQDMEKAVDKFLNG QNEATTGLNQALYQLKE ISKLNRRSESLRRASA SGYMSFQQYSNFTGDR RTVQQTYGGLKTANRE RVLELSGQATGISKELD RLNSKKGLTAREGEERK KLMRQLEGIDAELTARK KLNSSLDETTSNMEKFN QSLVDAQVSVKPERGT MRGMMYERAPAIALAIG GAITATIGKLYSEGGNH SKAMRPDEMYVGQQTG AVGANWRPNRTATMRS GLGNHLGFTGQEMMEF QSNYLSANGYHGAEDM KAATTGQATFARATGLG SDEVKDFNTAYRSGGI DGNQTKQFQNAFLGAM KQSGAVGREKDQLKAL NGILSSMSQNRTVSNQ DMMRTVGLQSAISSSG VASLQGTKGGALMEQL DNGIREGFNDPQMRVL FGQGTYQGMGGRAAL RKQMEKGISDPDNLNTL IDASKASAGQDPAEQAE VLATLASKMGVNMSSD QARGLIDLQPSGKLTKE NIDKVMKEGLKEGSIES AKRDKAYSESKASIDNS SEAATAKQATELNDMG SKLRQANAALGGLPAPL YTAIAAVVAFTA AVAGS ALMFKGASWLKGGMAS KYGGKGGKGGKGGGT GGGGGAGGAAATGAG AAAGAGGVGAAAAGEV
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				GAGVAAGGAAAGAAAAG GSKLAGVGKGFMMKGAG KLMLPLGILMGASEIMQ APEEAKGSAIGSAVGGI GGGIAGGAATGAIAGSF LGPIGTAVGGIAGGIAG GFAGSSLGETIGGWFD SGPKEDASAADKAKAD ASAAALAAAAGTSGAVG SSALQSQMAQGITGAP NMSQVGSMASALGISS GAMASALGISSGQENQI QTMTDKENTNTKKANE AKKGDNLSYERENISMY ERVLTRAEQILAQARAQ NGIMGVGGGGTAGAGG GINGFTGGGKLQFLAAG QKWSSSNLQQHDLGFT DQNLTAEDLDKWIDSKA PQGSMMRGMGATFLKA GQEYGLDPRYLIAHAAE ESGWGTSKIARDKGNF FGIGAFDDSPYSSAYEF KDGTGSAAERGIMGGA KWISEKYYGKGNTTLDK MKAAGYATNASWAPNI ASIMAGAPTGS GSGNVT ATINNVNKGDEKVSDKL KNSSDMKKAGKDIGSLL GFYSREMTIA (SEQ ID NO: 69)
<i>S. aureus</i>	ΦGH15	LysGH15	Amidase and endopeptidase	MAKTQAEINKRLDAYAK GTVDSPYRIKKATSYDP SFGVMEAGAIADAGYY HAQCQDLITDYVLWLT NKVRTWGNADQIKQS YGTGFKIHENKPSTVPK KGWIAVFTSGSYQQWG HIGIVYDGGNTSTFTILE QNWNGYANKKPTKRVD

				NYYGLTHFIEIPVKAGTT VKKETAKKSASKTPAPK KKATLKVSKNHINYTMD KRGKKPEGMVIHNDAG RSSGQQYENSLANAGY ARYANGIAHYYGSEGYV WEAIDAKNQIAWHTGD GTGANSNGNFRFAGIEVC QSMSASDAQFLKNEQA VFQFTAEEKFKEWGLTPN RKTVRLHMEFVPTACPH RSMVLHTGFNPVTQGR PSQAIMNKLKDYFIKQIK NYMDKGTSSSTVVKDG KTSSASTPATRPVTGS WKKNQYGTWYKPENAT FVNGNQPIVTRIGSPFLN APVGGNLPAGATIVYDE VCIQAGHIWIGYNAYNG DRVYCPVRTCQGVPPN HIPGVAWGVPFK (SEQ ID NO: 70)
<i>S. aureus</i>	ΦvB SauS-PLA88	HydH5	Endopeptidase and glycosidase	N/A
<i>E. faecalis</i>	ΦF168/08	Lys168	Endopeptidase	N/A
<i>E. faecalis</i>	ΦF170/08	Lys170	Amidase	N/A
<i>S. aureus</i>	ΦP-27/HP	P-27/HP	Nonspecified	N/A
<i>C. perfringens</i>	ΦSM101	Psm	Muramidase	N/A
<i>C. sporogenes</i>	Φ8074-B1	CS74L	Amidase	MKIGIDMGHTLSGADYG VVGLRPESVLTREVGTK VIYKLQKLGHVVVNCTV DKASSVSESLYTRYRA NQANVDLFISIHFNATPG GTGTEVYTYAGRQLGE ATRIRQEFKSLGLRDRG TKDGSGSLAVIRNTKAKA MLVECCFCNDPNMKL YNSESFSNAIVKGITGKL PNGESGNNNQGGNKVK

				AVVIYNEGADRRGAEYL ADYLNCPRTISNSRTFDY SCVEHVYAVGGKKEQY TKYLKTLLSGANRYDTM QQILNFINGGK (SEQ ID NO: 71)
<i>S. typhimurium</i>	ΦSPN1S	SPN1S	Glycosidase	MDINQFRRASGINEQLA ARWFPHITTAMNEFGIT KPDDQAMFIAQVGHE GGFTRLQENFNYSVNG LSGFIRAGRITPDQANAL GRKTYEKSPLERQRAI ANLVYSKRMGNNGPGD GWNYRGRGLIQITGLNN YRDCGNGLKVDLVAQP ELLAQDEYAARSAWFF SSKGCMKYTGDLVRVT QIINGGQNGIDDRTRY AAARKVLAL (SEQ ID NO: 72)
<i>C. michiganensis</i>	ΦCMP1	CMP1	Peptidase	N/A
<i>C. michiganensis</i>	ΦCN77	CN77	Peptidase	MGYWGYPNGQIPNDKM ALYRGCLLRADAAAQAY ALQDAYTRATGKPLVILE GYRDLTRQKYLRNLYLS GRGNIAAVPGLSNHGW GLACDFAAPLNSSGSEE HRWMRQNAPLFGFDW ARGKADNEPWHWEYG NVPVSRWASLDVTPIDR NDMADITEGQMQRIV LLDTEIQTPLGPRLVKHA LGDALLGQANANSIAE VPDKTWDVLVDHPLAK NEDGTPLKVRLGDVAKY EPLEHQNTRDAIAKLGT LQFTDKQLATIGAGVKPI DEASLVKKIVDGVRALF GRAAA (SEQ ID NO: 73)

<i>A. baumannii</i>	ΦAB2	LysAB2	Glycosidase	MILTKDGF SIIRNELFGG KLDQTQVD AIN FIVAKAT ESGLTYPEAAYLLATIYH ETGLPSGYRTMQPIKEA GSDSYLR SKKYYPIGY GYVQLTWKENYERIGKL IGVDLIK NPEKALEPLIAI QIAIKGMLNGWFTGVGF RRKRPVSKYNKQQYVA ARNIINGKDKAELIAKYAI IFERALRSL (SEQ ID NO: 74)
<i>B. cereus</i>	ΦB4	LysB4	Endopeptidase	MAMALQTLIDKANRKLN VSGMRKDVADRTRAVIT QMHAQGIYICVAQGFRS FAEQNALYAQGRTKPG SIVTNARGGQSNHNYG VAVDLCLYTQDGS DVIW TVEGNFRKVIAAMKAQG FKWGGDWVSFKDYPHF ELYDVVGGQKPPADNG GAVDNNGGSGSTGGS GGGSTGGGSTGGGYD SSWFTKETGTFVTNTSI KLRTAPFTSADVIATLPA GSPVNYNGFGIEYDGYV WIRQPRSNYGYLATG ESKGGKRQNYWGTFK (SEQ ID NO: 75)
<i>P. aeruginosa</i>	ΦKMV	KMV45	Nonspecified	N/A
<i>C. tyrobutyricum</i>	ΦCTP1	Ctp1I	Glycosidase	MKKIADISNLNGNVDVK LLFNLGYIGIIAKASEGG TFVDKYYKQNYTNTKAQ GKITGAYHFANFSTIAKA QQEANFFLNCIAGTTPD FVVDLEQQCTGDITDA CLAFLNIVAKKFKCVVYC NSSFIKEHLNSKICAYPL WIANYGVATPAFTLWTK YAMWQFTEKGQVSGIS GYIDFSYITDEFIKYIKGE

				DEVENLVVYNDGADQR AAEYLADRLACPTINNA RKFDYSNVKNVYAVGG NKEQYTSYLTTLIAGSTR YTTMQAVLDYIKNLK (SEQ ID NO: 76)
<i>P. aeruginosa</i>	ΦEL	EL188	Transglycosylase	N/A
<i>P. aeruginosa</i>	ΦKZ	KZ144	Transglycosylase	N/A
<i>S. aureus</i>		Ply187	Cell Wall Hydrolase	MALPKTGKPTAKQVVD WAINLIGSGVDVDGYYG RQCWDLPNYIFNRYWN FKTPGNARDMAWYRYP EGFKVFRNTSDFVPKPG DIAVWTGGNYNWNTW GHTGIVVGPSTKSYFYS VDQNWNNNSNSYVGSPA AKIKHSYFGVTHFVRPA YKAEPKPTPPAQNNPAP KDPEPSKKPESNKPIYK VVTKILFTTAHIEHVKAN RFVHYITKSDNHNKPN KIVIKNTNTALSTIDVYRY RDELDKDEIPHFFVDRL NVWACRPIEDSINGYHD SVVLSITETRTALSDNFK MNEIECLSLAESILKANN KKMSASNIIVDNKAWRT FKLHTGKDSLKSSSFTS KDYQKAVNELIKLFNDK DKLLNNKPKDVVERIRIR TIVKENTKFVPESELKPRN NIRDKQDSKIDRVINNYT LKQALNIQYKLNPKPQT SNGVSWYNASVNQIKS AMDTTKIFNNNVQVYQF LKLNQYQGIPVDKLNKL LVGKGTLANQGHAFAD GCKKYNINEIYLIAHRFL

				ESANGTSFFASGKTGVY NYFGIGAFDNNPNNAM AFARSHGWTSPKAIIG GAEFVGKGYFNVGQNT LYRMRWNPQKPGTHQY ATDISWAKVQAQMISAM YKEIGLTGDYFIYDQYKK (SEQ ID NO: 77)
<i>P. uorescens</i>	ΦOBP	OBPgp279	Glycosidase	N/A
<i>L. monocytogenes</i>	ΦP35	PlyP35	Amidase	MARKFTKAELVAKAEKK VGGLKPDVKKAVLSAVK EAYDRYGIGIIVSQGYRS IAEQNGLYAQGRTKPGN IVTNAKGGQSNHNFVGA VDFAIDLIDDGKIDSWQP SATIVNMMKRRGFKWG GDWKSFTDLPHFEACD WYRGERKYKVDTSWK KKENINIVIKDVGYFQDK PQFLNSKSVRQWKHGT KVKLTKHNSHWYTGTV KDGNSVRGYIYHSMA KVTSKNSDGSVNATINA HAFCDWNKKLNGGDFI NLKRGFKGITHPASDGF YPLYFASRKKTFYIPRY MFDIKK (SEQ ID NO: 78)
<i>L. fermentum</i>	ΦPYB5	Lyb5	Muramidase	N/A
<i>S. pneumoniae</i>	ΦCP-7	Cpl-7	Muramidase	MVKKNDLFVDVASHQG YDISGILEEAGTTNTIIV SESTSYLNPCLSAQVSQ SNPIGFYHFAWFGGNE EEAEAEARYFLDNVPTQ VKYLVLDYEDHASASVQ RNTTACLRFMQIIAEAG YTPYYSYKPFTLDNVDY QQILAQFPNSLWIAGYG LNDGTANFEYFPSMDGI RWWQYSSNPFDKNIVL LDDEKEDNINNENTLKS

				LTTVANEVIQGLWGNG QERYDSLANAGYDPQA VQDKVNEILNAREIADLT TVANEVIQGLWGNGQE RYDSLANAGYDPQAVQ DKVNEILNAREIADLTTV ANEVIQGLWGNGQERY DSLANAGYDPQAVQDK VNELLS (SEQ ID NO: 79)
<i>P. chlororaphis</i> 201	Φ2-1	201φ2- 1gp229	Glycosidase	N/A
<i>S. enterica</i>	ΦPVP-SE1)	PVP- SE1gp146	Glycosidase	N/A
<i>Corynebacterium</i>	ΦBKF20	BKF20	Amidase	N/A
<i>E. faecalis</i>	ΦEFAP-1	EFAL-1	Amidase	MKLKGILLSVVTTFGLLF GATNVQAYEVNNEFNL QPWEGSQQLAYPNKIIL HETANPRATGRNEATY MKNNWFNAHTTAIVGD GGIVYKVAPEGNVSWG AGNANPYAPVQIELQHT NDPELFKANYKAYVDYT RDMGKKFGIPMTLDQG GSLWEKGVVSHQWVTD FWWDHTDPYGYLAKM GISKAQLAHDLANGVSG NTATPTPKPDKPKPTQP SKPSNKKRFNYRVDGL EYVNGMWQIYNEHLGKI DFNWTENGIPVEVVDKV NPATGQPTKDQVLKVG DYFNFQENSTGVVQEQ TPYMGYTLSHVQLPNEF IWLFTDSKQALMYQ (SEQ ID NO: 80)
<i>Lactobacilli</i>	lamdaSA2	LysA, LysA2, and Lysga Y	Nonspecified	N/A
<i>S. aureus</i>		SAL-1	Nonspecified	N/A

In some instances, the lysin is a functionally active variant of the lysins described herein. In some instances, the variant of the lysin has at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a lysin described herein or a naturally occurring lysin.

In some instances, the lysin may be bioengineered to modulate its bioactivity, e.g., increase or decrease or regulate, or to specify a target microorganism. In some instances, the lysin is produced by the translational machinery (e.g. a ribosome, etc.) of a microbial cell. In some instances, the lysin is chemically synthesized. In some instances, the lysin is derived from a polypeptide precursor. The polypeptide precursor can undergo cleavage (for example, processing by a protease) to yield the polypeptide of the lysin itself. As such, in some instances, the lysin is produced from a precursor polypeptide. In some instances, the lysin includes a polypeptide that has undergone post-translational modifications, for example, cleavage, or the addition of one or more functional groups.

The lysins described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of lysins, such as at least about any one of 1 lysin, 2, 3, 4, 5, 10, 15, 20, or more lysins. A suitable concentration of each lysin in the composition depends on factors such as efficacy, stability of the lysin, number of distinct lysin, the formulation, and methods of application of the composition. In some instances, each lysin in a liquid composition is from about 0.1 ng/mL to about 100 mg/mL. In some instances, each lysin in a solid composition is from about 0.1 ng/g to about 100 mg/g. In some instances, wherein the composition includes at least two types of lysins, the concentration of each type of lysin may be the same or different.

A modulating agent including a lysin as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of lysin concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of lysin concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of lysin concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

30 (c) *Antimicrobial Peptides*

The modulating agent described herein may include an antimicrobial peptide (AMP). Any AMP suitable for inhibiting a microorganism resident in the host may be used. AMPs are a diverse group of molecules, which are divided into subgroups on the basis of their amino acid composition and structure. The AMP may be derived or produced from any organism that naturally produces AMPs, including AMPs derived from plants (e.g., copsin), insects (e.g., drosocin, scorpion peptide (e.g., Uy192, UyCT3, D3, D10, Uy17, Uy192), mastoparan, poneratoxin, cecropin, moricin, melittin), frogs (e.g., magainin, dermaseptin, aurein), and mammals (e.g., cathelicidins, defensins and protegrins). For example, the AMP may be a scorpion peptide, such as Uy192 (5'- FLSTIWNIGIKLL-3'; SEQ ID NO: 221), UyCT3 (5'- LSAIWSGIKSLF-3; SEQ ID NO: 222), D3 (5'- LWGKLWEGVKSLI-3'; SEQ ID NO: 223), and D10 (5'-

FPFLKLSLKIPKSAIKSAIKRL-3'; SEQ ID NO: 224), Uy17 (5'-ILSAIWSGIKGLL-3'; SEQ ID NO: 225), or a combination thereof. Other non-limiting examples of AMPs are listed in Table 6.

Table 6: Examples of Antimicrobial Peptides

Type	Characteristic	Example AMP	Sequence
Anionic peptides	rich in glutamic and aspartic acid	dermcidin	SSLLEKGLDGAKKAVGGLGKL GKDAVEDLESVGKGAVHDVKD VLDSVL (SEQ ID NO: 81)
Linear cationic α -helical peptides	lack cysteine	cecropin A	KWKLFKKIEKVGQNIRDGIKAG PAVAVVGQATQIAK (SEQ ID NO: 82)
		andropin	MKYFSLVVLTLILAIVDQSDAFI NLLDKVEDALHTGAQAGFKLIR PVERGATPKKSEKPEK (SEQ ID NO: 83)
		morcin	MNILKFFVFIVAMSLVSCSTAA PAKIPIKAIKTVGKAVGKGLRAI NIASTANDVFNFKPKKRKH (SEQ ID NO: 84)
		ceratotoxin	MANLKAVFLICIVAFIALQCVVA EPAAEDSVVVKRSIGSALKKAL PVAKKIGKIALPIAKAALPVAAG LVG (SEQ ID NO: 85)
Cationic peptide enriched for specific amino acid	rich in proline, arginine, phenylalanine, glycine, tryptophan	abaecin	MKVVIFIFALLATICAFAFAYVPLP NVPQPGRRPFPTFGQGPFNP KIKWPQGY (SEQ ID NO: 86)
		apidaecins	KNFALAILVVTFVAVFGNTNLD PPTRPTRLRREAKPEAEPGNN RPVYIPQPRPPHPRLRREAPE AEPGNNRPVYIPQPRPPHPRL RREAELAEAGNNRPVYISQP RPPHPRLRREAPEAEPGNNR PVYIPQPRPPHPRLRREAELAE EPGNNRPVYISQPRPPHPRLR REAPEAEPGNNRPVYIPQPR PPHPRLRREAPEAEPGNNRP VYIPQPRPPHPRLRREAPEAE

			PGNNRPVYIPQPRPPHPRLRR EAKPEAKPGNNRPVYIPQPRP PHPRI (SEQ ID NO: 87)
		prophenin	METQRASLCLGRWSLWLLLLA LVVPSASAQALSREAVLRAVD RLNEQSSEANLYRLELDQPPK ADEDPGTPKPVSTVKETVCP RPTRRPPELCDFKENGVRKQC VGTVTLDQIKDPLDITCNEGVR RFPWWWPFLRRPRLRRQAFP PPNVGPRFPPPNVPGPRFPP PNFPGPRFPPPNFPGPRFPPP NFGPPFPPIFGPWFP PPPP FRPPFGPPRFPGRR (SEQ ID NO: 88)
		indolicidin	MQTQRASLSLGRWSLWLLLLG LVVPSASAQALSREAVLRAVD QLNELSSEANLYRLELDPPPK DNEDLGTRKPVSTVKETVCP RTIQQPAEQCDFKEKGRVKQC VGTVTLDPSNDQFDLNCNELQ SVILPWKWPWWPWRRG (SEQ ID NO: 89)
Anionic and cationic peptides that contain cysteine and form disulfide bonds	contain 1-3 disulfide bond	protegrin	METQRASLCLGRWSLWLLLLA LVVPSASAQALSREAVLRAVD RLNEQSSEANLYRLELDQPPK ADEDPGTPKPVSTVKETVCP RPTRQPPELCDFKENGVRKQC VGTVTLDQIKDPLDITCNEVQG VRGGRLCYCRRRFCVCVGRG (SEQ ID NO: 90)
		tachyplesins	KWCFRVCYRGICYRRCR (SEQ ID NO: 91)
		defensin	MKCATIVCTIAVVLAATLLNGSV QAAPQEEAALSGGANLNTLLD ELPEETHHAALenyRAKRATC DLASGFGVGSLLCAAHCIARR YRGGYCNSKAVCVCRN (SEQ ID NO: 92)
		drosomycin	MMQIKYLFALFAVLMVLVVGAN EADADCLSGRYKGPCAVWDN

			ETCRRVCKEEGRSSGHCSPL KCWCEGC (SEQ ID NO: 93)
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The AMP may be active against any number of target microorganisms. In some instances, the AMP may have antibacterial and/or antifungal activities. In some instances, the AMP may have a narrow-spectrum bioactivity or a broad-spectrum bioactivity. For example, some AMPs target and kill only a few species of bacteria or fungi, while others are active against both gram-negative and gram-positive bacteria as well as fungi.

