COMPOSITIONS AND RELATED METHODS FOR CONTROLLING VECTOR-BORNE DISEASES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application No. 62/450,032, filed on January 24, 2017, and U.S. Provisional Application No. 62/583,925, filed on November 9, 2017, the contents of which are hereby incorporated herein by reference in their entireties.

BACKGROUND

Insects function as vectors for pathogens causing severe human disease such as dengue, trypanosomiases, and malaria. With 174 million diagnoses and 655,000 million deaths in 2011, malaria is considered as one of the most significant diseases worldwide. Thus, there is need in the art for methods and compositions to control insects that carry vector-borne diseases.

SUMMARY

Disclosed herein are compositions and methods for modulating the fitness of insects for controlling the spread of vector-borne diseases in humans. 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, the present disclosure refers to a method of decreasing fitness of an insect vector for a human pathogen, comprising: delivering to the insect vector a composition comprising an antimicrobial peptide and a cell penetrating peptide, wherein: (i) the antimicrobial peptide is chosen from scorpion peptide Uy192 (FLSTIWNGIKGLL), cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin (SEQ ID NO: 89), protegrin (SEQ ID NO: 90), tachyplesin (SEQ ID NO: 91), UyCT3 (LSAIWSGIKSLF), D3 (LWGKLWEGVKSLI), D10 (FPFLKLSLKIPKSAIKSAIKRL), Uy17 (ILSAIWSGIKGLL), and defensin (SEQ ID NO: 92); and (ii) the cell penetrating peptide has an amino acid sequence selected from the group consisting of SEQ ID NOs: 213 – 220 and SEQ ID NO: 247; wherein the antimicrobial peptide targets a microorganism resident in the insect vector resulting in a decrease in fitness of the insect vector, relative to a control insect vector not treated with the composition.

In one aspect, the present disclosure refers to use of an antimicrobial peptide and a cell penetrating peptide in the manufacture of a composition for decreasing fitness of an insect vector for a human pathogen, wherein the antimicrobial peptide targets a microorganism resident in an insect vector for the human pathogen resulting in a decrease in fitness of the insect vector relative to a control insect vector not treated with the composition, wherein: (i) the antimicrobial peptide is chosen from scorpion peptide Uy192 (FLSTIWNGIKGLL), cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin (SEQ ID NO: 89), protegrin (SEQ ID NO: 90), tachyplesin (SEQ ID NO: 91), UyCT3 (LSAIWSGIKSLF), D3 (LWGKLWEGVKSLI), D10 (FPFLKLSLKIPKSAIKSAIKRL), Uy17 (ILSAIWSGIKGLL), and defensin (SEQ ID NO: 92); and (ii) the cell penetrating peptide has an amino acid sequence selected from the group consisting of SEQ ID NOs: 213 – 220 and SEQ ID NO: 247.

In one example, provided herein is a method of decreasing fitness of a vector (e.g., insect vector) for a human pathogen, the method including delivering an antimicrobial peptide having at least 90% sequence identity (e.g., at least 90%, 92%, 94%, 96%, 98%, or 100% sequence identity) with one or more of the following: cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin (SEQ ID NO: 89), protegrin (SEQ ID NO: 90), tachyplesin (SEQ ID NO: 91), or defensin (SEQ ID NO: 92) to the vector.

In some examples, the delivery includes delivering the antimicrobial peptide to at least one habitat where the vector grows, lives, reproduces, feeds, or infests.

In some examples, the antimicrobial peptide may be delivered in an insect comestible composition for ingestion by the vector.

In some examples, the antimicrobial peptide may be formulated as a liquid, a solid, an aerosol, a paste, a gel, or a gas composition.

In some examples, the insect may be at least one of a mosquito, midge, louse, sandfly, tick, triatomine bug, tsetse fly, or flea.