Further, the AMP may function through a number of known mechanisms of action. For example, the cytoplasmic membrane is a frequent target of AMPs, but AMPs may also interfere with DNA and protein synthesis, protein folding, and cell wall synthesis. In some instances, AMPs with net cationic charge and amphipathic nature disrupt bacterial membranes leading to cell lysis. In some instances, AMPs may enter cells and interact with intracellular target to interfere with DNA, RNA, protein, or cell wall synthesis. In addition to killing microorganisms, AMPs have demonstrated a number of immunomodulatory functions that are involved in the clearance of infection, including the ability to alter host gene expression, act as chemokines and/or induce chemokine production, inhibit lipopolysaccharide induced pro-inflammatory cytokine production, promote wound healing, and modulating the responses of dendritic cells and cells of the adaptive immune response.

In some instances, the AMP is a functionally active variant of the AMPs described herein. In some instances, the variant of the AMP has at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of an AMP described herein or a naturally derived AMP.

In some instances, the AMP may be bioengineered to modulate its bioactivity, e.g., increase or decrease or regulate, or to specify a target microorganism. In some instances, the AMP is produced by the translational machinery (e.g. a ribosome, etc.) of a cell. In some instances, the AMP is chemically synthesized. In some instances, the AMP is derived from a polypeptide precursor. The polypeptide precursor can undergo cleavage (for example, processing by a protease) to yield the polypeptide of the AMP itself. As such, in some instances, the AMP is produced from a precursor polypeptide. In some instances, the AMP includes a polypeptide that has undergone post-translational modifications, for example, cleavage, or the addition of one or more functional groups.

The AMPs described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of AMPs, such as at least about any one of 1 AMP, 2, 3, 4, 5, 10, 15, 20, or more AMPs. For example, the compositions may include a cocktail of AMPs (e.g., a cocktail of scorpion peptides, e.g., UyCT3, D3, D10, and Uy17). A suitable concentration of each AMP in the composition depends on factors such as efficacy, stability of the AMP, number of distinct AMP in the composition, the formulation, and methods of application of the composition. In some instances, each AMP in a liquid composition is from about 0.1 ng/mL to about 100 mg/mL. In some instances, each AMP in a solid composition is from about 0.1 ng/g to about 100 mg/g.

In some instances, wherein the composition includes at least two types of AMPs, the concentration of each type of AMP may be the same or different.

A modulating agent including an AMP as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of AMP concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of AMP concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of AMP concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

(d) Nodule C-rich Peptides

The modulating agent described herein may include a nodule C-rich peptide (NCR peptide). NCR peptides are produced in certain leguminous plants and play an important role in the mutualistic, nitrogen-fixing symbiosis of the plants with bacteria from the *Rhizobiaceae* family (rhizobia), resulting in the formation of root nodules where plant cells contain thousands of intracellular endosymbionts. NCR peptides possess anti-microbial properties that direct an irreversible, terminal differentiation process of bacteria, e.g., to permeabilize the bacterial membrane, disrupt cell division, or inhibit protein synthesis. For example, in *Medicago truncatula* nodule cells infected with *Sinorhizobium meliloti*, hundreds of NCR peptides are produced which direct irreversible differentiation of the bacteria into large polyploid nitrogen-fixing bacteroids.). Non-limiting examples of NCR peptides are listed in Table 7.

Table 7: Examples of NCR Peptides

NAME	Peptide sequence	Producer
>gi 152218086 gb ABS31477.1 NCR 340	MTKIVVFYVILLTIFHVS AKKKRYI ECETHEDCSQVFMPPFVMRCVIHE CKIFNGEHLRY (SEQ ID NO: 94)	<i>Medicago truncatula</i>
>gi 152218084 gb ABS31476.1 NCR 339	MAKIMKFVYNMIPFLSIFIITLQVNVV VCEIDADCPQICMPPEVRCVNHRC GWVNTDDSLFLTQEFTRSKQYIIS (SEQ ID NO: 95)	<i>Medicago truncatula</i>
>gi 152218082 gb ABS31475.1 NCR 338	MYKVVESIFIRYMHRKPNMTKFFKF VYTMFILISLFLVVTNANAHNCTDISD CSSNHCSYEGVSLCMNGQCICIYE (SEQ ID NO: 96)	<i>Medicago truncatula</i>
>gi 152218080 gb ABS31474.1 NCR 337	MVETLRLFYIMILFVSLCLVVDGES KLEQTCSEDFECYIKNPHVPFGHLR CFEGFCQQLNGPA (SEQ ID NO: 97)	<i>Medicago truncatula</i>

>gi 152218078 gb ABS31473. 1 NCR 336	MAKIVNFVYSMIVFLFLVATKAAR GYLCVTDSHCPPHMCPPGMEPRCV RRMCKCLPIGWRYFVP (SEQ ID NO: 98)	<i>Medicago truncatula</i>
>gi 152218076 gb ABS31472. 1 NCR 335	MQIGKNMVETPKLDYVIFFLYFFF RQMILRLNTTFRPLNFKMLRFWGQ NRNIMKHRGQKVHFSLILSDCKTNK DCPKLRRANVRCRKSVCVPI (SEQ ID NO: 99)	<i>Medicago truncatula</i>
>gi 152218074 gb ABS31471. 1 NCR 334	MLRLYLVSFYLLKRTLLVSYSYFST YIECKTDNDPISQLKIYAWKCVKN GCHLFDVIPMMYE (SEQ ID NO: 100)	<i>Medicago truncatula</i>
>gi 152218072 gb ABS31470. 1 NCR 333	MAEILKFVYIVILFVSLLLIVVASEREC VTDDDCEKLYPTNEYRMMCDSGYC MNLLNGKIIYLLCLKKKKFLIISVLL (SEQ ID NO: 101)	<i>Medicago truncatula</i>
>gi 152218070 gb ABS31469. 1 NCR 332	MAEIKFVYIMILCVSLLLIEVAGEECV TDADCDKLYPDIRKPLMCSIGECYSL YKGKFSLSIISKTSFSLMVYNVVTLVI CLRLAYISLLKFL (SEQ ID NO: 102)	<i>Medicago truncatula</i>
>gi 152218068 gb ABS31468. 1 NCR 331	MAEILKDFYAMNLFIFLILPAKIRGET LSLTHPKCHHIMLPSELFITEVFQRT DDGCPKPVNHLRVVKCIEHICEYGY NYRPDFASQIPESTKMPRKRE (SEQ ID NO: 103)	<i>Medicago truncatula</i>
>gi 152218066 gb ABS31467. 1 NCR 330	MVEILKNFYAMNLFIFLILAVKIRGAH FPCVTDDDCPKPVNKLRLVIKCIDHIC QYARNLPDFASEISESTKMPCKGE (SEQ ID NO: 104)	<i>Medicago truncatula</i>
>gi 152218064 gb ABS31466. 1 NCR 329	MFHAQAENMAKVSNFVCIMILFLALF FITMNDAAARFECREDSHCVTRIKCV LPRKPECRNYACGCYDSNKYR (SEQ ID NO: 105)	<i>Medicago truncatula</i>
>gi 152218062 gb ABS31465. 1 NCR 328	MQMRQNMATILNFVFIILFISLLLVV TKGYREPFSSTFTEGPTCKEDIDCPSI SCVNPQVPKCMFECHCKYIPTTLK (SEQ ID NO: 106)	<i>Medicago truncatula</i>
>gi 152218060 gb ABS31464. 1 NCR 327	MATILMYVYITILFISILTVLTEGLYEPL YNFRRDPDCRRNIDCPSYLCVAPKV PRCIMFECHCKDIPSDH (SEQ ID NO: 107)	<i>Medicago truncatula</i>

>gi 152218058 gb ABS31463. 1 NCR 326	MTTSLKFVYVAILFLSLLLVMGGIR RFECRQSDCPSYFCEKLTVPKCF WSKCYCK (SEQ ID NO: 108)	<i>Medicago truncatula</i>
>gi 152218056 gb ABS31462. 1 NCR 325	MTTSLKFVYVAILFLSLLLVMGGIR KKECRQSDCPSYFCEKLTIAKCIHS TCLCK (SEQ ID NO: 109)	<i>Medicago truncatula</i>
>gi 152218054 gb ABS31461. 1 NCR 324	MQIGKNMVETPKLVYFIILFLSIFLCIT VSNSSFQIFNSACKTDKDCPKFGR VNVRCRKGNCPVI (SEQ ID NO: 110)	<i>Medicago truncatula</i>
>gi 152218046 gb ABS31457. 1 NCR 320	MTAILKKFINAVFLFIVLFLATTNVED FVGGSNDECVPDVFQCINNICKCV SHHRT (SEQ ID NO: 111)	<i>Medicago truncatula</i>
>gi 152218044 gb ABS31456. 1 NCR 319	MQKRKNMAQIIFYVYALIILFSPFLAA RLVFVNPEKPCVTDADCDRYRHES AIYSDMFCKDGYCFIDYHHPYP (SEQ ID NO: 112)	<i>Medicago truncatula</i>
>gi 152218042 gb ABS31455. 1 NCR 318	MQMRKNMAQILFYVYALLILFTPFLV ARIMVVNPNNPCVTDADCQRYRHK LATRMICNQGFCLMDFTHDPYAPSL P (SEQ ID NO: 113)	<i>Medicago truncatula</i>
>gi 152218040 gb ABS31454. 1 NCR 317	MNHISKFYVALIFLSIYLVLDGLPIS CKDHFECRRKINILRCIYRQEKPMCI NSICTCVKLL (SEQ ID NO: 114)	<i>Medicago truncatula</i>
>gi 152218038 gb ABS31453. 1 NCR 316	MQREKNMAKIFEFVYAMIIFILLFLVE KNVVAYLKFECKTDDDCQKSLLKTY VWKCVKNECYFFAKK (SEQ ID NO: 115)	<i>Medicago truncatula</i>
>gi 152218036 gb ABS31452. 1 NCR 315	MAGIIKFVHVLIIFLSLFHVVKNDGGS FCFKDSDCPDEMCPSPLEKMCYFL QCKCGVDTIA (SEQ ID NO: 116)	<i>Medicago truncatula</i>
>gi 152218034 gb ABS31451. 1 NCR 314	MANTHKLVSMLFIFLFLASNNEGY VNCETDADCPPSTRVKRFKCVKGE CRWTRMSYA (SEQ ID NO: 117)	<i>Medicago truncatula</i>

>gi 152218032 gb ABS31450. 1 NCR 313	MQRRKKKAQVVMFVHDLIICIYLFIVI TTRKTDIRCRFYDCPRLEYHFCECI EDFCAYIRLN (SEQ ID NO: 118)	<i>Medicago truncatula</i>
>gi 152218030 gb ABS31449. 1 NCR 312	MAKVYMFVYALIIFVSPFLLATFRTL PCEKDDDCPEAFLPPVMKCVNRFC QYEILE (SEQ ID NO: 119)	<i>Medicago truncatula</i>
>gi 152218028 gb ABS31448. 1 NCR 310	MIKQFSVCYIQMRRNMTTILKFPYIM VICLLLLHVAAYEDFEKEIFDCKKDG DCDHMCVTPGIPKCTGYVCFCFENL (SEQ ID NO: 120)	<i>Medicago truncatula</i>
>gi 152218026 gb ABS31447. 1 NCR 309	MQRSRNMTTIFKFAYIMIICVLLNIA AQEIENGIHPCKKNEDCNHMCVMP GLPWCHENNLCFCYENAYGNTR (SEQ ID NO: 121)	<i>Medicago truncatula</i>
>gi 152218024 gb ABS31446. 1 NCR 304	MTIIKFVNVLIIFLSLFHVAKNDDNKL LLSFIEEGFLCFKDSDCPYNMCPSP LKEMCYFIKCVCGVYGPIRERRLYQ SHNPMIQ (SEQ ID NO: 122)	<i>Medicago truncatula</i>
>gi 152218022 gb ABS31445. 1 NCR 303	MRKNMTKILMIGYALMIFILSIASIT GNLARASRKKPVDVIPCIYDHDCPR KLYFLERCVGRVCKYL (SEQ ID NO: 123)	<i>Medicago truncatula</i>
>gi 152218020 gb ABS31444. 1 NCR 301	MAHKLVAITLFI FLIANNIEDDIFCI TDNDCPPNTLVQRYRCINGKCNLSF VSYG (SEQ ID NO: 124)	<i>Medicago truncatula</i>
>gi 152218018 gb ABS31443. 1 NCR 300	MDETLLKFVYILILFVSLCLVVADGVK NINRECTQTSDCYKKYPFIPWGKVR CVKGRCRLDM (SEQ ID NO: 125)	<i>Medicago truncatula</i>
>gi 152218016 gb ABS31442. 1 NCR 290	MAKIIKFVYVLAIFFLVAKNVNG WTCVEDSDCPANICQPPMQRMCFY GECACVRSKFCT (SEQ ID NO: 126)	<i>Medicago truncatula</i>
>gi 152218014 gb ABS31441. 1 NCR 289	MVKIIKFVYFMTLFLSMLLVTTKEDG SVECIANIDCPQIFMLPFVMRCINFR CQIVNSEDT (SEQ ID NO: 127)	<i>Medicago truncatula</i>

>gi 152218012 gb ABS31440.1 NCR 286	MDEILKFVYTLIIFFSLFFAANNVDANI MNCQSTFDCPRDMCSHIRDVICIFK KCKCAGGRYMPQVP (SEQ ID NO: 128)	<i>Medicago truncatula</i>
>gi 152218008 gb ABS31438.1 NCR 278	MQRRKNMANNHMLIYAMIICLFPYL VVTFKTAITCDCNEDCLNFFFTPLDNL KCIDNVCEVFM (SEQ ID NO: 129)	<i>Medicago truncatula</i>
>gi 152218006 gb ABS31437.1 NCR 266	MVNILKFIYVIFFILMFFVLIDVDGHV LVECIENRDCEKGMCKFPFIVRCLM DQCKCVRIHNL (SEQ ID NO: 130)	<i>Medicago truncatula</i>
>gi 152218004 gb ABS31436.1 NCR 265	MIIQFSIYYMQRRKLNLMVEILKFSHA LIIFLFLSALVTNANIFFCSTDEDCTW NLCRQPWWQKCRMHMCSEKN (SEQ ID NO: 131)	<i>Medicago truncatula</i>
>gi 152218002 gb ABS31435.1 NCR 263	MDEVFKFVYVMIIFFPFLILDVATNAEK IRRCFNDAHCPPDMCTLGVIPKCSR FTICIC (SEQ ID NO: 132)	<i>Medicago truncatula</i>
>gi 152218000 gb ABS31434.1 NCR 244	MHRKPNMTKFFKFVYTMFILISLFLV VTNANANNCTDTSDCSSNHCSYEG VSLCMNGQCICIYE (SEQ ID NO: 133)	<i>Medicago truncatula</i>
>gi 152217998 gb ABS31433.1 NCR 239	MQMKMATILKFVYLIILLIYPLLVTTE ESHYMKFSICKDDTDCPTLFCVLPN VPKIGSKCHCKLMVN (SEQ ID NO: 134)	<i>Medicago truncatula</i>
>gi 152217996 gb ABS31432.1 NCR 237	MVETLRLFYIMILFVSLYLVVVDGVS KLAQSCSEDFECYIKNPHAPFGQLR CFEGYCQRLDKPT (SEQ ID NO: 135)	<i>Medicago truncatula</i>
>gi 152217994 gb ABS31431.1 NCR 228	MTTFLKVAYIMICVFVHLAAQVDS QKRLHGCKEDRDCDNICSVHAVTK CIGNMCRCLANVK (SEQ ID NO: 136)	<i>Medicago truncatula</i>
>gi 152217992 gb ABS31430.1 NCR 224	MRINRTPAIFKFVYTIILYFLLRVVAK DLPFNICEKDEDCLEFCAHDKVAKC MLNICFCF (SEQ ID NO: 137)	<i>Medicago truncatula</i>

>gi 152217990 gb ABS31429. 1 NCR 221	MAEILKILYVFIIFLSLILAVISQHPFTP CETNADCKCRNHKRPDCLWHKCYC Y (SEQ ID NO: 138)	<i>Medicago truncatula</i>
>gi 152217988 gb ABS31428. 1 NCR 217	MRKSMATILKFVYVIMLFIYSLFVIES FGHRFLIYNCKNDTECPNDGCPHE QAKCILYACYCVE (SEQ ID NO: 139)	<i>Medicago truncatula</i>
>gi 152217986 gb ABS31427. 1 NCR 209	MNTILKFIFVVFLLSIFLSAGNSKSY GPCTTLQDCETHNWFEVCSCIDFEC KCWSSL (SEQ ID NO: 140)	<i>Medicago truncatula</i>
>gi 152217984 gb ABS31426. 1 NCR 206	MAEIIKFVYIMILCVSLLIAEASGKEC VTDADCENLYPGNKKPMFCNNTGY CMSLYKEPSRYM (SEQ ID NO: 141)	<i>Medicago truncatula</i>
>gi 152217982 gb ABS31425. 1 NCR 201	MAKIIKFVYIMILCVSLLLIVEAGGKEC VTDVDCEKIYPGNKKPLICSTGYCYS LYEEPPLYHK (SEQ ID NO: 142)	<i>Medicago truncatula</i>
>gi 152217980 gb ABS31424. 1 NCR 200	MAKVTKFGYIIHFLSLFFLAMNVAG GRECHANSCHCVGKITCVLPQKPEC WNYACVCYDSNKYR (SEQ ID NO: 143)	<i>Medicago truncatula</i>
>gi 152217978 gb ABS31423. 1 NCR 192	MAKIFNYVYALIMFLSLFLMGTSGMK NGCKHTGHCPKRMCGAKTTKCRN NKCQCV (SEQ ID NO: 144)	<i>Medicago truncatula</i>
>gi 152217976 gb ABS31422. 1 NCR 189	MTEILKFVCMIIFFISFIVSKSLNGG GKDKCFRSDCPKHMCPSSLVAKCI NRLCRCRRPELQVQLNP (SEQ ID NO: 145)	<i>Medicago truncatula</i>
>gi 152217974 gb ABS31421. 1 NCR 187	MAHIIMFVYALIYALIIFFSLFVRDGIP CLSDDECPEMSHYFKCENKICEYD LGEMSDDDYLEMSRE (SEQ ID NO: 146)	<i>Medicago truncatula</i>
>gi 152217972 gb ABS31420. 1 NCR 181	MYREKNMAKTLKFVYVIVLFLSLFLA AKNIDGRVSYNSFIALPVCQTAADC PEGTRGRTYKCINNKCORYPKLLKPI Q (SEQ ID NO: 147)	<i>Medicago truncatula</i>