In another example, provided herein is a composition including an antimicrobial peptide having at least 90% sequence identity (e.g., at least 90%, 92%, 94%, 96%, 98%, or 100% sequence identity) with one or more of the following: cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin

CLAIMS

1. A method of decreasing fitness of an insect vector for a human pathogen, comprising: delivering to the insect vector a composition comprising an antimicrobial peptide and a cell penetrating peptide, wherein:

(i) the antimicrobial peptide is chosen from scorpion peptide Uy192 (FLSTIWNGIKGLL), cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin (SEQ ID NO: 89), protegrin (SEQ ID NO: 90), tachyplesin (SEQ ID NO: 91), UyCT3 (LSAIWSGIKSLF), D3 (LWGKLWEGVKSLI), D10 (FPFLKLSLKIPKSAIKSAIKRL), Uy17 (ILSAIWSGIKGLL), and defensin (SEQ ID NO: 92); and

(ii) the cell penetrating peptide has an amino acid sequence selected from the group consisting of SEQ ID NOs: 213 – 220 and SEQ ID NO: 247;

wherein the antimicrobial peptide targets a microorganism resident in the insect vector resulting in a decrease in fitness of the insect vector, relative to a control insect vector not treated with the composition.

2. Use of an antimicrobial peptide and a cell penetrating peptide in the manufacture of a composition for decreasing fitness of an insect vector for a human pathogen, wherein the antimicrobial peptide targets a microorganism resident in an insect vector for the human pathogen resulting in a decrease in fitness of the insect vector relative to a control insect vector not treated with the composition, wherein:

(i) the antimicrobial peptide is chosen from scorpion peptide Uy192 (FLSTIWNGIKGLL), cecropin (SEQ ID NO: 82), melittin, copsin, drosomycin (SEQ ID NO: 93), dermcidin (SEQ ID NO: 81), andropin (SEQ ID NO: 83), moricin (SEQ ID NO: 84), ceratotoxin (SEQ ID NO: 85), abaecin (SEQ ID NO: 86), apidaecin (SEQ ID NO: 87), prophenin (SEQ ID NO: 88), indolicidin (SEQ ID NO: 89), protegrin (SEQ ID NO: 90), tachyplesin (SEQ ID NO: 91), UyCT3 (LSAIWSGIKSLF), D3 (LWGKLWEGVKSLI), D10 (FPFLKLSLKIPKSAIKSAIKRL), Uy17 (ILSAIWSGIKGLL), and defensin (SEQ ID NO: 92); and

(ii) the cell penetrating peptide has an amino acid sequence selected from the group consisting of SEQ ID NOs: 213 – 220 and SEQ ID NO: 247.

3. The method of claim 1 or use of claim 2, wherein the microorganism is an obligate symbiont of the insect vector.

4. The method of claim 1, the use of claim 2, or the method or use of claim 3, wherein the composition further comprises at least one agent selected from an antibiotic and a natural antimicrobial.

5. The method or use of any one of claims 1-4, wherein the antimicrobial peptide is scorpion peptide Uy192 (SEQ ID NO: 227) or dermcidin (SEQ ID NO: 81).

6. The method or use of claim 4, wherein the antibiotic is at least one chosen from oxytetracycline, rifampicin, ciprofloxacin, doxycycline, ampicillin, polymyxin B, timentin, and azithromycin.

7. The method or use of claim 4, wherein the natural antimicrobial is chitosan.

8. The method of claim 1, the use of claim 2, or the method or use of any one of claims 3-7, wherein targeting comprises altering at least one of a level, activity, or metabolism of the microorganism.

9. The method of claim 1, the use of claim 2, or the method or use of any one of claims 3-8, wherein delivering comprises providing the composition to at least one habitat where the insect vector grows, lives, reproduces, feeds, or infests.

10. The method of claim 1, the use of claim 2, or the method or use of any one of claims 3-9, wherein composition is formulated as an insect comestible composition for ingestion by the insect vector.

11. The method of claim 1, the use of claim 2, or the method or use of any one of claims 3-10, wherein the antimicrobial peptide and the cell penetrating peptide are a fusion peptide.

12. The method or use of claim 11, wherein the fusion peptide has the amino acid sequence of SEQ ID NO: 246.