>gi 152217970 gb ABS31419.1 NCR 176	MAHIFNYVYALLVFLSLFLMVTNGIHI GCDKDRDCPKQMCHLNQTPKCLKN ICKCV (SEQ ID NO: 148)	<i>Medicago truncatula</i>
>gi 152217968 gb ABS31418.1 NCR 175	MAEILKCFYTMNLFIFLIILPAKIREHI QCVIDDDCPKSLNKLIIKCINHVQCQY VGNLPDFASQIPKSTKMPYKGE (SEQ ID NO: 149)	<i>Medicago truncatula</i>
>gi 152217966 gb ABS31417.1 NCR 173	MAYISRIFYVLIIFLSLFFVINGVKSL LLIKVRSFIPCQRSDDCPRNLCVDQII PTCVWAKCKCKNYND (SEQ ID NO: 150)	<i>Medicago truncatula</i>
>gi 152217964 gb ABS31416.1 NCR 172	MANVTKFVYIAIYFLSLFFIAKNDATA TFCHDDSHCVTKIKCVLPRTQPQRN EACGCYHSNKFR (SEQ ID NO: 151)	<i>Medicago truncatula</i>
>gi 152217962 gb ABS31415.1 NCR 171	MGEIMKFVYVMIIYLFMFNVATGSEF IFTKKLTSCDSSKDCRSFLCYSPKFP VCKRGICECI (SEQ ID NO: 152)	<i>Medicago truncatula</i>
>gi 152217960 gb ABS31414.1 NCR 169	MGEMFKFIYTFILFVHLFLVVIFEDIG HIKYCGIVDDCYKSKPLFKIWKCVE NVCVLWYK (SEQ ID NO: 153)	<i>Medicago truncatula</i>
>gi 152217958 gb ABS31413.1 NCR 165	MARTLKFFVYSMILFLSLFLVANGLKIF CIDVADCPKDLPLLYKCIYNKCIVFT RIPFPFDWI (SEQ ID NO: 154)	<i>Medicago truncatula</i>
>gi 152217956 gb ABS31412.1 NCR 159	MANITKFVYIAILFLSLFFIGMNDAAIL ECREDSHCVTKIKCVLPKPECRNN ACTCYKGGFSFHH (SEQ ID NO: 155)	<i>Medicago truncatula</i>
>gi 152217954 gb ABS31411.1 NCR 147	MQRVKKMSETLKFVYVLILFISIFHV IVCDSIYFPVSRPCITDKDCPNMKHY KAKCRKGFCISSVR (SEQ ID NO: 156)	<i>Medicago truncatula</i>
>gi 152217952 gb ABS31410.1 NCR 146	MQIRKIMSGVLKFVYAILFLFLFLVA REVGGLETIECETDGDGCPRSMIKM WNKNYRHKCIDGKCEWIKKLP (SEQ ID NO: 157)	<i>Medicago truncatula</i>

>gi 152217950 gb ABS31409.1 NCR 145	MFVYDLILFISLILVVTGINAEADTSC HSFDDCPWVAHHYRECIEGLCAYRI LY (SEQ ID NO: 158)	<i>Medicago truncatula</i>
>gi 152217948 gb ABS31408.1 NCR 144	MQRRKKSMAKMLKFFFAIILLLSLFL VATEVGGAYIECEVDDDCPKPMKN SHPDTYYKCVKHRCQWAWK (SEQ ID NO: 159)	<i>Medicago truncatula</i>
>gi 152217946 gb ABS31407.1 NCR 140	MFVYTLIIFLFP SHVITNKIAIYCVSDD DCLKTFTPLDLKCDNVCEFNLRCK GKCGERDEK FVFLKALKKMDQKLVL EEQGNAREVKIPKLLFDRIQVPTPA TKDQVEEDDYDDDDDEEEEEEDDV DMWFHLPDVVCH (SEQ ID NO: 160)	<i>Medicago truncatula</i>
>gi 152217944 gb ABS31406.1 NCR 138	MAKFSMFVYALINFLSLFLVETAITNI RCVSDDDCPKVIKPLVMKCIGNYCY FFMIYEGP (SEQ ID NO: 161)	<i>Medicago truncatula</i>
>gi 152217942 gb ABS31405.1 NCR 136	MAHKFVYAIILFIFLFLVAKNVKGYVV CRTVDDCPPDTRDLRYRCLNGKCK SYRLSYG (SEQ ID NO: 162)	<i>Medicago truncatula</i>
>gi 152217940 gb ABS31404.1 NCR 129	MQRKKNMGQILIFVFALINFLSPILVE MTTTTIPCTFIDDCPKMPLVVKCIDN FCNYFEIK (SEQ ID NO: 163)	<i>Medicago truncatula</i>
>gi 152217938 gb ABS31403.1 NCR 128	MAQTLMLVYALIIFTSLFLVVISRQTD IPCKSDDACPRVSSHIECVKGFCT YWKLD (SEQ ID NO: 164)	<i>Medicago truncatula</i>
>gi 152217936 gb ABS31402.1 NCR 127	MLRRKNTVQILMFVSALLIYIFLFLVIT SSANIPCNSDSDCPWKIYYTYRCND GFCVYKSIDPSTIPQYMTDLIFPR (SEQ ID NO: 165)	<i>Medicago truncatula</i>
>gi 152217934 gb ABS31401.1 NCR 122	MAVILKFVYIMIIIFLLYVVNGTRCN RDEDCPFICTGPQIPKCVSHICFLS SGKEAY (SEQ ID NO: 166)	<i>Medicago truncatula</i>
>gi 152217932 gb ABS31400.1 NCR 121	MDAILKFIYAMFLFLFVTTTRNVEAL FECNRDFVCGNDDECVPYAVQCI HRYCKCLKSRN (SEQ ID NO: 167)	<i>Medicago truncatula</i>

>gi 152217930 gb ABS31399.1 NCR 119	MQIGRKKMGETPKLVYVILFLSIFLC TNSSFSQMINFRGCKRDKDCPQFR GVNIRCRSGFCTPIDS (SEQ ID NO: 168)	<i>Medicago truncatula</i>
>gi 152217928 gb ABS31398.1 NCR 118	MQMRKNMAQILFYVYALLILFSPFLV ARIMVVNPNNPCVTDADCQRYRHK LATRMVCNIGFCLMDFTHDPYAPSL P (SEQ ID NO: 169)	<i>Medicago truncatula</i>
>gi 152217926 gb ABS31397.1 NCR 111	MYVYYIQMGKNMAQRFMFIYALIIFL SQFFVINTSDIPNNSNRNSPKEDVF CNSNDDCPTILYYVSKCVYNFCEYW (SEQ ID NO: 170)	<i>Medicago truncatula</i>
>gi 152217924 gb ABS31396.1 NCR 103	MAKIVNFVYSMIIFVSLFLVATKGGG KPFLTRPYPCNTGSDCPQNMCPPG YKPGCEDGYCNHCYKRW (SEQ ID NO: 171)	<i>Medicago truncatula</i>
>gi 152217922 gb ABS31395.1 NCR 101	MVRTLKFYVYVILSLFLVAKGGGKK IYCENAASCPRMLYPLVYKCLDNKC VKFMMKSRFV (SEQ ID NO: 172)	<i>Medicago truncatula</i>
>gi 152217920 gb ABS31394.1 NCR 96	MARTLKFYVYAVILFLSLFLVAKGDDV KIKCVVAANCPDLMYPLVYKCLNGIC VQFTLTFFV (SEQ ID NO: 173)	<i>Medicago truncatula</i>
>gi 152217918 gb ABS31393.1 NCR 94	MSNTLMFVITFIVLVTFLGPKNVYA FQPCVTTADCMKTLKTDENIWYECI NDFCIPFPIPKGRK (SEQ ID NO: 174)	<i>Medicago truncatula</i>
>gi 152217916 gb ABS31392.1 NCR 93	MKRNVNMAKIVKYVYVYVILFLSLFLVA TKIEGYYYKCFKSDCVKLLCRIPLR PKCMYRHICKCKVVLQNNYVLT (SEQ ID NO: 175)	<i>Medicago truncatula</i>
>gi 152217914 gb ABS31391.1 NCR 90	MKRGKNMSKILKFIYATLVLYLFLVV TKASDDECKIDGDCPISWQKFHTYK CINQKCKWVLRFFEY (SEQ ID NO: 176)	<i>Medicago truncatula</i>
>gi 152217912 gb ABS31390.1 NCR 88	MAKTLNFMFALILFISLFLVSKNVAID FVCQTDADCPKSELSMYTWKCIDN ECNLFKVMQQMV (SEQ ID NO: 177)	<i>Medicago truncatula</i>

>gi 152217910 gb ABS31389.1 NCR 86	MANTHKLVSMLFIFLFLVANNVEGY VNCETDADCPPSTRVKRFKCVKGE CRWTRMSYA (SEQ ID NO: 178)	<i>Medicago truncatula</i>
>gi 152217908 gb ABS31388.1 NCR 77	MAHFLMFVYALITCLSLFLVEMGHLS IHCVSVD DCPKVEKPITMKCINNYCK YFVDHKL (SEQ ID NO: 179)	<i>Medicago truncatula</i>
>gi 152217906 gb ABS31387.1 NCR 76	MNQIPMFGYTLIIFFSLFPVITNGDRI PCVTNGDCPVMRLPLYMRCITYSCE LFFDGP NLCAVERI (SEQ ID NO: 180)	<i>Medicago truncatula</i>
>gi 152217904 gb ABS31386.1 NCR 74	MRKDMARISLFFVYALIIFFSLFFVLTN GELEIRCVSDADCP LPLPLHNRCID DVCHLFTS (SEQ ID NO: 181)	<i>Medicago truncatula</i>
>gi 152217902 gb ABS31385.1 NCR 68	MAQILMFVYFLIIFLSLFLVESIKIFTE HRCRTDADCPARELPEYLK CQGGM CRLLIKD (SEQ ID NO: 182)	<i>Medicago truncatula</i>
>gi 152217900 gb ABS31384.1 NCR 65	MARVISLIFYALIIFLFLVATNGDLS PCLRSGDCSKDECPSHLVPKIGLT CYCI (SEQ ID NO: 183)	<i>Medicago truncatula</i>
>gi 152217898 gb ABS31383.1 NCR 62	MQRRKNMAQILLFAYVFIISLFLVV TNGVKIPCVKDTDCPTLPCPLYSKC VDGFCKMLSI (SEQ ID NO: 184)	<i>Medicago truncatula</i>
>gi 152217896 gb ABS31382.1 NCR 57	MNHISKFYALIIFLSVYLVVLDGRPV SCKDHYDCRRKVKIVGCIFPQEKPM CINSMTCTCIREIVP (SEQ ID NO: 185)	<i>Medicago truncatula</i>
>gi 152217894 gb ABS31381.1 NCR 56	MKSQNHAKFISFYKNDLFKIFQNND SHFKVFFALIIFLYTYLHVTNGV FVSC NSHIHCRVNNHKIGCNIPEQYLLCVN LFCLWLDY (SEQ ID NO: 186)	<i>Medicago truncatula</i>
>gi 152217892 gb ABS31380.1 NCR 54	MTYISKVVYALIIFLSIYVGVNDCMLV TCEDHFD CRQNVQVGCSFREIPQ CINSICKCMKG (SEQ ID NO: 187)	<i>Medicago truncatula</i>

>gi 152217890 gb ABS31379.1 NCR 53	MTHISKFVFALIIFLSIYVGVNDCKRIP CKDNNDCCNNNWQLLACRFEREVPR CINSICKCMPM (SEQ ID NO: 188)	<i>Medicago truncatula</i>
>gi 152217888 gb ABS31378.1 NCR 43	MVQTPKLVYVIVLLLSIFLGMTICNSS FSHFFEGACKSDKDCPKLHRSNVR CRKGQCVQI (SEQ ID NO: 189)	<i>Medicago truncatula</i>
>gi 152217886 gb ABS31377.1 NCR 28	MTKILMLFYAMIVFHSIFLVASYTDEC STDADCEYILCLFPPIIKRCIHNHCKCV PMGSIEPMSTIPNGVHKFHIINN (SEQ ID NO: 190)	<i>Medicago truncatula</i>
>gi 152217884 gb ABS31376.1 NCR 26	MAKTLNFCAMILFISLFLVSKNVAL YIECKTDADCPISKLNMYNWRICKS SCHLYKVIQFMV (SEQ ID NO: 191)	<i>Medicago truncatula</i>
>gi 152217882 gb ABS31375.1 NCR 24	MQKEKNMAKTFFVYAMIIFILLFLVE NNFAAYIECQTDDDCPKSQLEMFA WKCVKNGCHLFGMYEDDDDP (SEQ ID NO: 192)	<i>Medicago truncatula</i>
>gi 152217880 gb ABS31374.1 NCR 21	MAATRKFYVLSHFLFLVTKITDAR VCKSDKDCKDIIYRYILKCRNGECV KIKI (SEQ ID NO: 193)	<i>Medicago truncatula</i>
>gi 152217878 gb ABS31373.1 NCR 20	MQRLDNMAKNVKFIYVILLFIFLVII VCDSAFVPNSGPCTTDKCKQVKG YIARCRKGYCMQSVKRTWSSYSR (SEQ ID NO: 194)	<i>Medicago truncatula</i>
>gi 152217876 gb ABS31372.1 NCR 19	MKFIYIMILFSLFLVQFLTCKGLTVP CENPTTCPEDFCTPPMITRCINFICL CDGPEYAEPEYDGPEPEYDHKGDF LSVKPKIINENMMMRRERHMMKEIEV (SEQ ID NO: 195)	<i>Medicago truncatula</i>
>gi 152217874 gb ABS31371.1 NCR 12	MAQFLMFIYVLIIFLYFYVEAAMFEL TKSTIRCVTADCPNVVKPLPKPCV DGFCEYT (SEQ ID NO: 196)	<i>Medicago truncatula</i>
>gi 152217872 gb ABS31370.1 NCR 10	MKMRIHMAQIIMFFYALIIFLSPFLVD RRSFPSSFVSPKSYTSEIPCKATRD CPYELYYETKCVDSLCTY (SEQ ID NO: 197)	<i>Medicago truncatula</i>

Any NCR peptide known in the art is suitable for use in the methods or compositions described herein. NCR peptide-producing plants include but are not limited to *Pisum sativum* (pea), *Astragalus sinicus* (IRLC legumes), *Phaseolus vulgaris* (bean), *Vigna unguiculata* (cowpea), *Medicago truncatula* (barrelclover), and *Lotus japonicus*. For example, over 600 potential NCR peptides are predicted from the *M. truncatula* genome sequence and almost 150 different NCR peptides have been detected in cells isolated from root nodules by mass spectrometry.

The NCR peptides described herein may be mature or immature NCR peptides. Immature NCR peptides have a C-terminal signal peptide that is required for translocation into the endoplasmic reticulum and cleaved after translocation. The N-terminus of a NCR peptide includes a signal peptide, which may be cleavable, for targeting to a secretory pathway. NCR peptides are generally small peptides with disulfide bridges that stabilize their structure. Mature NCR peptides have a length in the range of about 20 to about 60 amino acids, about 25 to about 55 amino acids, about 30 to about 50 amino acids, about 35 to about 45 amino acids, or any range therebetween. NCR peptides may include a conserved sequence of cysteine residues with the rest of the peptide sequence highly variable. NCR peptides generally have about four or eight cysteines.

NCR peptides may be anionic, neutral, or cationic. In some instances, synthetic cationic NCR peptides having a pI greater than about eight possess antimicrobial activities. For example, NCR247 (pI = 10.15) (RNGCIVDPRCPYQQCRRPLYCRRR; SEQ ID NO: 198) and NCR335 (pI = 11.22) (MAQFLLFVYSLIIFLSLFFGEAAFERTETRLTIPCTSDDNCPKVISPCHTKCFDGFCEGWYIEGSYEGP; SEQ ID NO: 199) are both effective against gram-negative and gram-positive bacteria as well as fungi. In some instances, neutral and/or anionic NCR peptides, such as NCR001, do not possess antimicrobial activities at a pI greater than about 8.

In some instances, the NCR peptide is effective to kill bacteria. In some instances, the NCR peptide is effective to kill *S. meliloti*, *Xenorhabdus spp*, *Photorhabdus spp*, *Candidatus spp*, *Buchnera spp*, *Blattabacterium spp*, *Baumania spp*, *Wigglesworthia spp*, *Wolbachia spp*, *Rickettsia spp*, *Orientia spp*, *Sodalis spp*, *Burkholderia spp*, *Cupriavidus spp*, *Frankia spp*, *Snirrhizobium spp*, *Streptococcus spp*, *Wolinella spp*, *Xylella spp*, *Erwinia spp*, *Agrobacterium spp*, *Bacillus spp*, *Paenibacillus spp*, *Streptomyces spp*, *Micrococcus spp*, *Corynebacterium spp*, *Acetobacter spp*, *Cyanobacteria spp*, *Salmonella spp*, *Rhodococcus spp*, *Pseudomonas spp*, *Lactobacillus spp*, *Enterococcus spp*, *Alcaligenes spp*, *Klebsiella spp*, *Paenibacillus spp*, *Arthrobacter spp*, *Corynebacterium spp*, *Brevibacterium spp*, *Thermus spp*, *Pseudomonas spp*, *Clostridium spp*, or *Escherichia spp*.

In some instances, the NCR peptide is a functionally active variant of a NCR peptide described herein. In some instances, the variant of the NCR peptide has at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a NCR peptide described herein or naturally derived NCR peptide.

In some instances, the NCR peptide may be bioengineered to modulate its bioactivity, e.g., increase or decrease or regulate, or to specify a target microorganism. In some instances, the NCR peptide is produced by the translational machinery (e.g. a ribosome, etc.) of a cell. In some instances, the NCR peptide is chemically synthesized. In some instances, the NCR peptide is derived from a

polypeptide precursor. The polypeptide precursor can undergo cleavage (for example, processing by a protease) to yield the NCR peptide itself. As such, in some instances, the NCR peptide is produced from a precursor polypeptide. In some instances, the NCR peptide includes a polypeptide that has undergone post-translational modifications, for example, cleavage, or the addition of one or more functional groups.

5 The NCR peptide described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type of NCR peptides, such as at least about any one of 1 NCR peptide, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, or more NCR peptides. A suitable concentration of each NCR peptide in the composition depends on factors such as efficacy, stability of the NCR peptide, number of distinct NCR peptide, the formulation, and methods of application of the composition. In some instances, each NCR peptide in a liquid composition is from about 0.1 ng/mL to about 100 mg/mL. In some instances, each NCR peptide in a solid composition is from about 0.1 ng/g to about 100 mg/g. In some instances, wherein the composition includes at least two types of NCR peptides, the concentration of each type of NCR peptide may be the same or different.

A modulating agent including a NCR peptide as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of NCR peptide concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of NCR peptide concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of NCR peptide concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

(e) *Bacteriocyte Regulatory Peptides*

The modulating agent described herein may include a bacteriocyte regulatory peptide (BRP). BRPs are peptides expressed in the bacteriocytes of insects. These genes are expressed first at a developmental time point coincident with the incorporation of symbionts and their bacteriocyte-specific expression is maintained throughout the insect's life. In some instances, the BRP has a hydrophobic amino terminal domain, which is predicted to be a signal peptide. In addition, some BRPs have a cysteine-rich domain. In some instances, the bacteriocyte regulatory peptide is a bacteriocyte-specific cysteine rich (BCR) protein. Bacteriocyte regulatory peptides have a length between about 40 and 150 amino acids. In some instances, the bacteriocyte regulatory peptide has a length in the range of about 45 to about 145, about 50 to about 140, about 55 to about 135, about 60 to about 130, about 65 to about 125, about 70 to about 120, about 75 to about 115, about 80 to about 110, about 85 to about 105, or any range therebetween. Non-limiting examples of BRPs and their activities are listed in Table 8.

35 Table 8: Examples of Bacteriocyte Regulatory Peptides

Name	Peptide Sequence
Bacteriocyte-specific cysteine rich proteins BCR family, peptide BCR1	MKLLHGFLIIMLTMHLSIQYAYGGPFLTKYLCDRVCHKLC GDEFVCSCIQYKSLKGLWFPHCPTGKASVVLHNFLTSP (SEQ ID NO: 200)

Bacteriocyte-specific cysteine rich proteins BCR family, peptide BCR2	MKLLYGFLIIMLTIHLSVQYFESPFETKYNCDDTHCNKLCGK IDHCSCIQYHSM EGLWFP HCRTGSAAQMLHDFLSNP (SEQ ID NO: 201)
Bacteriocyte-specific cysteine rich proteins BCR family, peptide BCR3	MSVRKNVLPTMFVLLIMSPVTPTSVFISAVCYSGCGSLA LVCFVSNGITNGLDYFKSSAPLSTSETSCGEAFDTCTDH CLANFKF (SEQ ID NO: 202)
Bacteriocyte-specific cysteine rich proteins BCR family, peptide BCR4	MRLLYGFLIIMLTIHLSVQDFDPTEFKGPFTIEICSKYCAV VCNYTSRPCYCVEAAKERDQWFPYCYD (SEQ ID NO: 203)
Bacteriocyte-specific cysteine rich proteins BCR family, peptide BCR5	MRLLYGFLIIMLTIHLSVQDIDPNTLRGPYPTKEICSKYCEY NVVCGASLPCICVQDARQLDHWFACCYDGGPEMLM (SEQ ID NO: 204)
Secreted proteins SP family, peptide SP1	MKLFVVVVLVAVGIMFVFASDTAAAPTDYEDTNDMISLSS LVGDNSPYVRVSSADSGGSSKTSSKNPILGLLKSVIKLLT KIFGTYSDAAPAMPPIPPALRKNRGMLA (SEQ ID NO: 205)
Secreted proteins SP family, peptide SP2	MVACKVILAVAVVFVAAVQGRPGGEPEWAAPIFAELKSV SDNITNLVGLDNAGEYATAAKNNLNAFAESLKTEAAVFSK SFEGKASASDVFEKSTKNFQAVVDYIKNLPKDLTLKDFT EKSEQALKYMEVHGTEITKKAQGNTEKEIKEFFKKQIE NLIGQGKALQAKIAEAKKA (SEQ ID NO: 206)
Secreted proteins SP family, peptide SP3	MKTSSSKVFASCVAIVCLASVANALPVQKSVAATTENPIV EKHGCRAHKNLVRQNVVDLKYDMSMLITNEVVQKQSNE VQSSEQSNEGQNSEQSNEGQNSEQSNVQSSEHSNEG QNSKQSNEGQNSEQSNVQSSEHSNEGQNSEQSNVQ SSEHSNEGQNSKQSNEGQNSKQSNVQSSEHWNEGQ NSKQSNEDQNSEQSNEGQNSKQSNEGQNSKQSNEDQ NSEQSNEGQNSKQSNVQSSEQSNEGQNSKQSNEGQS SEQSNEGQNSKQSNVQSP EEHYDLPDPESSYESEETK GSHESGDDSEHR (SEQ ID NO: 207)
Secreted proteins SP family, peptide SP4	MKTIILGLCLFGALFWSTQSMPVGEVAPAVPAVPSEAVP QKQVEAKPETNAASPVS DAKPESDSKPVDAEVKPTVSEV KAESQKPSGEPKPESDAKPVVASESKPESDPKPAAVVE SKPENDAVAPETNNDAPENAAAPVSENKPATDAKAETE LIAQAKPESKPASDLKAEPEAAKPNSEVPVALPLNPTETK ATQQSVETNQVEQAAPAAAQADPAAAPAADPAPAPAAA PVAAEEAKLSESAPSTENKAAEPPSKPAEQQSAKPVEDA VPAASEISETKVSPAVPAVPEVPASPSAPAVADPVSAPEA EKNAEPAKAANSAEPAVQSEAKPAEDIQKSGAVVSAENP

	KPVEEQKPAEVAKPAEQSKSEAPAEAPKPTEQSAAEPPK KPESANDEKKEQHSVNKRDATKEKKPTDSIMKKQKQKK AN (SEQ ID NO: 208)
Secreted proteins SP family, peptide SP5a	MNGKIVLCFAVFIGQAMSAATGTTPEVEDIKKVAEQMS QTFMSVANHLVGITPNSADAQKSIEKIRTIMNKGFTDMET EANKMKDIVRKNADPKLVEKYDELEKELKKHLSTAKDMF EDKVVKPIGEKVELKKITENVIKTTKDMEATMNKAIDGFKK Q (SEQ ID NO: 209)
Secreted proteins SP family, peptide SP6	MHLFLALGLFIVCGMVDATFYNPRSQTFNQLMERRQSI PIPYSGYHYNPIEPSINVLDLSEGLDSRINTFKPIYQNV KMSTQDVNSVPRTQYQPKNSLYDSEYISAKDIPSLFP DSYDYKYLGSPLNKYLTRPSTQESGIAINLVAIKETSVFDY GFPTYKSPYSSDSVWNFGSKIPNTVFEDPQSVESDPNTF KVSSPTIKIVKLLPETPEQESIITTTKNYELNYKTTQETPTE AELYPITSEEFQTEDEWHMPVKENTTKDESSFITTEEPL TEDKSNSITIEKTQTEDESNSIEFNSIRTEEKSNISITTEENQ KEDDESMTTSQETTTAFNLNDTFDTNRYSSSHESLMRL IRELMKNIADQQNKSQFRTVDNIPAKSQSNLSSDESTNQ QFEPQLVNGADTYK (SEQ ID NO: 210)
Colepotericin A, ColA peptide	MTRTMLFLACVAALYVCISATAGKPEEFAKLSDEAPSND QAMYESIQRYRRFVDGNRYNGGQQQQQKQWEVRP DLSRDQRGNTKAQVEINKKGDNDINAGWGKNINGPDS HKDTWHVGGSVRW (SEQ ID NO: 211)
RlpA type I	MKETTVVWAKLFLILILAKPLGLKAVNECKRLGNNSCRSH GECCSGFCFIEPGWALGVCKRLGTPKKSDDSNNGKNIK NNGVHERIDDVFERGVCSYYKGPSITANGDVFDENEMTA AHRTLFPNTMVKVEGMGTSSVVVKINDRKTAAADGKVMLLS RAAAESLNIDENTGPVQCQLKFVLDGSGCTPDYGDTCVL HHECCSQNCFREMFSDKGFCLPK (SEQ ID NO: 212)

In some instances, the BRP alters the growth and/or activity of one or more bacteria resident in the bacteriocyte of the host. In some instances, the BRP may be bioengineered to modulate its bioactivity (e.g., increase, decrease, or regulate) or to specify a target microorganism. In some instances, the BRP is produced by the translational machinery (e.g. a ribosome, etc.) of a cell. In some instances, the BRP is chemically synthesized. In some instances, the BRP is derived from a polypeptide precursor. The polypeptide precursor can undergo cleavage (for example, processing by a protease) to yield the polypeptide of the BRP itself. As such, in some instances, the BRP is produced from a precursor

polypeptide. In some instances, the BRP includes a polypeptide that has undergone post-translational modifications, for example, cleavage, or the addition of one or more functional groups.

Functionally active variants of the BRPs as described herein are also useful in the compositions and methods described herein. In some instances, the variant of the BRP has at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity, e.g., over a specified region or over the entire sequence, to a sequence of a BRP described herein or naturally derived BRP.

The BRP described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of BRPs, such as at least about any one of 1 BRP, 2, 3, 4, 5, 10, 15, 20, or more BRPs. A suitable concentration of each BRP in the composition depends on factors such as efficacy, stability of the BRP, number of distinct BRP, the formulation, and methods of application of the composition. In some instances, each BRP in a liquid composition is from about 0.1 ng/mL to about 100 mg/mL. In some instances, each BRP in a solid composition is from about 0.1 ng/g to about 100 mg/g. In some instances, wherein the composition includes at least two types of BRPs, the concentration of each type of BRP may be the same or different.

A modulating agent including a BRP as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of BRP concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of BRP concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of BRP concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

iii. Small Molecules

Numerous small molecules (e.g., an antibiotic or a metabolite) may be used in the compositions and methods described herein. In some instances, an effective concentration of any small molecule described herein may alter the level, activity, or metabolism of one or more microorganisms (as described herein) resident in a host, the alteration resulting in an increase in the host's fitness.

A modulating agent comprising a small molecule as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of a small molecule concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of small molecule concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of a small molecule concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

(a) Antibiotics

The modulating agent described herein may include an antibiotic. Any antibiotic known in the art may be used. Antibiotics are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity.

The antibiotic described herein may target any bacterial function or growth processes and may be either bacteriostatic (e.g., slow or prevent bacterial growth) or bactericidal (e.g., kill bacteria). In some instances, the antibiotic is a bactericidal antibiotic. In some instances, the bactericidal antibiotic is one that targets the bacterial cell wall (e.g., penicillins and cephalosporins); one that targets the cell membrane (e.g., polymyxins); or one that inhibits essential bacterial enzymes (e.g., rifamycins, lipiarmycins, quinolones, and sulfonamides). In some instances, the bactericidal antibiotic is an aminoglycoside. In some instances, the antibiotic is a bacteriostatic antibiotic. In some instances the bacteriostatic antibiotic targets protein synthesis (e.g., macrolides, lincosamides and tetracyclines). Additional classes of antibiotics that may be used herein include cyclic lipopeptides (such as daptomycin), glycylicyclines (such as tigecycline), oxazolidinones (such as linezolid), or lipiarmycins (such as fidaxomicin). Examples of antibiotics include oxytetracycline, doxycycline, rifampicin, ciprofloxacin, ampicillin, and polymyxin B. Other non-limiting examples of antibiotics are found in Table 9.

Table 9: Examples of Antibiotics

Antibiotics	Action
Penicillins, cephalosporins, vancomycin	Cell wall synthesis
Polymixin, gramicidin	Membrane active agent, disrupt cell membrane
Tetracyclines, macrolides, chloramphenicol, clindamycin, spectinomycin	Inhibit protein synthesis
Sulfonamides	Inhibit folate-dependent pathways
Ciprofloxacin	Inhibit DNA-gyrase
Isoniazid, rifampicin, pyrazinamide, ethambutol, (myambutol), streptomycin	Antimycobacterial agents

The antibiotic described herein may have any level of target specificity (e.g., narrow- or broad-spectrum). In some instances, the antibiotic is a narrow-spectrum antibiotic, and thus targets specific types of bacteria, such as gram-negative or gram-positive bacteria. Alternatively, the antibiotic may be a broad-spectrum antibiotic that targets a wide range of bacteria.

The antibiotics described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of antibiotics, such as at least about any one of 1 antibiotic, 2, 3, 4, 5, 10, 15, 20, or more antibiotics (e.g., a combination of rifampicin and doxycycline, or a combination of ampicillin and rifampicin). A suitable concentration of each antibiotic in the composition depends on factors such as efficacy, stability of the antibiotic, number of distinct antibiotics, the formulation, and methods of application of the composition. In some instances, wherein the composition includes at least two types of antibiotics, the concentration of each type of antibiotic may be the same or different.

A modulating agent including an antibiotic as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of antibiotic concentration inside a target host; (b) reach a target level (e.g., a predetermined or

threshold level) of antibiotic concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of antibiotic concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

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(b) *Secondary Metabolites*

In some instances, the modulating agent of the compositions and methods described herein includes a secondary metabolite. Secondary metabolites are derived from organic molecules produced by an organism. Secondary metabolites may act (i) as competitive agents used against bacteria, fungi, amoebae, plants, insects, and large animals; (ii) as metal transporting agents; (iii) as agents of symbiosis between microbes and plants, insects, and higher animals; (iv) as sexual hormones; and (v) as differentiation effectors. Non-limiting examples of secondary metabolites are found in Table 10.

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Table 10: Examples of Secondary Metabolites

Phenyl-propanoids	Alkaloids	Terpenoids	Quinones	Steroids	Polyketides
Anthocyanins	Acridines	Carotenes	Anthro-quinones	Cardiac	Erythromycin
Coumarins	Betalaines	Monoterpenes	Bezo-quinones	Glycosides	Lovastatin and other statins
Flavonoids	Quino-lozidines	Sesquiterpenes	Naphtho-quinones	Pregnen-olone	Discoder-molide
Hydroxy-cinnamoyl	Furono-quinones	Diterpenes		Derivatives	Aflatoxin B1
Derivatives	Harring-tonines	Triterpenes			Avermectins
Isoflavonoids	Isoquino-lines				Nystatin
Lignans	Indoles				Rifamycin
Phenolenones	Purines				
Proantho-cyanidins	Pyridines				
Stilbenes	Tropane				
Tanins	Alkaloids				

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The secondary metabolite used herein may include a metabolite from any known group of secondary metabolites. For example, secondary metabolites can be categorized into the following groups: alkaloids, terpenoids, flavonoids, glycosides, natural phenols, e.g., gossypol acetic acid), enals (e.g., trans-cinnamaldehyde), phenazines, biphenols and dibenzofurans, polyketides, fatty acid synthase peptides, nonribosomal peptides, ribosomally synthesized and post-translationally modified peptides, polyphenols, polysaccharides (e.g., chitosan), and biopolymers. For an in-depth review of secondary metabolites see, for example, Vining, *Annu. Rev. Microbiol.* 44:395-427, 1990. Secondary metabolites useful for compositions and methods described herein include those that alter a natural function of an endosymbiont (e.g., primary or secondary endosymbiont), bacteriocyte, or extracellular symbiont. In some instances, one or more secondary metabolites described herein is isolated from a high throughput screening (HTS) for antimicrobial compounds. For example, a HTS screen identified 49 antibacterial

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extracts that have specificity against gram positive and gram negative bacteria from over 39,000 crude extracts from organisms growing in diverse ecosystems of one specific region. In some instances, the secondary metabolite is transported inside a bacteriocyte.

In some instances, the small molecule is an inhibitor of vitamin synthesis. In some instances, the vitamin synthesis inhibitor is a vitamin precursor analog. In certain instances, the vitamin precursor analog is pantothenol.

In some instances, the small molecule is an amino acid analog. In certain instances, the amino acid analog is L-canvanine, D-arginine, D-valine, D-methionine, D-phenylalanine, D-histidine, D-tryptophan, D-threonine, D-leucine, L-NG-nitroarginine, or a combination thereof.

In some instances the small molecule is a natural antimicrobial compound, such as propionic acid, levulinic acid, trans-cinnemaldehyde, nisin, or low molecular weight chitosan.

The secondary metabolite described herein may be formulated in a composition for any of the uses described herein. The compositions disclosed herein may include any number or type (e.g., classes) of secondary metabolites, such as at least about any one of 1 secondary metabolite, 2, 3, 4, 5, 10, 15, 20, or more secondary metabolites. A suitable concentration of each secondary metabolite in the composition depends on factors such as efficacy, stability of the secondary metabolite, number of distinct secondary metabolites, the formulation, and methods of application of the composition. In some instances, wherein the composition includes at least two types of secondary metabolites, the concentration of each type of secondary metabolite may be the same or different.

A modulating agent including a secondary metabolite as described herein can be contacted with the target host in an amount and for a time sufficient to: (a) reach a target level (e.g., a predetermined or threshold level) of secondary metabolite concentration inside a target host; (b) reach a target level (e.g., a predetermined or threshold level) of secondary metabolite concentration inside a target host gut; (c) reach a target level (e.g., a predetermined or threshold level) of secondary metabolite concentration inside a target host bacteriocyte; (d) modulate the level, or an activity, of one or more microorganism (e.g., endosymbiont) in the target host; or/and (e) modulate fitness of the target host.

iv. Bacteria as modulating agents

In some instances, the modulating agent described herein includes one or more bacteria. Numerous bacteria are useful in the compositions and methods described herein. In some instances, the agent is a bacterial species endogenously found in the host. In some instances, the bacterial modulating agent is an endosymbiotic bacterial species. Non-limiting examples of bacteria that may be used as modulating agents include all bacterial species described herein in Section II of the detailed description and those listed in Table 1. For example, the modulating agent may be a bacterial species from any bacterial phyla present in insect guts and/or haemocoel, including *Gammaproteobacteria*, *Alphaproteobacteria*, *Betaproteobacteria*, *Bacteroidetes*, *Firmicutes* (e.g., *Lactobacillus* and *Bacillus* spp.), *Clostridia*, *Actinomycetes*, *Spirochetes*, *Verrucomicrobia*, and *Actinobacteria*.

In some instances, the modulating agent is a bacterium that promotes microbial diversity or otherwise alters the microbiota of the host in a favorable manner. In one instance, bacteria may be provided to promote microbiome development in insects.

The bacterial modulating agents discussed herein can be used to alter the level, activity, or metabolism of target microorganisms as indicated in the sections for increasing the fitness of insects, such as, crickets, grasshoppers, or locusts.

In some instances, such bacterial modulating agents are bacteria which are capable of producing nutrients, including amino acids (e.g., methionine). The nutrient-producing bacteria may be naturally occurring bacteria, e.g., naturally occurring bacteria exogenous to the insect host. Such bacteria may be isolated from a population of bacteria, such as that found in an environmental sample. Bacteria can be isolated that produce one or more amino acids in a manner that increases production of amino acids in the host relative to a host who has not been administered the amino-acid producing bacteria. Amino acids that can be produced by the bacteria in the host include methionine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glutamate, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine. In certain instances, the amino acid-producing bacteria is a methionine-producing bacteria.

In some instances, the nutrient-producing bacteria (e.g., amino acid-producing bacteria, e.g., methionine-producing bacteria) are at a concentration of at least 100,000 cells/ml (e.g., at least about 100,000 cells/ml, at least about 150,000 cells/ml, at least about 200,000 cells/ml, at least about 250,000 cells/ml, at least about 300,000 cells/ml, at least about 350,000 cells/ml, at least about 400,000 cells/ml, at least about 450,000 cells/ml, or at least about 500,000 cells/ml).

Examples 1 to 4 and 8 describe how methionine-producing microorganisms can be identified which can then be used as modulating agents in insect hosts, such as crickets or in the model organism *Drosophila*, to increase the fitness of the hosts (e.g., increase amino acid content (e.g., methionine content). For example, in certain instances, nutrient content is increased in the host prior to use of the host in manufacturing of food or feed.

In some instances, such bacterial modulating agents are bacteria which are capable of degrading pesticides as laid out in Table 12 including insecticides. Such insecticides include neonicotinoids such as imidacloprid, or organophosphorus insecticides, such as fenitrothion. In some instances, the pesticide-metabolizing bacteria are at a concentration of at least 100,000 cells/ml (e.g., at least about 100,000 cells/ml, at least about 150,000 cells/ml, at least about 200,000 cells/ml, at least about 250,000 cells/ml, at least about 300,000 cells/ml, at least about 350,000 cells/ml, at least about 400,000 cells/ml, at least about 450,000 cells/ml, or at least about 500,000 cells/ml).

Examples 5 and 6 describe how imidacloprid and fenitrothion degrading microorganisms can be identified which can then be used as modulating agents in insect hosts, such as crickets, giving the treated insect hosts a competitive advantage. Administering such pesticide-degrading microorganisms, for example imidacloprid- or fenitrothion-degrading microorganisms to insect hosts such as honeybees is understood to be encompassed by the alteration of a level, activity, or metabolism of one or more microorganisms resident in the host.

v. Modifications to modulating agents

(a) Fusions

Any of the modulating agents described herein may be fused or linked to an additional moiety. In some instances, the modulating agent includes a fusion of one or more additional moieties (e.g., 1 additional moiety, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more additional moieties). In some instances, the additional moiety is any one of the modulating agents described herein (e.g., a peptide, polypeptide, small molecule, or antibiotic). Alternatively, the additional moiety may not act as modulating agent itself but may instead serve a secondary function. For example, the additional moiety may help the modulating agent access, bind, or become activated at a target site in the host (e.g., at a host gut or a host bacteriocyte) or at a target microorganism resident in the host (e.g., a cricket, a grasshopper, or a locust).

In some instances, the additional moiety may help the modulating agent penetrate a target host cell or target microorganism resident in the host. For example, the additional moiety may include a cell penetrating peptide. Cell penetrating peptides (CPPs) may be natural sequences derived from proteins; chimeric peptides that are formed by the fusion of two natural sequences; or synthetic CPPs, which are synthetically designed sequences based on structure–activity studies. In some instances, CPPs have the capacity to ubiquitously cross cellular membranes (e.g., prokaryotic and eukaryotic cellular membranes) with limited toxicity. Further, CPPs may have the capacity to cross cellular membranes via energy-dependent and/or independent mechanisms, without the necessity of a chiral recognition by specific receptors. CPPs can be bound to any of the modulating agents described herein. For example, a CPP can be bound to an antimicrobial peptide (AMP), e.g., a scorpion peptide, e.g., UY192 fused to a cell penetrating peptide (e.g., YGRKKRRQRRFLSTIWNIGIKGLLFAM; SEQ ID NO: 226). Non-limiting examples of CPPs are listed in Table 11.

Table 11: Examples of Cell Penetrating Peptides (CPPs)

Peptide	Origin	Sequence
<u>Protein-derived</u>		
Penetratin	Antennapedia	RQIKIWFQNRRMKWKK (SEQ ID NO: 213)
Tat peptide	Tat	GRKKRRQRRPPQ (SEQ ID NO: 214)
pVEC	Cadherin	LLIILRRRIRKQAHASK (SEQ ID NO: 215)
<u>Chimeric</u>		
Transportan	Galanine/Mastoparan	GWTLNSAGYLLGKINLKALAALAKKIL (SEQ ID NO: 216)
MPG	HIV-gp41/SV40 T-antigen	GALFLGFLGAAGSTMGAWSQPKKKRKV (SEQ ID NO: 217)
Pep-1	HIV-reverse transcriptase/SV40 T-antigen	KETWWETWWTEWSQPKKKRKV (SEQ ID NO: 218)

<i>Synthetic</i>		
Polyarginines	Based on Tat peptide	$(R)_n$; $6 < n < 12$
MAP	de novo	KLALKLALKALKAAALKLA (SEQ ID NO: 219)
R ₆ W ₃	Based on penetratin	RRWRRRWR (SEQ ID NO: 220)

In other instances, the additional moiety helps the modulating agent bind a target microorganism (e.g., a fungi or bacterium) resident in the host. The additional moiety may include one or more targeting domains. In some instances, the targeting domain may target the modulating agent to one or more microorganisms (e.g., bacterium or fungus) resident in the gut of the host. In some instances, the targeting domain may target the modulating agent to a specific region of the host (e.g., host gut or bacteriocyte) to access microorganisms that are generally present in said region of the host. For example, the targeting domain may target the modulating agent to the foregut, midgut, or hindgut of the host. In other instances, the targeting domain may target the modulating agent to a bacteriocyte in the host and/or one or more specific bacteria resident in a host bacteriocyte.

(b) Pre- or Pro-domains

In some instances, the modulating agent may include a pre- or pro- amino acid sequence. For example, the modulating agent may be an inactive protein or peptide that can be activated by cleavage or post-translational modification of a pre- or pro-sequence. In some instances, the modulating agent is engineered with an inactivating pre- or pro-sequence. For example, the pre- or pro-sequence may obscure an activation site on the modulating agent, e.g., a receptor binding site, or may induce a conformational change in the modulating agent. Thus, upon cleavage of the pre- or pro-sequence, the modulating agent is activated.

Alternatively, the modulating agent may include a pre- or pro-small molecule, e.g., an antibiotic. The modulating agent may be an inactive small molecule described herein that can be activated in a target environment inside the host. For example, the small molecule may be activated upon reaching a certain pH in the host gut. For example, the targeting domain may be *Galanthus nivalis* lectin or agglutinin (GNA) bound to a modulating agent described herein, e.g., an AMP, e.g., a scorpion peptide, e.g., Uy192.

(c) Linkers

In instances where the modulating agent is connected to an additional moiety, the modulating agent may further include a linker. For example, the linker may be a chemical bond, e.g., one or more covalent bonds or non-covalent bonds. In some instances, the linker may be a peptide linker (e.g., 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 20, 25, 30, 35, 40, or more amino acids longer). The linker may include any flexible, rigid, or cleavable linkers described herein.

A flexible peptide linker may include any of those commonly used in the art, including linkers having sequences having primarily Gly and Ser residues ("GS" linker). Flexible linkers may be useful for

joining domains that require a certain degree of movement or interaction and may include small, non-polar (e.g. Gly) or polar (e.g. Ser or Thr) amino acids.

Alternatively, a peptide linker may be a rigid linker. Rigid linkers are useful to keep a fixed distance between moieties and to maintain their independent functions. Rigid linkers may also be useful when a spatial separation of the domains is critical to preserve the stability or bioactivity of one or more components in the fusion. Rigid linkers may, for example, have an alpha helix-structure or Pro-rich sequence, (XP)_n, with X designating any amino acid, preferably Ala, Lys, or Glu.

In yet other instances, a peptide linker may be a cleavable linker. In some instances, linkers may be cleaved under specific conditions, such as the presence of reducing reagents or proteases. *In vivo* cleavable linkers may utilize the reversible nature of a disulfide bond. One example includes a thrombin-sensitive sequence (e.g., PRS) between two Cys residues. *In vitro* thrombin treatment of CPRSC results in the cleavage of the thrombin-sensitive sequence, while the reversible disulfide linkage remains intact. Such linkers are known and described, e.g., in Chen et al., *Adv. Drug Deliv. Rev.* 65(10):1357-1369, 2013. Cleavage of linkers in fusions may also be carried out by proteases that are expressed *in vivo* under conditions in specific cells or tissues of the host or microorganisms resident in the host. In some instances, cleavage of the linker may release a free functional, modulating agent upon reaching a target site or cell.

Fusions described herein may alternatively be linked by a linking molecule, including a hydrophobic linker, such as a negatively charged sulfonate group; lipids, such as a poly (—CH₂—) hydrocarbon chains, such as polyethylene glycol (PEG) group, unsaturated variants thereof, hydroxylated variants thereof, amidated or otherwise N-containing variants thereof, non-carbon linkers; carbohydrate linkers; phosphodiester linkers, or other molecule capable of covalently linking two or more molecules, e.g., two modulating agents. Non-covalent linkers may be used, such as hydrophobic lipid globules to which the modulating agent is linked, for example, through a hydrophobic region of the modulating agent or a hydrophobic extension of the modulating agent, such as a series of residues rich in leucine, isoleucine, valine, or perhaps also alanine, phenylalanine, or even tyrosine, methionine, glycine, or other hydrophobic residue. The modulating agent may be linked using charge-based chemistry, such that a positively charged moiety of the modulating agent is linked to a negative charge of another modulating agent or an additional moiety.

IV. Formulations and Compositions

The compositions described herein may be formulated either in pure form (e.g., the composition contains only the modulating agent) or together with one or more additional agents (such as excipient, delivery vehicle, carrier, diluent, stabilizer, etc.) to facilitate application or delivery of the compositions.

Examples of suitable excipients and diluents include, but are not limited to, lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, cellulose, water, saline solution, syrup, methylcellulose, methyl- and propylhydroxybenzoates, talc, magnesium stearate, and mineral oil.

In some instances, the composition includes a delivery vehicle or carrier. In some instances, the delivery vehicle includes an excipient. Exemplary excipients include, but are not limited to, solid or liquid

carrier materials, solvents, stabilizers, slow-release excipients, colorings, and surface-active substances (surfactants). In some instances, the delivery vehicle is a stabilizing vehicle. In some instances, the stabilizing vehicle includes a stabilizing excipient. Exemplary stabilizing excipients include, but are not limited to, epoxidized vegetable oils, antifoaming agents, e.g. silicone oil, preservatives, viscosity regulators, binding agents and tackifiers. In some instances, the stabilizing vehicle is a buffer suitable for the modulating agent. In some instances, the composition is microencapsulated in a polymer bead delivery vehicle. In some instances, the stabilizing vehicle protects the modulating agent against UV and/or acidic conditions. In some instances, the delivery vehicle contains a pH buffer. In some instances, the composition is formulated to have a pH in the range of about 4.5 to about 9.0, including for example pH ranges of about any one of 5.0 to about 8.0, about 6.5 to about 7.5, or about 6.5 to about 7.0.

Depending on the intended objectives and prevailing circumstances, the composition may be formulated into emulsifiable concentrates, suspension concentrates, directly sprayable or dilutable solutions, coatable pastes, diluted emulsions, spray powders, soluble powders, dispersible powders, wettable powders, dusts, granules, encapsulations in polymeric substances, microcapsules, foams, aerosols, carbon dioxide gas preparations, tablets, resin preparations, paper preparations, nonwoven fabric preparations, or knitted or woven fabric preparations. In some instances, the composition is a liquid. In some instances, the composition is a solid. In some instances, the composition is an aerosol, such as in a pressurized aerosol can. In some instances, the composition is present in the waste (such as feces) of the pest. In some instances, the composition is present in or on a live pest.

In some instances, the delivery vehicle is the food or water of the host. In other instances, the delivery vehicle is a food source for the host. In some instances, the delivery vehicle is a food bait for the host. In some instances, the composition is a comestible agent consumed by the host. In some instances, the composition is delivered by the host to a second host, and consumed by the second host. In some instances, the composition is consumed by the host or a second host, and the composition is released to the surrounding of the host or the second host via the waste (such as feces) of the host or the second host. In some instances, the modulating agent is included in food bait intended to be consumed by a host or carried back to its colony.

In some instances, the modulating agent may make up about 0.1% to about 100% of the composition, such as any one of about 0.01% to about 100%, about 1% to about 99.9%, about 0.1% to about 10%, about 1% to about 25%, about 10% to about 50%, about 50% to about 99%, or about 0.1% to about 90% of active ingredients (such as phage, lysin or bacteriocin). In some instances, the composition includes at least any of 0.1%, 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more active ingredients (such as phage, lysin or bacteriocin). In some instances, the concentrated agents are preferred as commercial products, the final user normally uses diluted agents, which have a substantially lower concentration of active ingredient.

Any of the formulations described herein may be used in the form of a bait, a coil, an electric mat, a smoking preparation, a fumigant, or a sheet.

i. Liquid Formulations

The compositions provided herein may be in a liquid formulation. Liquid formulations are generally mixed with water, but in some instances may be used with crop oil, diesel fuel, kerosene or other light oil as a carrier. The amount of active ingredient often ranges from about 0.5 to about 80 percent by weight.

An emulsifiable concentrate formulation may contain a liquid active ingredient, one or more petroleum-based solvents, and an agent that allows the formulation to be mixed with water to form an emulsion. Such concentrates may be used in agricultural, ornamental and turf, forestry, structural, food processing, livestock, and public health pest formulations. These may be adaptable to application equipment from small portable sprayers to hydraulic sprayers, low-volume ground sprayers, mist blowers, and low-volume aircraft sprayers. Some active ingredients are readily dissolve in a liquid carrier. When mixed with a carrier, they form a solution that does not settle out or separate, e.g., a homogenous solution. Formulations of these types may include an active ingredient, a carrier, and one or more other ingredients. Solutions may be used in any type of sprayer, indoors and outdoors.

In some instances, the composition may be formulated as an invert emulsion. An invert emulsion is a water-soluble active ingredient dispersed in an oil carrier. Invert emulsions require an emulsifier that allows the active ingredient to be mixed with a large volume of petroleum-based carrier, usually fuel oil. Invert emulsions aid in reducing drift. With other formulations, some spray drift results when water droplets begin to evaporate before reaching target surfaces; as a result the droplets become very small and lightweight. Because oil evaporates more slowly than water, invert emulsion droplets shrink less and more active ingredient reaches the target. Oil further helps to reduce runoff and improve rain resistance. It further serves as a sticker-spreader by improving surface coverage and absorption. Because droplets are relatively large and heavy, it is difficult to get thorough coverage on the undersides of foliage. Invert emulsions are most commonly used along rights-of-way where drift to susceptible non-target areas can be a problem.

A flowable or liquid formulation combines many of the characteristics of emulsifiable concentrates and wettable powders. Manufacturers use these formulations when the active ingredient is a solid that does not dissolve in either water or oil. The active ingredient, impregnated on a substance such as clay, is ground to a very fine powder. The powder is then suspended in a small amount of liquid. The resulting liquid product is quite thick. Flowables and liquids share many of the features of emulsifiable concentrates, and they have similar disadvantages. They require moderate agitation to keep them in suspension and leave visible residues, similar to those of wettable powders.

Flowables/liquids are easy to handle and apply. Because they are liquids, they are subject to spilling and splashing. They contain solid particles, so they contribute to abrasive wear of nozzles and pumps. Flowable and liquid suspensions settle out in their containers. Because flowable and liquid formulations tend to settle, packaging in containers of five gallons or less makes remixing easier.

Aerosol formulations contain one or more active ingredients and a solvent. Most aerosols contain a low percentage of active ingredients. There are two types of aerosol formulations—the ready-to-use type commonly available in pressurized sealed containers and those products used in electrical or gasoline-powered aerosol generators that release the formulation as a smoke or fog.

Ready to use aerosol formulations are usually small, self-contained units that release the formulation when the nozzle valve is triggered. The formulation is driven through a fine opening by an inert gas under pressure, creating fine droplets. These products are used in greenhouses, in small areas inside buildings, or in localized outdoor areas. Commercial models, which hold five to 5 pounds of active ingredient, are usually refillable.

Smoke or fog aerosol formulations are not under pressure. They are used in machines that break the liquid formulation into a fine mist or fog (aerosol) using a rapidly whirling disk or heated surface.

ii. Dry or Solid Formulations

Dry formulations can be divided into two types: ready-to-use and concentrates that must be mixed with water to be applied as a spray. Most dust formulations are ready to use and contain a low percentage of active ingredients (less than about 10 percent by weight), plus a very fine, dry inert carrier made from talc, chalk, clay, nut hulls, or volcanic ash. The size of individual dust particles varies. A few dust formulations are concentrates and contain a high percentage of active ingredients. Mix these with dry inert carriers before applying. Dusts are always used dry and can easily drift to non-target sites.

iii. Granule or Pellet Formulations

In some instances, the composition is formulated as granules. Granular formulations are similar to dust formulations, except granular particles are larger and heavier. The coarse particles may be made from materials such as clay, corncobs, or walnut shells. The active ingredient either coats the outside of the granules or is absorbed into them. The amount of active ingredient may be relatively low, usually ranging from about 0.5 to about 15 percent by weight. Granular formulations are most often used to apply to the soil, insects living in the soil, or absorption into plants through the roots. Granular formulations are sometimes applied by airplane or helicopter to minimize drift or to penetrate dense vegetation. Once applied, granules may release the active ingredient slowly. Some granules require soil moisture to release the active ingredient. Granular formulations also are used to control larval mosquitoes and other aquatic pests. Granules are used in agricultural, structural, ornamental, turf, aquatic, right-of-way, and public health (biting insect) pest-control operations.

In some instances, the composition is formulated as pellets. Most pellet formulations are very similar to granular formulations; the terms are used interchangeably. In a pellet formulation, however, all the particles are the same weight and shape. The uniformity of the particles allows use with precision application equipment.

iv. Powders

In some instances, the composition is formulated as a powder. In some instances, the composition is formulated as a wettable powder. Wettable powders are dry, finely ground formulations that look like dusts. They usually must be mixed with water for application as a spray. A few products, however, may be applied either as a dust or as a wettable powder—the choice is left to the applicator. Wettable powders have about 1 to about 95 percent active ingredient by weight; in some cases more than about 50 percent. The particles do not dissolve in water. They settle out quickly unless constantly

agitated to keep them suspended. They can be used for most pest problems and in most types of spray equipment where agitation is possible. Wettable powders have excellent residual activity. Because of their physical properties, most of the formulation remains on the surface of treated porous materials such as concrete, plaster, and untreated wood. In such cases, only the water penetrates the material.

5 In some instances, the composition is formulated as a soluble powder. Soluble powder formulations look like wettable powders. However, when mixed with water, soluble powders dissolve readily and form a true solution. After they are mixed thoroughly, no additional agitation is necessary. The amount of active ingredient in soluble powders ranges from about 15 to about 95 percent by weight; in some cases more than about 50 percent. Soluble powders have all the advantages of wettable
10 powders and none of the disadvantages, except the inhalation hazard during mixing.

In some instances, the composition is formulated as a water-dispersible granule. Water-dispersible granules, also known as dry flowables, are like wettable powders, except instead of being dust-like, they are formulated as small, easily measured granules. Water-dispersible granules must be mixed with water to be applied. Once in water, the granules break apart into fine particles similar to
15 wettable powders. The formulation requires constant agitation to keep it suspended in water. The percentage of active ingredient is high, often as much as 90 percent by weight. Water-dispersible granules share many of the same advantages and disadvantages of wettable powders, except they are more easily measured and mixed. Because of low dust, they cause less inhalation hazard to the applicator during handling

20 *v. Bait*

In some instances, the composition includes a bait. The bait can be in any suitable form, such as a solid, paste, pellet or powdered form. The bait can also be carried away by the host back to a population of said host (e.g., a colony or hive). The bait can then act as a food source for other members of the
25 colony, thus providing an effective modulating agent for a large number of hosts and potentially an entire host colony.

The baits can be provided in a suitable "housing" or "trap." Such housings and traps are commercially available and existing traps can be adapted to include the compositions described herein. The housing or trap can be box-shaped for example, and can be provided in pre-formed condition or can
30 be formed of foldable cardboard for example. Suitable materials for a housing or trap include plastics and cardboard, particularly corrugated cardboard. The inside surfaces of the traps can be lined with a sticky substance in order to restrict movement of the host once inside the trap. The housing or trap can contain a suitable trough inside which can hold the bait in place. A trap is distinguished from a housing because the host cannot readily leave a trap following entry, whereas a housing acts as a "feeding station" which
35 provides the host with a preferred environment in which they can feed and feel safe from predators.

vi. Attractants

In some instances, the composition includes an attractant (e.g., a chemoattractant). The attractant may attract an adult host or immature host (e.g., larva) to the vicinity of the composition.

40 Attractants include pheromones, a chemical that is secreted by an animal, especially an insect, which

influences the behavior or development of others of the same species. Other attractants include sugar and protein hydrolysate syrups, yeasts, and rotting meat. Attractants also can be combined with an active ingredient and sprayed onto foliage or other items in the treatment area.

Various attractants are known which influence host behavior as a host's search for food, oviposition or mating sites, or mates. Attractants useful in the methods and compositions described herein include, for example, eugenol, phenethyl propionate, ethyl dimethylisobutyl-cyclopropane carboxylate, propyl benzodioxanecarboxylate, cis-7,8-epoxy-2-methyloctadecane, trans-8,trans-0-dodecadienol, cis-9-tetradecenal (with cis-11-hexadecenal), trans-11-tetradecenal, cis-11-hexadecenal, (Z)-11,12-hexadecadienal, cis-7-dodecenyl acetate, cis-8-dodecenyl acetate, cis-9-dodecenyl acetate, cis-9-tetradecenyl acetate, cis-11-tetradecenyl acetate, trans-11-tetradecenyl acetate (with cis-11), cis-9,trans-11-tetradecadienyl acetate (with cis-9,trans-12), cis-9,trans-12-tetradecadienyl acetate, cis-7,cis-11-hexadecadienyl acetate (with cis-7,trans-11), cis-3,cis-13-octadecadienyl acetate, trans-3,cis-13-octadecadienyl acetate, anethole and isoamyl salicylate.

Means other than chemoattractants may also be used to attract insects, including lights in various wavelengths or colors.

vii. Nanocapsules/Microencapsulation/Liposomes

In some instances, the composition is provided in a microencapsulated formulation. Microencapsulated formulations are mixed with water and sprayed in the same manner as other sprayable formulations. After spraying, the plastic coating breaks down and slowly releases the active ingredient.

viii. Carriers

Any of the compositions described herein may be formulated to include the modulating agent described herein and an inert carrier. Such carrier can be a solid carrier, a liquid carrier, gel carrier, and/or a gaseous carrier. In certain instances, the carrier can be a seed coating. The seed coating is any non-naturally occurring formulation that adheres, in whole or part, to the surface of the seed. The formulation may further include an adjuvant or surfactant. The formulation can also include one or more modulating agents to enlarge the action spectrum.

A solid carrier used for formulation includes finely-divided powder or granules of clay (e.g. kaolin clay, diatomaceous earth, bentonite, Fubasami clay, acid clay, etc.), synthetic hydrated silicon oxide, talc, ceramics, other inorganic minerals (e.g., sericite, quartz, sulfur, activated carbon, calcium carbonate, hydrated silica, etc.), a substance which can be sublimated and is in the solid form at room temperature (e.g., 2,4,6-triisopropyl-1,3,5-trioxane, naphthalene, p-dichlorobenzene, camphor, adamantane, etc.); wool; silk; cotton; hemp; pulp; synthetic resins (e.g., polyethylene resins such as low-density polyethylene, straight low-density polyethylene and high-density polyethylene; ethylene-vinyl ester copolymers such as ethylene-vinyl acetate copolymers; ethylene-methacrylic acid ester copolymers such as ethylene-methyl methacrylate copolymers and ethylene-ethyl methacrylate copolymers; ethylene-acrylic acid ester copolymers such as ethylene-methyl acrylate copolymers and ethylene-ethyl acrylate copolymers; ethylene-vinylcarboxylic acid copolymers such as ethylene-acrylic acid copolymers; ethylene-

tetracyclododecene copolymers; polypropylene resins such as propylene homopolymers and propylene-ethylene copolymers; poly-4-methylpentene-1, polybutene-1, polybutadiene, polystyrene; acrylonitrile-styrene resins; styrene elastomers such as acrylonitrile-butadiene-styrene resins, styrene-conjugated diene block copolymers, and styrene-conjugated diene block copolymer hydrides; fluororesins; acrylic resins such as poly(methyl methacrylate); polyamide resins such as nylon 6 and nylon 66; polyester resins such as polyethylene terephthalate, polyethylene naphthalate, polybutylene terephthalate, and polycyclohexylenedimethylene terephthalate; polycarbonates, polyacetals, polyacrylsulfones, polyarylates, hydroxybenzoic acid polyesters, polyetherimides, polyester carbonates, polyphenylene ether resins, polyvinyl chloride, polyvinylidene chloride, polyurethane, and porous resins such as foamed polyurethane, foamed polypropylene, or foamed ethylene, etc.), glasses, metals, ceramics, fibers, cloths, knitted fabrics, sheets, papers, yarn, foam, porous substances, and multifilaments.

A liquid carrier may include, for example, aromatic or aliphatic hydrocarbons (e.g., xylene, toluene, alkylnaphthalene, phenylxylethane, kerosine, gas oil, hexane, cyclohexane, etc.), halogenated hydrocarbons (e.g., chlorobenzene, dichloromethane, dichloroethane, trichloroethane, etc.), alcohols (e.g., methanol, ethanol, isopropyl alcohol, butanol, hexanol, benzyl alcohol, ethylene glycol, etc.), ethers (e.g., diethyl ether, ethylene glycol dimethyl ether, diethylene glycol monomethyl ether, diethylene glycol monoethyl ether, propylene glycol monomethyl ether, tetrahydrofuran, dioxane, etc.), esters (e.g., ethyl acetate, butyl acetate, etc.), ketones (e.g., acetone, methyl ethyl ketone, methyl isobutyl ketone, cyclohexanone, etc.), nitriles (e.g., acetonitrile, isobutyronitrile, etc.), sulfoxides (e.g., dimethyl sulfoxide, etc.), amides (e.g., N,N-dimethylformamide, N,N-dimethylacetamide, cyclic imides (e.g. N-methylpyrrolidone) alkylidene carbonates (e.g., propylene carbonate, etc.), vegetable oil (e.g., soybean oil, cottonseed oil, etc.), vegetable essential oils (e.g., orange oil, hyssop oil, lemon oil, etc.), or water.

A gaseous carrier may include, for example, butane gas, flon gas, liquefied petroleum gas (LPG), dimethyl ether, and carbon dioxide gas.

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ix. Adjuvants

In some instances, the composition provided herein may include an adjuvant. Adjuvants are chemicals that do not possess activity. Adjuvants are either pre-mixed in the formulation or added to the spray tank to improve mixing or application or to enhance performance. They are used extensively in products designed for foliar applications. Adjuvants can be used to customize the formulation to specific needs and compensate for local conditions. Adjuvants may be designed to perform specific functions, including wetting, spreading, sticking, reducing evaporation, reducing volatilization, buffering, emulsifying, dispersing, reducing spray drift, and reducing foaming. No single adjuvant can perform all these functions, but compatible adjuvants often can be combined to perform multiple functions simultaneously.

Among nonlimiting examples of adjuvants included in the formulation are binders, dispersants and stabilizers, specifically, for example, casein, gelatin, polysaccharides (e.g., starch, gum arabic, cellulose derivatives, alginic acid, etc.), lignin derivatives, bentonite, sugars, synthetic water-soluble polymers (e.g., polyvinyl alcohol, polyvinylpyrrolidone, polyacrylic acid, etc.), PAP (acidic isopropyl phosphate), BHT (2,6-di-t-butyl-4-methylphenol), BHA (a mixture of 2-t-butyl-4-methoxyphenol and 3-t-butyl-4-methoxyphenol), vegetable oils, mineral oils, fatty acids and fatty acid esters.

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x. Surfactants

In some instances, the composition provided herein includes a surfactant. Surfactants, also called wetting agents and spreaders, physically alter the surface tension of a spray droplet. For a formulation to perform its function properly, a spray droplet must be able to wet the foliage and spread out evenly over a leaf. Surfactants enlarge the area of formulation coverage, thereby increasing the pest's exposure to the chemical. Surfactants are particularly important when applying a formulation to waxy or hairy leaves. Without proper wetting and spreading, spray droplets often run off or fail to cover leaf surfaces adequately. Too much surfactant, however, can cause excessive runoff and reduce efficacy.

Surfactants are classified by the way they ionize or split apart into electrically charged atoms or molecules called ions. A surfactant with a negative charge is anionic. One with a positive charge is cationic, and one with no electrical charge is nonionic. Formulation activity in the presence of a nonionic surfactant can be quite different from activity in the presence of a cationic or anionic surfactant. Selecting the wrong surfactant can reduce the efficacy of a pesticide product and injure the target plant. Anionic surfactants are most effective when used with contact pesticides (pesticides that control the pest by direct contact rather than being absorbed systemically). Cationic surfactants should never be used as stand-alone surfactants because they usually are phytotoxic.

Nonionic surfactants, often used with systemic pesticides, help pesticide sprays penetrate plant cuticles. Nonionic surfactants are compatible with most pesticides, and most EPA-registered pesticides that require a surfactant recommend a nonionic type. Adjuvants include, but are not limited to, stickers, extenders, plant penetrants, compatibility agents, buffers or pH modifiers, drift control additives, defoaming agents, and thickeners.

Among nonlimiting examples of surfactants included in the compositions described herein are alkyl sulfate ester salts, alkyl sulfonates, alkyl aryl sulfonates, alkyl aryl ethers and polyoxyethylenated products thereof, polyethylene glycol ethers, polyvalent alcohol esters and sugar alcohol derivatives.

xi. Combinations

In formulations and in the use forms prepared from these formulations, the modulating agent may be in a mixture with other active compounds, such as pesticidal agents (e.g., insecticides, sterilants, acaricides, nematocides, molluscicides, or fungicides; see, e.g., pesticides listed in Table 12), attractants, growth-regulating substances, or herbicides. As used herein, the term "pesticidal agent" refers to any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. A pesticide can be a chemical substance or biological agent used against pests including insects, pathogens, weeds, and microbes that compete with humans for food, destroy property, spread disease, or are a nuisance. The term "pesticidal agent" may further encompass other bioactive molecules such as antibiotics, antivirals pesticides, antifungals, antihelminthics, nutrients, pollen, sucrose, and/or agents that stun or slow insect movement.

In instances where the modulating agent is applied to plants, a mixture with other known compounds, such as herbicides, fertilizers, growth regulators, safeners, semiochemicals, or else with agents for improving plant properties is also possible.

V. Delivery

A host described herein can be exposed to any of the compositions described herein in any suitable manner that permits delivering or administering the composition to the insect. The modulating agent may be delivered either alone or in combination with other active or inactive substances and may be applied by, for example, spraying, microinjection, through plants, pouring, dipping, in the form of concentrated liquids, gels, solutions, suspensions, sprays, powders, pellets, briquettes, bricks and the like, formulated to deliver an effective concentration of the modulating agent. Amounts and locations for application of the compositions described herein are generally determined by the habits of the host, the lifecycle stage at which the microorganisms of the host can be targeted by the modulating agent, the site where the application is to be made, and the physical and functional characteristics of the modulating agent. The modulating agents described herein may be administered to the insect by oral ingestion, but may also be administered by means which permit penetration through the cuticle or penetration of the insect respiratory system.

In some instances, the insect can be simply "soaked" or "sprayed" with a solution including the modulating agent. Alternatively, the modulating agent can be linked to a food component (e.g., comestible) of the insect for ease of delivery and/or in order to increase uptake of the modulating agent by the insect. Methods for oral introduction include, for example, directly mixing a modulating agent with the insect's food, spraying the modulating agent in the insect's habitat or field, as well as engineered approaches in which a species that is used as food is engineered to express a modulating agent, then fed to the insect to be affected. In some instances, for example, the modulating agent composition can be incorporated into, or overlaid on the top of, the insect's diet. For example, the modulating agent composition can be sprayed onto a field of crops which an insect inhabits.

In some instances, the composition is sprayed directly onto a plant e.g., crops, by e.g., backpack spraying, aerial spraying, crop spraying/dusting etc. In instances where the modulating agent is delivered to a plant, the plant receiving the modulating agent may be at any stage of plant growth. For example, formulated modulating agents can be applied as a seed-coating or root treatment in early stages of plant growth or as a total plant treatment at later stages of the crop cycle. In some instances, the modulating agent may be applied as a topical agent to a plant, such that the host insect ingests or otherwise comes in contact with the plant upon interacting with the plant.

Further, the modulating agent may be applied (e.g., in the soil in which a plant grows, or in the water that is used to water the plant) as a systemic agent that is absorbed and distributed through the tissues (e.g., stems or leafs) of a plant or animal host, such that an insect feeding thereon will obtain an effective dose of the modulating agent. In some instances, plants or food organisms may be genetically transformed to express the modulating agent such that a host feeding upon the plant or food organism will ingest the modulating agent.

Delayed or continuous release can also be accomplished by coating the modulating agent or a composition containing the modulating agent(s) with a dissolvable or bioerodable coating layer, such as gelatin, which coating dissolves or erodes in the environment of use, to then make the modulating agent available, or by dispersing the agent in a dissolvable or erodable matrix. Such continuous release and/or

dispensing means devices may be advantageously employed to consistently maintain an effective concentration of one or more of the modulating agents described herein in a specific host habitat.

The modulating agent can also be incorporated into the medium in which the insect grows, lives, reproduces, feeds, or infests. For example, a modulating agent can be incorporated into a food container, feeding station, protective wrapping, or a hive. For some applications the modulating agent may be bound to a solid support for application in powder form or in a "trap" or "feeding station." As an example, for applications where the composition is to be used in a trap or as bait for a particular host insect, the compositions may also be bound to a solid support or encapsulated in a time-release material. For example, the compositions described herein can be administered by delivering the composition to at least one habitat where the insect grows, lives, reproduces, or feeds.

VI. Screening

Included herein are screening assays for identifying a modulating agent, wherein the modulating agent is effective to alter the microbiota of a host and thereby increase host fitness (e.g., insect fitness). For example, the screening assay may be used to identify one or more modulating agents that target specific microorganisms and/or specific hosts. Further, the screening assays may be used to identify one or more microorganisms with enhanced functionalities. For example, the screening assay may be effective to isolate one or more microorganisms with an enhanced ability to metabolize (e.g., degrade) a pesticide (e.g., insecticide, e.g., neonicotinoid) or plant allelochemical (e.g., caffeine, soyacystatin N, monoterpenes, diterpene acids, or phenolic compounds). Delivery and colonization of an isolated microorganism in the host may increase the host's resistance to the pesticide or plant allelochemical, thereby increasing host fitness. The methods may also be useful for the isolation of microorganisms with an enhanced ability to colonize any of the hosts described herein.

For example, to screen for microorganisms that increase a host's resistance to a pesticide, a starting culture may be used that includes microorganisms (e.g., bacteria) and high concentrations of a pesticide (e.g., a pesticide listed in Table 12 or a pesticide known in the art, e.g., a neonicotinoid). In some instances, the pesticide may be provided in the form of an environmental sample enriched with the pesticide (e.g., a soil sample). Alternatively, the pesticide (e.g., a pesticide listed in Table 12) may be provided in pure form or in combination with other carriers. Further, the one or more microorganism isolates may be inoculated directly into the media (e.g., from a laboratory strain) or may be an environmental sample including one or more microorganism species. The growth media may be either liquid or solid. In some instances, the pesticide of interest is the sole carbon or nitrogen source for the microorganisms in the media. The culture may be sub-cultured (e.g., inoculated into fresh media with high levels of the pesticide) any number of times to enrich for and/or isolate microbial strains (e.g., bacterial strains) capable of metabolizing the pesticide. The original culture or the subcultures may be assessed using any methods known in the art to test for alterations (e.g., decrease) in the levels of the pesticide in the sample (e.g., using HPLC). Isolates that reduce the concentration of the pesticide (e.g., a pesticide listed in Table 12 or a pesticide known in the art, e.g., neonicotinoid) may be isolated for use as a modulating agent in any of the methods or compositions described herein.

- The methods may be used to further select for microorganisms described herein, including those isolated from a screening assay, with an enhanced ability to colonize and survive in a host (e.g., insect). For example, a host may be inoculated with a bacterial isolate (e.g., one with the ability to degrade a pesticide). The host may then be tested at regular intervals for the presence of the bacterial isolate (e.g., via culturing or 16s RNA from guts isolated from the host). Bacterial isolates that survive in the host (e.g., the midgut of an insect) may be isolated for use as a modulating agent in any of the methods or compositions described herein.

Table 12. Pesticides

Aclonifen	Fenchlorazole-ethyl	Pendimethalin
Acetamiprid	Fenothiocarb	Penflufen
Alanycarb	Fenitrothion	Penflufen
Amidosulfuron	Fenpropidin	Pentachlorobenzene
Aminocyclopyrachlor	Fluazolate	Penthiopyrad
Amisulbrom	Flufenoxuron	Penthiopyrad
Anthraquinone	Flumetralin	Pirimiphos-methyl
Asulam, sodium salt	Fluxapyroxad	Prallethrin
Benfuracarb	Fuberidazole	Profenofos
Bensulide	Glufosinate-ammonium	Proquinazid
beta-HCH; beta-BCH	Glyphosate	Prothiofos
Bioresmethrin	Group: Borax, borate salts (see	Pyraclofos
Blasticidin-S	Group: Paraffin oils, Mineral	Pyrazachlor
Borax; disodium tetraborate	Halfenprox	Pyrazophos
Boric acid	Imiprothrin	Pyridaben
Bromoxynil heptanoate	Imidacloprid	Pyridalyl
Bromoxynil octanoate	Ipconazole	Pyridiphenthion
Carbosulfan	Isopyrazam	Pyrifeno
Chlorantraniliprole	Isopyrazam	Quinmerac
Chlordimeform	Lenacil	Rotenone
Chlorfluazuron	Magnesium phosphide	Sedaxane
Chlorphropham	Metaflumizone	Sedaxane
Climbazole	Metazachlor	Silafluofen
Clopyralid	Metazachlor	Sintofen
Copper (II) hydroxide	Metobromuron	Spinetoram
Cyflufenamid	Metoxuron	Sulfoxaflo
Cyhalothrin	Metsulfuron-methyl	Temephos
Cyhalothrin, gamma	Milbemectin	Thiocloprid
Decahydrate	Naled	Thiamethoxam
Diafenthiuron	Napropamide	Tolfenpyrad
Dimefuron	Nicosulfuron	Tralomethrin
Dimoxystrobin	Nitenpyram	Tributyltin compounds
Dinotefuran	Nitrobenzene	Tridiphane

Diquat dichloride	o-phenylphenol	Triflumizole
Dithianon	Oils	Validamycin
E-Phosphamidon	Oxadiargyl	Zinc phosphide
EPTC	Oxycarboxin	
Ethaboxam	Paraffin oil	
Ethirimol	Penconazole	

EXAMPLES

The following is an example of the methods of the invention. It is understood that various other embodiments may be practiced, given the general description provided above.

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Example 1: Generation of a library of natural microbes

This Example demonstrates the isolation of bacteria from soil that naturally produce the amino acid, methionine.

The medium used for isolation of microorganisms is Starch-Casein-Nitrate agar (Starch, 10.0 g; Casein, 0.003 g; KNO₃, 0.02 g; NaCl, 0.02 g; MgSO₄, 0.5 mg; CaCO₃, 0.2 mg; FeSO₄, 0.1 mg; Agar, 12.0 g; H₂O, 1L; pH 7.0) (Kuster and Williams, 1964). Each environmental soil sample (1.0 g) is suspended in 9 ml of sterile water, and 1 ml of the suspension is serially diluted ten-fold in sterile distilled water. One milliliter of the 10⁻⁵ dilution is inoculated onto the agar medium and incubated for 7 days at 30°C. At the end of this period, the plates are observed for growth. White discrete and leathery colonies are picked and grown on new Starch-Casein-Nitrate agar plates to create a library of isolates. After 7 days of growth at 30°C, the plates are kept at 4°C.

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Example 2: Screen for isolates that produce methionine

This Example demonstrates the screening assay of isolates from Example 1 that naturally produce the amino acid, methionine.

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Screening for methionine production:

A modified basal medium (K₂HPO₄, 0.3 g; KH₂PO₄, 0.7 g; Na₂CO₃, 1.0 g; CaCl₂, 5.0 mg; MgSO₄, 0.3 g; FeSO₄, 1.0 mg; H₂O, 1L) containing sucrose (20.0 g) and NH₄Cl (10.0 g) is used for fermentation (Chay, B.P., Galvez, F.C.F., and Padolina, W.G.P.U.L.B.P. (1992). Methionine production by batch fermentation from various carbohydrates. ASEAN Food Journal (Malaysia)). The pH of the medium is 7.2.

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Culture conditions: Two loops of the 7 day isolate culture of Example 1 are inoculated into a 250 ml Erlenmeyer flask containing 30 ml of the fermentation medium. Methionine production is assayed after incubation of the flask for 5 days on a rotary shaker (160 rpm) at 30°C. Duplicate flasks are prepared and non-inoculated flasks served as control in all experiments.

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The presence of methionine in the culture broths of the isolates is examined by paper chromatography following a modified method of Khanna and Nag (Khanna et al., "Production of amino acids in vitro tissue culture," *Indian Journal of Experimental Biology* (1973)). The broth culture is centrifuged at 5000 x g for 20 min and 2 µL of the supernatant is applied 1.5 cm above one edge of

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Whatman No.1 filter paper, with dimensions of 18 cm x 22 cm. 1 μ L of volume of a standard methionine solution (0.1 mg/mL) is applied alongside with the supernatant, and the chromatogram is developed in a solvent mixture of n-butanol, acetic acid and water (4: 1: 1) for 18 h. The chromatogram is air-dried at room temperature, sprayed with 0.15% ninhydrin solution in butanol and dried again before heating at 60°C for 5 min in an oven. The value of the ninhydrin-positive spot (bluish-violet) of the supernatant that corresponds with the value of the standard methionine solution indicates presence of methionine in the broth culture. The concentration of methionine produced in the broth culture of the isolate is estimated as follows. The ninhydrin-positive spot of the supernatant of the isolate on the chromatogram is eluted in 10% ethanol and the spectrophotometric reading of the eluate at 520 nm recorded. The methionine concentration in the supernatant is determined from a standard curve. A plot of the values of optical densities against varying concentrations (0.1 to 0.9 mg/ml) of a methionine solution serve as the standard methionine curve.

Isolates that produce methionine are kept on fresh agar plates and a stock solution is created by suspending two loopfuls of microorganism in an aliquot of 50% glycerol solution.

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Example 3: Administration of methionine producing isolates to increase of crickets' amino acid content

This example demonstrates the ability to treat crickets with methionine producing bacteria to improve their nutritional content.

The world's appetite for meat is growing, and the production of animal feed is an increasing strain on land and water. Insects could provide much of the protein animals need at a much lower environmental cost; many insect species can feed on manure, like Grant's maggots, or other types of organic waste, such as leftover food, offal, and grains discarded by breweries. Insects produce body mass at an astonishing rate, in part because as cold-blooded animals they don't expend energy on regulating their body temperature. Crickets, e.g., *Acheta domesticus*, need only 1.7 kilograms of feed to gain a kilogram of body weight; a typical U.S. chicken consumes 2.5 kilograms, pigs 5 kilograms, and cattle 10 kilograms. Another advantage: most insects can be eaten whole. Only about half of a chicken or a pig is edible; for a cow the fraction is even less. As a result, raising a kilogram of insect protein produces less CO₂ than rearing pigs or cattle, and takes up only one-tenth the land.

Insect meal could replace between 25% and 100% of soymeal or fishmeal in the animals' diets with no adverse effects, but most insect meals are deficient in the amino acids methionine and lysine. Synthetic production of methionine requires hazardous chemicals and its use is banned in organic farming. By introducing methionine-producing bacteria into the crickets' microbiome, crickets are expected to naturally increase their nutritional content.

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Therapeutic design: Isolated bacteria identified as methionine producing from the Example 2, are formulated with a solution of 10⁷ cells/mL mixed with the feeding substrate, e.g., poultry starter feed and rice bran (Poultry Feed-PF), for crickets.

Experimental design:

The experimental units in which the crickets are bred are modified gaylord shipping boxes, which have the footprint of standard international shipping pallets (1.2m (L) x 1.0m (W) x 0.61m (H)). The interior of each enclosure is lined with a 4mm clear plastic liner and covered with 122cm x 137cm of nylon mosquito netting to serve as a physical barrier to entrance or exit. To prevent cannibalism and stress-related mortality, 96 egg cartons, 30 cm x 30 cm in size, are placed on-edge around the periphery of each box. This provides approximately 172800 cm² of crawl-able surface area. Access to water is provided by 2 quart-sized poultry water dispensers with cotton and gravel inserted in the dispensing basin to prevent the drowning of newly hatched nymphs. Sides of the water dispensers are sanded to provide purchase for the crickets to crawl vertically. Misting tips with check valves to prevent dripping are affixed at the top interior of each enclosure. To maintain acceptable humidity and provide a dispersed, alternative water source for the large population of crickets, these tips provided pulses of water aimed at the center of the enclosure at automated intervals. Temperature (T) and relative humidity (RH) within the greenhouse are maintained at 29.0 ± 2.1 standard deviation (SD) °C and 67.2 ± 14.7 SD %, respectively, over the course of the experiment. Light is provided 24 hr/day.

An egg substrate from Timberline Fisheries (<http://timberlinefresh.com>) consisting of approximately 50,000 *Acheta domesticus* eggs with a hatch rate of 70% is placed into each of the enclosures. The egg substrate is maintained between 80–90% humidity until they hatch. Once hatching is observed, the substrate is misted twice daily until the nymphs fully emerge. Population growth is monitored every 3 to 4 days by counting and weighing a random sample of 70 individuals from each experimental unit.

From 14 days after hatching until they are either harvested or experienced complete mortality, *Acheta domesticus* populations are administered the following: 2 feed treatments *ad libitum*: 1) a 5:1 ratio of non-medicated poultry starter feed and rice bran (Poultry Feed-PF), as control; 2) a 5:1 ratio of non-medicated poultry starter feed and rice bran (Poultry Feed-PF) sprayed with 100 mL of a solution of 10^9 cells/ml of the isolated bacteria described in Example 2 diluted in growth medium described herein.

Once a week for five weeks of culture, the insects are harvested. The insects are stored for half an hour in the freezer at -50°C. Next, the frozen insects are submerged in liquid nitrogen and subsequently grinded using a blender for 15 minutes (Braun Multiquick 5, 600 W, Kronberg, Germany). Amino acid composition of freeze-dried insect powder is analyzed using ion exchange chromatography, following the International standard ISO 13903:2005 following the technique of Yi, L. et al. (2013).

Crickets fed with the methionine producing microbes identified in Example 2 are expected to contain more methionine content than crickets fed the control feed.

Example 4: Administration of methionine producing strains of bacteria to *Drosophila melanogaster* raised on methionine deficient food to increase their body mass, development rate, and survival

This example demonstrates the ability to treat *Drosophila melanogaster* raised on methionine poor diet with methionine producing bacteria to increase the body mass, development rate, and survival.

This experimental design is also applicable to increase the nutritional content of other insects such as crickets which can be used to produce animal feed rich in methionine.

Experimental design:

5 Bacterial strains isolated in Example 2 that produce methionine, as well as the strains that do not produce methionine are grown in nutrient broth at 30°C.

Chemically defined (CD) fly food is prepared as described in Nature, Vol. 11, No. 1, 100-105, 2014. CD food is prepared that lacks methionine, and is referred to as CD-M. The fly food formulations are used for all experiments described in this Example.

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Development rate and body mass assays

On day one, 10^9 of the methionine producing bacteria as described in Example 1, or bacteria that do not produce methionine (control), are resuspended in 100 µl of phosphate-buffered saline and added to CD-M fly food. These two cohorts are left to dry for 24 hrs at 25°C.

15 On day two, fertilized embryos collected from flies are treated with 2% hypochlorite solution for 5 min and then washed with sterile water to remove any extracellular microbes from the embryos. 10µl of the embryo suspension in water (1:3 embryo:water suspension) is added to both the bacterial-seeded and control samples. The fly food cohorts with the embryos is maintained at 25°C with 12h light and 12 dark cycle for the rest of the experiment.

20 The time to puparium formation and the number of pupa formed is measured in each cohort. The time to adult emergence and the rate of emergence is measured in each sample. From the time the first adult emerges from the pupa, the number of emerging adult flies is counted every 12 hours and rate of emergence is computed.

25 For the body mass assay, ten larvae are collected from both cohorts and their weights, areas, and the total protein content are measured.

Embryos in the CD-M fly food seeded with methionine producing bacteria identified in Example 2 are expected to develop faster and have higher protein content than the embryos on CD-M fly food with non-methionine producing bacteria.

30 *Survival assay*

12 days before day one, sterile embryos are generated as described previously and raised on sterile CD fly food. Sterile adults start to emerge from their pupae 11 days from the time the embryos are collected when raised at 25°C with 12 h light and 12 h dark cycle.

35 On day one, 10^9 of the methionine producing bacteria, or bacteria that do not produce methionine (control), are resuspended in 100 µl phosphate-buffered saline and added to CD-M fly food. These two cohorts are left to dry for 24 hrs at 25°C.

10 newly emerged sterile adult males and females are introduced to CD-M fly food with methionine producing bacteria or control on day two of the experiment. The fly food with the flies is maintained at 25°C with 12h light and 12 dark cycle for the rest of the experiment. The number of

surviving male and female flies are counted every day until all the flies are dead. Survival analysis are performed to assess the fitness benefit of the methionine producing bacteria on fly survival.

Flies raised on CD-M fly food seeded with methionine producing microbes identified in Example 2 are expected to survive longer than the control.

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Example 5: Isolation of microorganisms that degrade fenitrothion, an organophosphorus insecticide

This Example demonstrates the acquisition of a library of microorganisms able to degrade fenitrothion, an organophosphorus insecticide.

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Experimental design

Soil samples are obtained from various regions where fenitrothion was previously utilized for insect control. Fenitrothion degrading bacteria will be isolated from the soil samples as described in (Microbes Environ. Vol. 21, No. 1, 58–64, 2006). Briefly, 1 g of the soil sample is mixed thoroughly with 9 ml of sterile distilled water. The soil particles are then centrifuged at 1000 rcf for 5 min, and 100µl of the supernatant is then plated onto fenitrothion with mineral salts medium (0.4 g/l of yeast extract, 0.4 g/l fenitrothion, 15 g/l bacteriological agar). The plates are cloudy when prepared as the fenitrothion is an emulsion.

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Colonies that develop clear zones around them and are likely to be degrading or metabolizing fenitrothion, and these colonies are isolated and regrown on LB agar, nutrient agar, yeast glucose agar, TSA agar, BHI agar, or MRS agar. Once unique bacterial colonies are identified, their genomes are extracted using a genomic DNA extraction kit, (Qiagen, DNeasy Blood and Tissue Kit) as per the manufacturer's protocol.

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The 16S rRNA gene is amplified using universal bacterial primers 27F (5'-AGAGTTTGATCMTGGCTCAG-3'; SEQ ID NO: 227) and 1492R (5'-TACCTTGTTACGACTT-3'; SEQ ID NO: 228), and using PCR conditions of 94°C for 2 min, 30 cycles of 94°C for 1 min, 56°C for 1 min, and 72°C for 2 min, and a final extension of 72°C for 5min. Gel electrophoresis is used to confirm that the amplicons are of the correct size (~1500 bp), and the products are excised from the gel and purified using a gel extraction kit (Qiagen, QIAquick) as per the manufacturer's protocol. The correct size amplicons are Sanger sequenced and BLAST is used to match the sequence against various repositories of 16s rRNA gene sequences to identify the bacteria.

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To determine whether the isolated bacteria is degrading fenitrothion, ~10⁷ bacterial cells are incubated in 1 ml of 20mM sodium-potassium phosphate buffer (pH 7) with 1mM fenitrothion, as described in PNAS, Vol. 109, No. 22, 8618-8622, 2012. After 30 min of incubation at 30°C, the reaction is stopped by adding an equal volume of methanol. Then fenitrothion and its metabolite, 3-methyl-4-nitrophenol, are analyzed by HPLC. The retention times and peak areas of the HPLC profiles are compared to known standards.

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Unique bacterial isolates that have fenitrothion degrading capabilities are then stored as frozen glycerol at -80 °C.

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Example 6: Increasing *Drosophila melanogaster*'s resistance to fenitrothion through the administration of fenitrothion-degrading bacteria

This Example demonstrates the ability to produce an insect model, *Drosophila melanogaster*, that is resistant to one or more negative effects of insecticides in their diet, more specifically fenitrothion, to produce a more robust insect. The following approach is a surrogate for other insects, such as crickets or other insects disclosed herein, e.g., insect sources useful to produce animal feed rich in protein. Many insecticides including fenitrothion have been shown to be toxic to crickets.

Experimental design:

Therapeutic design: The bacterial isolates selected in Example 5 are formulated at 10^9 organisms in 100 μ l of fly food medium with and without fenitrothion.

The media used to rear flies is cornmeal, molasses and yeast medium (11 g/l yeast, 54 g/l yellow cornmeal, 5 g/l agar, 66 ml/l molasses, and 4.8 ml/l propionic acid). For experimental procedures, fenitrothion at 0, 10, and 100 p.p.m. or phosphate-buffered saline as negative controls are infused into sterile fly food medium.

Development rate assay

On day one, 10^9 fenitrothion-degrading bacteria described in Example 5 are suspended in 100 μ l phosphate-buffered saline or equal volumes of saline (negative controls) are added to sterile fly food medium with or without fenitrothion. All are left to dry for a day at 25°C as described in *Appl. Environ. Microbiol.* Vol. 82, No. 20, 6204-6213, 2016.

On day two, fertilized embryos collected from flies are treated with 2% hypochlorite solution for 5 min and then washed with sterile water to remove any extracellular microbes from the embryos. 10 μ l of the embryo suspension in water (1:3 embryo:water suspension) is added to the bacteria-seeded or negative control fly food with or without the fenitrothion. The fly food cohorts with the embryos are maintained at 25°C with 12h light and 12 dark cycle for the rest of the experiment.

The time to puparium formation and the number of pupa formed is measured in each cohort. The time to adult emergence and the rate of emergence is measured in each sample. From the time the first adult emerges from the pupa, the number of emerging adult flies are counted every 12 hours and rate of emergence is computed.

Embryos in the fenitrothion infused fly food seeded with Fenitrothion-degrading bacteria are expected to develop faster than the the embryos on fenitrothion infused food without the fenitrothion-degrading bacteria.

Survival assay

About 12 days before day one, sterile embryos are generated as described previously and raised on sterile fly food. Adults start to emerge from their pupae 11 days from embryo collection when raised in sterile fly food without fenitrothion at 25°C with 12 h light and 12 h dark cycle.

On day one, 10^9 of the fenitrothion-degrading bacteria in phosphate-buffered saline are added to sterile fly food medium as described in a previous Example.

On day two, 10 newly emerged sterile adult males and females are introduced to bacteria-seeded or negative control fly food with or without fenitrothion. The fly food with the flies is maintained at 25°C with 12h light and 12 dark cycle for the rest of the experiment. The number of surviving male and female flies are counted every day until all the flies are dead. Survival analysis is performed to assess the fitness benefit of fenitrothion-degrading bacteria on the fly survival.

Flies raised on fenitrothion infused fly food seeded with fenitrothion-degrading bacteria are expected to survive longer than flies raised on fenitrothion infused food without the fenitrothion-degrading bacteria.

10 **Example 7: Elimination of entomopathogenic bacteria from *Drosophila melanogaster* using naturally occurring phages**

This Example demonstrates the ability to eliminate insect bacterial pathogens (such as *Serratia marcescens*, *Erwinia carotovora*, and *Pseudomonas entomophila*) from *Drosophila melanogaster* using naturally occurring phages. This procedure can be useful as a surrogate assay for eliminating bacteria in other insect species, such as in bees.

Experimental design:

Therapeutic design: Phage library collections are used having the following phage families:

Myoviridae, Siphoviridae, Podoviridae, Lipothruxviridae, Rudiviridae, Ampullaviridae, Bicaudaviridae, Clavaviridae, Corticoviridae, Cystoviridae, Fuselloviridae, Gluboloviridae, Guttaviridae, Inoviridae, Leviviridae, Microviridae, Plasmaviridae, Tectiviridae.

Multiple environmental samples (soil, pond sediments, and sewage water) are collected in sterile 1L flasks over a period of 2 weeks and are immediately processed after collection and stored thereafter at 4 °C. Solid samples are homogenized in sterile double-strength difco luria broth (LB) or tryptic soy broth (TSB) supplemented with 2mM CaCl₂ to a final volume of 100mL. The pH and phosphate levels are measured using phosphate test strips. For purification, all samples are centrifuged at 3000–6000 g for 10–15 min at 4 °C, and filtered through 0.2-µm low protein filters to remove all remaining bacterial cells. The supernatant that contains the phage library is then stored at 4 °C in the presence of chloroform in a glass bottle.

20–30 ml of the phage library is diluted to a volume of 30–40 ml with LB-broth. The target bacterial strain (e.g., *Serratia marcescens*, *Erwinia carotovora*, and *Pseudomonas entomophila*) is added (50–200 µl overnight culture grown in LB-broth) to enrich phages that target this specific bacterial strain in the culture. This culture is incubated overnight at 37 °C, shaken at 230 rpm. Bacteria from this enrichment culture are removed by centrifugation (3000–6000 g 15–20 min, 4 °C) and filtered (0.2 or 0.45 µm filter). 2.5 ml of the bacteria free culture is added to 2.5 ml of LB-broth and 50–100 µl of the target bacteria are added back to the culture to further enrich the phages. The enrichment culture is grown overnight as above. A sample from this enrichment culture is centrifuged at 13,000 g for 15 min at room temperature and 10 µl of the supernatant is plated on an LB-agar petri dish along with 100–300 µl of the target bacteria and 3 ml of melted 0.7% soft-agar. The plates are incubated overnight at 37 °C.

Each of the plaques observed on the bacterial lawn are picked and transferred into 500 µl of LB-broth. A sample from this plaque-stock is further plated on the target bacteria. Plaque-purification is performed three times for all discovered phages in order to isolate a single homogenous phage from the heterogeneous phage mix.

5 Lysates from plates with high-titer phages ($>1 \times 10^{10}$ PFU/ml) are prepared by harvesting overlay plates of a host bacterium strain exhibiting confluent lysis. After being flooded with 5 ml of buffer, the soft agar overlay is macerated, clarified by centrifugation, and filter sterilized. The resulting lysates are stored at 4 °C. High-titer phage lysates are further purified by isopycnic CsCl centrifugation, as described in Summer et al., *J. Bacteriol.* 192:179-190, 2010.

10 DNA is isolated from CsCl-purified phage suspensions as described in Summer, *Methods Mol. Biol.* 502:27-46, 2009. An individual isolated phage is sequenced as part of two pools of phage genomes by using a 454 pyrosequencing method. Briefly, phage genomic DNA is mixed in equimolar amounts to a final concentration of about 100 ng/L. The pooled DNA is sheared, ligated with a multiplex identifier (MID) tag specific for each of the pools, and sequenced by pyrosequencing using a full-plate reaction on a
15 sequencer (Roche) according to the manufacturer's protocols. The pooled phage DNA is present in two sequencing reactions. The output corresponding to each of the pools is assembled individually by using software (454 Life Sciences), by adjusting the settings to include only reads with a single MID per assembly. The identity of individual contigs is determined by PCR using primers generated against contig sequences and individual phage genomic DNA preparations as the template. Sequence software (Gene
20 Codes Corporation) is used for sequence assembly and editing.

Phage chromosomal end structures are determined experimentally. Cohesive (cos) ends for phages are determined by sequencing off the ends of the phage genome and sequencing the PCR products derived by amplification through the ligated junction of circularized genomic DNA, as described in Summer, *Methods Mol. Biol.* 502:27-46, 2009. Protein-coding regions are initially predicted using gene
25 prediction software (Lukashin et al. *Nucleic Acids Res.* 26:1107-1115, 1998), refined through manual analysis in Artemis (Rutherford et al., *Bioinformatics* 16:944-945, 2000), and analyzed through the use of BLAST (E value cutoff of 0.005) (Camacho et al., *BMC Bioinformatics* 10:421, 2009). Proteins of particular interest are additionally analyzed by sequence searching software (Hunter et al., *Nucleic Acids Res.* 40:D306-D312, 2012).

30 Electron microscopy of CsCl-purified phage ($>1 \times 10^{11}$ PFU/ml) that lysed the *Drosophila's* pathogenic bacterial species is performed by diluting phage stock with the tryptic soy broth buffer. Phages are applied onto thin 400-mesh carbon-coated grids, stained with 2% (wt/vol) uranyl acetate, and air dried. Specimens are observed on a transmission electron microscope operating at an acceleration voltage of 100 kV. Five virions of each phage are measured to calculate mean values and standard
35 deviations for dimensions of capsid and tail, where appropriate.

Incorporating phages into a meal

The media used to rear flies is cornmeal, molasses and yeast medium (11 g/l yeast, 54 g/l yellow cornmeal, 5 g/l agar, 66 ml/l molasses, and 4.8 ml/l propionic acid). Phage solutions are infused into the fly food to obtain final concentrations of phages between 0 and 10^8 pfu/ml.

- 5 *S. Marcescens*, *Erwinia carotovora*, and *Pseudomonas entomophila* bacteria are grown at 30 °C in nutrient broth or LB broth.

- Sterile fly embryos are generated by treating fertilized embryos collected from flies with 2% hypochlorite solution for 5 min and then washed with sterile water to remove any extracellular microbes. Fly larvae with the target bacteria are generated by seeding 10^9 CFUs of bacteria in sterile fly food and adding sterile fly embryos to this food. After 2 days, ten *S. marcescens* infected first instar fly larvae are added to the fly food with a range (0- 10^8 pfu/ml) of the phage concentrations. The larvae are left to grow in the food with the phages for 3 days until they become third instars. The larvae are then collected and individually homogenized in nutrient broth or LB broth, and plated on nutrient agar or LB agar plates, and incubated at 30 °C. The number of CFUs of *S. marcescens* obtained from larvae in fly food with varying phage concentrations are recorded. This shows the number of live bacteria that were present in the flies.

 The number of live bacteria are expected to be reduced in the larvae grown on fly food with the phages against the bacteria.

Example 8: Administration of amino acid producing strain of bacteria to *Drosophila melanogaster* through diet to increase their development rate

- 20 This Example demonstrates the ability to treat the insect *Drosophila melanogaster* with amino acid producing bacteria to improve their nutritional content. This experimental design can be extended to reduce the growth time and produce more biomass of other insects, such as crickets, which can be used to produce animal feed rich in protein.

- 25 The world's appetite for meat is growing, and the production of animal feed is an increasing strain on land and water. Insects could provide much of the protein humans and animals need at a much lower environmental cost; many insect species can feed on manure, like Grant's maggots, or other types of organic waste, such as leftover food, offal, and grains discarded by breweries. Insects produce body mass at an astonishing rate, in part because as cold-blooded animals they don't expend energy on regulating their body temperature. Crickets, e.g., *Acheta domesticus*, need only 1.7 kilograms of feed to gain a kilogram of body weight; a typical U.S. chicken consumes 2.5 kilograms, pigs 5 kilograms, and cattle 10 kilograms. Another advantage: most insects can be eaten whole. Only about half of a chicken or a pig is edible; for a cow the fraction is even less. As a result, raising a kilogram of insect protein produces less CO₂ than rearing pigs or cattle, and takes up only one-tenth the land.

Insect meal could replace between 25% and 100% of soymeal or fishmeal in animals' diets with no adverse effects. However, most insect meals are deficient in the amino acids methionine and lysine. Synthetic production of methionine requires hazardous chemicals and its use is banned in organic farming. In this Example, the introduction of methionine-producing bacteria into an insect's microbiome naturally increased their nutritional content.

Therapeutic design:

Isolated bacteria *Corynebacterium glutamicum* that are glutamate or methionine producing, are formulated with a solution of 10⁹ colony forming units (CFUs) mixed to the feeding substrate for *Drosophila* flies.

Experimental design:

Corynebacterium glutamicum strains that produce glutamate or methionine were grown in nutrient broth at 30°C.

The media used to rear flies is cornmeal, molasses and yeast medium (11 g/l yeast, 54 g/l yellow cornmeal, 5 g/l agar, 66 ml/l molasses, and 4.8 ml/l propionic acid). All the components of the diet except propionic acid are heated together to 80°C in deionized water with constant mixing for 30 minutes and let to cool to 60°C. Propionic acid is then mixed in and 50ml of the diet is aliquoted into individual bottles and allowed to cool down and solidify. The flies are raised at 26°C, 16:8 hour light:dark cycle, at around 60% humidity.

For the experimental setup to measure the larval growth rate, defined diet was used (Piper et al., 2014, *Nature Methods*). Defined diet eliminates the effects of batch to batch variation in the ingredients used for the cornmeal based diet. In addition, the defined diet allows for the exclusion of individual components to test their effects on fly development.

Development rate assay

On day one, 100 ul of a *Corynebacterium glutamicum* suspension in nutrient broth consisting of 10⁹ colony forming units (CFUs) were added to five replicates of fly food. As controls, nutrient broth without the bacteria was added to five more bottles of fly food. Fertilized embryos collected from fruit flies were treated with 2% hypochlorite solution for five minutes and then washed with sterile water to remove any extracellular microbes from the embryos. 10ul of the embryo suspension in water (one:three embryo:water suspension) was added to all the bacteria seeded and control fly food bottles. The fly food with the embryos was maintained at 26°C, 16:8 hour light:dark cycle, at around 60% humidity for the rest of the experiment. The time to adult emergence and the rate of emergence was measured in every replicate. From the time the first adult emerges from the pupa, the number of adult flies emerging was counted every 12 hours and rate of emergence was be computed.

Larval mass assay

To test whether the presence of bacteria producing amino acids can increase the body mass of developing larvae when raised on defined diet, we produced larvae that are axenic, and mono-associated

with a single strain of bacterium. For these assays, three different bacteria were used, *Corynebacterium glutamicum* - a strain that produces glutamate, *Corynebacterium glutamicum* – a strain that produces methionine, and *E. coli*.

First, axenic embryos were generated. Fertilized embryos were collected from fruit flies over a 6
5 hour period on grape juice agar plates with yeast. To eliminate any bacterial contamination, the embryos were treated with 2% hypochlorite solution for five minutes and then washed thrice with sterile water. One volume of embryos was then suspended in 3 volumes of water.

The defined diet was aliquoted into vials and nine replicates were used for every condition being tested. The conditions were:

- 10 1. No bacteria added to the food
2. Food containing *C. glutamicum*, strain that produces glutamate (C.glu-Glu)
3. Food containing *C. glutamicum*, a strain that produces methionine (C.glu-Met)
4. Food containing *E. coli*

To each vial of the food that were in conditions 2, 3, and 4, 100ul of overnight stationary phase
15 cultures was added.

To each of the nine replicates in every condition, 10ul of the sterile embryo+water suspension was added. The vials were then incubated at 26°C, 60% humidity, 16:8 light:dark cycle.

After 13 days, 10-15 randomly chosen larvae from each replicate were sampled, and their areas were measured, as a proxy to their biomass and weight. The larvae were scooped out from the food with
20 a sterile spatula, rinsed in water to clean the food from their bodies, and an image of every larvae sampled was acquired individually for every replicate in each condition. An Image J script was used to identify, outline and measure the area of the larva in every image.

Amino acid producing bacteria treatment increases insect development rate.

25 Embryos that developed on diet that was seeded with the amino acid producing strain of bacterium reached adulthood significantly faster than those that were raised on the sterile diet (Fig. 1). Further, this effect was slightly stronger in female flies than in male flies (Figs. 2A and 2B).

Amino acid producing bacteria treatment increases larval body mass.

30 Larvae from the diet supplemented with *C. glu-Met* had the largest body size on average, followed by those in diet with *C.glu-Glu*, *E.coli*, and no bacteria (Fig. 3). This shows that augmenting the diet of insects with bacteria that produce amino acids produced insect biomass faster than un-supplemented diet.

Together this data demonstrates that augmenting the diet of insects with bacteria that were
35 capable of producing amino acids produced insect biomass faster than un-supplemented diet. Extending this to other insects such as crickets, supplementing their diet with bacteria that are capable of producing methionine can increase their biomass and protein content.

Example 9: Insects treated with a solution of purified phage

This Example demonstrates the isolation and purification of phages from environmental samples that targeted specific insect bacteria. This Example also demonstrates the efficacy of isolated phages against the target bacteria in vitro by plaque assays, by measuring their oxygen consumption rate, and the extracellular acidification rate. Finally, this Example demonstrates the efficacy of the phages in vivo, by measuring the ability of the phage to the target bacteria from flies by treating them with a phage isolated against the bacteria. This Example demonstrates that a pathogenic bacterium that decreased the fitness of an insect can be cleared using a phage to target the bacteria. Specifically, *Serratia marcescens* which is a pathogenic bacterium in flies can be cleared with the use of a phage that was isolated from garden compost.

There are several beneficial and commercially useful insects that are affected by naturally occurring bacterial pathogens.

*Experimental design**Isolation of specific bacteriophages from natural samples:*

Bacteriophages against target bacteria were isolated from environmental source material. Briefly, a saturated culture of *Serratia marcescens* was diluted into fresh double-strength tryptic soy broth (TSB) and grown for ~120 minutes to early log-phase at 24-26°C, or into double-strength Luria-Bertani (LB) broth and grown for ~90 min at 37°C. Garden compost was prepared by homogenization in PBS and sterilized by 0.2 µm filtration. Raw sewage was sterilized by 0.2 µm filtration. One volume of filtered source material was added to log-phase bacterial cultures and incubation was continued for 24 h. Enriched source material was prepared by pelleting cultures and filtering supernatant fluid through 0.45 µm membranes.

Phages were isolated by plating samples onto double-agar bacterial lawns. Stationary bacterial cultures were combined with molten 0.6% agar LB or TSB and poured onto 1.5% agar LB or TSB plates. After solidification, 2.5 µL of phage sample dilutions were spotted onto the double-agar plates and allowed to absorb. Plates were then wrapped and incubated overnight at 25°C (TSA) or 37°C (LB), then assessed for the formation of visible plaques. Newly isolated plaques were purified by serial passaging of individual plaques on the target strain by picking plaques into SM Buffer (50 mM Tris-HCl [pH 7.4], 10 mM MgSO₄, 100 mM NaCl) and incubating for 15 min at 55°C, then repeating the double-agar spotting method from above using the plaque suspension.

Bacteriophages were successfully isolated from both sewage and compost, as detailed above. Plaque formation was clearly evident after spotting samples onto lawns of the *S. marcescens* bacteria used for the enrichments.

Passaging, quantification, and propagation of bacteriophages:

Propagation and generation of phage lysates for use in subsequent experiments was performed using bacteriophages isolated and purified as above. Briefly, saturated bacterial cultures were diluted 100-fold into fresh medium and grown for 60-120 minutes to achieve an early-logarithmic growth state for effective phage infection. Phage suspensions or lysates were added to early log phase cultures and

incubation was continued until broth clearing, indicative of phage propagation and bacterial lysis, was observed, or until up to 24 h post-infection. Lysates were harvested by pelleting cells at 7,197 x g for 20 min, then filtering the supernatant fluid through 0.45 or 0.2 µm membranes. Filtered lysates were stored at 4°C.

5 Enumeration of infective phage particles was performed using the double-agar spotting method. Briefly, a 1:10 dilution series of samples was performed in PBS and dilutions were spotted onto solidified double-agar plates prepared with the host bacteria as above. Plaque-forming units (PFU) were counted after overnight incubation to determine the approximate titer of samples.

10 *In vitro analysis of isolated phages measuring bacterial respiration:*

A Seahorse XFe96 Analyzer (Agilent) was used to measure the effects of phages on bacteria by monitoring oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) during infection. XFe96 plates were coated the day prior to experiments by 15 µL of a 1 mg/mL poly-L-lysine stock per well and dried overnight at 28°C and XFe96 probes were equilibrated by placing into wells containing 200 µL
15 of XF Calibrant and incubating in the dark at room temperature. The following day, poly-L-lysine coated plates were washed twice with ddH₂O. Saturated overnight cultures of *E. coli* BL21 (LB, 37°C) or *S. marcescens* (TSB, 25°C) were subcultured at 1:100 into the same media and grown with aeration for ~2.5 h at 30°C. Cultures were then diluted to O.D._{600nm} ~ 0.02 using the same media. Treatments were prepared by diluting stocks into SM Buffer at 10x final concentration and loading 20 µL of the 10x
20 solutions into the appropriate injection ports of the probe plate. While the probes were equilibrating in the XFe96 Flux Analyzer, bacterial plates were prepared by adding 90 µL of bacterial suspensions or media controls and spun at 3,000 rpm for 10 min. Following centrifugation, an additional 90 µL of the appropriate media were added gently to the wells so as not to disturb bacterial adherence, bringing the total volume to 180 µL per well.

25 The XFe96 Flux Analyzer was run at ~30°C, following a Mix, Wait, Read cycling of 1:00, 0:30, 3:00. Four cycles were completed to permit equilibration/normalization of bacteria, then the 20 µL treatments were injected and cycling continued as above, for a total time of approximately 6 h. Data were analyzed using the Seahorse XFe96 Wave software package.

The effects of isolated bacteriophages were assayed by measuring oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) of bacteria with a Seahorse XFe96 Analyzer. When
30 *E. coli* was infected with phage T7 and *S. marcescens* infected with the newly isolated ΦSmVL-C1, dramatic decreases in OCR were observed following brief bursts in this rate (Fig. 4). For both phages with both host organisms, the Seahorse assay permitted the detection of successful phage infection without the need for plaque assays. Thus, this method is applicable for detecting phage infection of a
35 host organism not amenable to traditional phage detection methods.

SYBR Gold transduction assay for infection identification:

Bacteriophage preparations were prepared for staining by pretreating with nucleases to remove
40 extracellular nucleic acids that could interfere with fluorescent signal interpretation. Briefly, MgCl₂ was added to 10 mL of phage lysate at 10 mM final concentration, and RNase A (Qiagen) and DNase I

(Sigma) were both added to final concentrations of 10 µg/mL. Samples were incubated for 1 h at room temperature. After nuclease treatment, 5 mL of lysates were combined with 1 µL of SYBR Gold (Thermo, 10,000x) and incubated at room temperature for ~1.5 h. Excess dye was subsequently removed from samples using Amicon ultrafiltration columns. Briefly, Amicon columns (15 mL, 10k MWCO) were
5 washed by adding 10 mL of SM Buffer and spinning at 5,000 x g, 4°C for 5 min. Labeled phage samples were then spun through the columns at 5,000 x g, 4°C until the volume had decreased by approximately 10-fold (15-30 min). To wash samples, 5 mL SM Buffer was added to each reservoir and the spin repeated, followed by two additional washes. After the third wash, the retained samples were pipetted out from the Amicon reservoirs and brought up to approximately 1 mL using SM Buffer. To remove larger
10 contaminants, washed and labeled phage samples were spun at 10,000 x g for 2 min, and the supernatants were subsequently filtered through 0.2 µm membranes into black microtubes and stored at 4°C.

Saturated bacterial cultures (*E. coli* MG1655 grown in LB at 37°C, *S. marcescens* and *S. symbiotica* grown in TSB at 26°C) were prepared by spinning down 1 mL aliquots and washing once
15 with 1 mL PBS before a final resuspension using 1 mL PBS. Positive control labeled bacteria were stained by combining 500 µL of washed bacteria with 1 µL of SYBR Gold and incubating for 1 h in the dark at room temperature. Bacteria were pelleted by spinning at 8,000 x g for 5 min and washed twice with an equal volume of PBS, followed by resuspension in a final volume of 500 µL PBS. A volume of 25 µL of stained bacteria was combined with 25 µL of SM Buffer in a black microtube, to which 50 µL of 10%
20 formalin (5% final volume, ~2% formaldehyde) was added and mixed by flicking. Samples were fixed at room temperature for ~3 h and then washed using Amicon ultrafiltration columns. Briefly, 500 µL of picopure water was added to Amicon columns (0.5 mL, 100k MWCO) and spun at 14,000 x g for 5 min to wash membranes. Fixed samples were diluted by adding 400 µL of PBS and then transferred to pre-washed spin columns and spun at 14,000 x g for 10 min. Columns were transferred to fresh collection
25 tubes, and 500 µL of PBS was added to dilute out fixative remaining in the retentate. Subsequently, two additional PBS dilutions were performed, for a total of three washes. The final retentates were diluted to roughly 100 µL, then columns were inverted into fresh collection tubes and spun at 1,000 x g for 2 min to collect samples. Washed samples were transferred to black microtubes and stored at 4°C.

For transduction experiments and controls, 25 µL of bacteria (or PBS) and 25 µL of SYBR Gold
30 labeled phage (or SM Buffer) were combined in black microtubes and incubated static for 15-20 min at room temperature to permit phage adsorption and injection into recipient bacteria. Immediately after incubation, 50 µL of 10% formalin was added to samples and fixation was performed at room temperature for ~4 h. Samples were washed with PBS using Amicon columns, as above.

Injection of bacteriophage nucleic acid was required for a phage to successfully infect a host
35 bacterial cell. Coliphage P1kc labeled with SYBR Gold and co-incubated with *S. marcescens* revealed the presence of fluorescent bacteria by microscopy, validating the use of this assay in a phage isolation pipeline. As with the Seahorse assay, this approach provided an alternative to traditional phage methods to permit expansion to organisms not amenable to plaque assay. Additionally, the SYBR Gold transduction assay did not require bacterial growth, so is applicable to analysis of phages targeting
40 difficult or even non-culturable organisms, including endosymbionts such as *Buchnera*.

Testing in vivo efficacy of the phages against S. marcescens in Drosophila melanogaster flies

S. marcescens cultures were grown in Tryptic Soy Broth (TSB) at 30°C with constant shaking at 200rpm.

The media used to rear fly stocks was cornmeal, molasses and yeast medium (11 g/l yeast, 54 g/l yellow cornmeal, 5 g/l agar, 66 ml/l molasses, and 4.8 ml/l propionic acid). All the components of the diet except propionic acid were heated together to 80°C in deionized water with constant mixing for 30 minutes and let to cool to 60°C. Propionic acid was then mixed in and 50ml of the diet was aliquoted into individual bottles and allowed to cool down and solidify. The flies were raised at 26°C, 16:8 hour light:dark cycle, at around 60% humidity.

To infect the flies with *S. marcescens*, a fine needle (About 10um wide tip) was dipped in a dense overnight stationary phase culture and the thorax of the flies was punctured. For this experiment, four replicates of 10 males and 10 females each were infected with *S. marcescens* using the needle puncturing method as the positive control for fly mortality. For the treatment group, four replicates of 10 males and 10 females each were pricked with *S. marcescens* and a phage solution containing about 10⁸ phage particles/ml. Finally, two replicates of 10 males and 10 females each that were not pricked or treated in anyway were used as a negative control for mortality.

Flies in all conditions were placed in food bottles and incubated at 26°C, 16:8 light:dark cycle, at 60% humidity. The number of alive and dead flies were counted every day for four days after the pricking. All The flies pricked with *S. marcescens* alone were all dead within 24 hours of the treatment. In comparison, more than 60% of the flies in the phage treatment group, and all the flies in the untreated control group were alive at that time point (Fig. 5). Further, most of the flies in the phage treatment group and the negative control group went on to survive for four more days when the experiment was terminated.

To ascertain the reason of death of the flies, dead flies from both the *S. marcescens* and *S. marcescens* + phage pricked flies were homogenized and plated out. Four dead flies from each of the four replicates of both the *S. marcescens* and the *S. marcescens* + phage treatment were homogenized in 100ul of TSB. A 1:100 dilution was also produced by diluting the homogenate in TSB. 10ul of the concentrated homogenate as well as the 1:100 dilution was plated out onto TSA plates, and incubated overnight at 30°C. Upon inspection of the plates for bacteria growth, all the plates from the dead *S. marcescens* pricked flies had a lawn of bacteria growing on them, whereas the plates from the dead *S. marcescens* + phage pricked flies had no bacteria on them. This shows that in the absence of the phage, *S. marcescens* likely induced septic shock in the flies leading to their fatality. However, in the presence of the phage, the mortality may have been due to injury caused by the pricking with the needle.

OTHER EMBODIMENTS

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, the descriptions and examples should not be construed as limiting the scope of the invention. The disclosures of all patent and scientific literature cited herein are expressly incorporated in their entirety by reference.

CLAIMS

1. A method for increasing a nutritional profile of an insect, the method comprising:
delivering an effective amount of a methionine-producing bacteria to the insect.
2. The method of claim 1, wherein the insect is a cricket, a grasshopper, or a locust.
3. The method of any one of claims 1-2, wherein the insect is developmentally an embryo, larva, pupa, or adult.
4. The method of any one of claims 1-3, wherein the delivery comprises delivering the composition to at least one habitat where the insect grows, lives, reproduces, or feeds.
5. The method of any one of claims 1-4, wherein the methionine-producing bacteria is delivered in an insect comestible composition for ingestion by the insect.
6. The method of any one of claims 1-5, wherein the methionine-producing bacteria is formulated with an agriculturally acceptable carrier as a liquid, a solid, an aerosol, a paste, a gel, or a gas composition.
7. The method of claim 6, wherein the carrier is a seed coating.
8. A modified insect comprising exogenous methionine-producing bacteria resident in the insect.
9. The insect of claim 8, wherein the insect is developmentally an embryo, larva, pupa, or an adult.
10. The insect of any one of claims 8-9, wherein the methionine-producing bacteria alters microbiota in a gut and/or haemocoel of the insect.