disfigurement of nails and/or pain. Treatments for dermatophytoses includes antifungal topical products (*e.g.*, terbinafine, itraconazole, miconazole, etc.) and/or systemic therapy. The ineffectiveness and toxicity of some long-term treatments as well as anti-fungal drug resistance and recurrence of infection has resulted in a need for an alternative treatment.

[005] Described herein are compositions and methods for using human-derived Janthinobacterium lividum for treating, inhibiting or preventing pathogenic microorganisms. The compositions and methods are useful in modulating the microbiome to effectively inhibit, treat or prevent microbial infections. These compositions and methods comprise products of the object of this invention, human-derived Janthinobacterium lividum.

[006] Also described herein are topical and cosmetic compositions and methods for improving skin health, reducing the effects of exposure to sun, and aging, using human-derived Janthinobacterium lividum.

4. SUMMARY

[007] Disclosed herein are pharmaceutical compositions comprising at least one human-isolated Janthinobacterium lividum in an amount effective for use in the inhibition, treatment or prevention of topical pathogenic microorganisms. Also disclosed herein are pharmaceutical compositions comprising one or more metabolite of human-derived Janthinobacterium lividum in an amount effective for use in the inhibition, treatment or prevention of a topical pathogenic microorganism. Also disclosed herein are pharmaceutical compositions comprising cell lysate of human-derived Janthinobacterium lividum in an amount effective for use in the inhibition, treatment or prevention of a topical pathogenic microorganism. Disclosed herein are pharmaceutical compositions comprising an excipient and human-derived Janthinobacterium lividum, and/or materials originating from human-derived Janthinobacterium lividum, in an amount effective for use in the inhibition, treatment or prevention of a topical pathogenic microorganism; and methods for using these pharmaceutical compositions to inhibit, treat or prevent pathogenic microorganisms. These pharmaceutical compositions can be formulated for application to the skin, mucosa, hair, and/or nails.

[007a] In one aspect, the present disclosure refers to a composition comprising human-derived Janthinobacterium lividum, formulated for topical application to a human subject.

[007b] In one aspect, the present disclosure refers to a pharmaceutical formulation comprising the composition disclosed herein in an amount effective to treat, inhibit, reduce a symptom of, or prevent a skin disease, disorder, or condition in a human subject, wherein the

pharmaceutical composition is to be administered in an amount effective to inhibit the growth of a topical pathogenic microorganism present on or in a tissue of the human subject.

[007c] In one aspect, the present disclosure refers to a pharmaceutical composition comprising an excipient suitable for formulation with at least one human-derived Janthinobacterium lividum in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.

[007d] In one aspect, the present disclosure refers to the use of a human-derived Janthinobacterium lividum in the manufacture of a medicament for inhibiting or preventing growth of a pathogenic microorganism in a human subject in need thereof.

[007e] In one aspect, the present disclosure refers to an isolated human-derived Janthinobacterium lividum that over-produces 2-(alpha-D-mannosyl)-D-glyceric acid, 2-ketogluconate, 2-O-ethyl ascorbic acid, anthramycin, Aprobarbital, bendiocarb, Bis(2-ethylhexyl) phthalate, cis-5- Tetradecenoylcarnitine, Dibutyl phthalate, imidazole propionate, indole-3-carboxaldehyde, indolin-2-one, N-Acetyl-L-aspartic acid, Phosphoric acid, Phthalic acid, Pimilprost, trimethadione, or Vernolate, wherein the Janthinobacterium lividum is present in a composition in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.

[008] Disclosed herein are synthetic compositions comprising the probiotic human-derived Janthinobacterium lividum, metabolites from the probiotic human-derived Janthinobacterium lividum, cell lysate of the probiotic human-derived Janthinobacterium lividum, and/or postbiotics from human-derived Janthinobacterium lividum formulated for topical application. These synthetic compositions can be formulated for application to the subject

(*e.g.* skin, mucosa, hair, nails) or to objects that come in contact with the subject (*e.g.* cloth, floors, etc.). In some examples these synthetic compositions are cosmetic compositions.

[008a] In one aspect, the present disclosure refers to a cosmetic formulation comprising the composition disclosed herein, further comprising a sunscreen, moisturizer, anti-aging, probiotic, or health promoting composition.

[009] In some examples the compositions of this disclosure further comprise a prebiotic. In preferred examples, the prebiotic, is selected from one or more of an amino acid, biotin, glycerol, fructooligosaccharide, galactooligosaccharides, inulin, lactulose, mannan oligosaccharide, oligofructose-enriched inulin, oligofructose, oligodextrose, tagatose, trans-galactooligosaccharide, and xylooligosaccharide. In some examples, the pharmaceutical composition further comprises an isolated non-pathogenic additional microbe. In preferred examples, the additional isolated microbe is selected from a Lactobacillus species, a Lactococcus species, a benign fungal species typically found on human skin, or a Propionibacterium species. In some examples, the composition is formulated for administration with additional antifungal or antibacterial compounds. In some examples, the pharmaceutical composition is formulated for topical administration to the skin or mucosa. In some examples, the compositions are part of a delivery device for mucosa cavities.

[0010] In some examples the human-derived Janthinobacterium lividum nucleic acid sequence is identified by SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7. In some examples the human-derived Janthinobacterium lividum comprises a nucleic acid sequence at least 90% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7; or at least 93% identical to, or at least 95%, or at least 97%, or at least 98%, or at least 99%, or 100% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7 at the 16s rRNA gene sequence. In some examples the human-derived Janthinobacterium lividum comprises a nucleic acid sequence at least 90% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID No: 7, at least 92% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7; or at least 93% identical, or at least 95%, or at least 97%, or at least 98%, or at least 99%, or 100% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7. In some examples SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7 is at least 90% identical to the human-derived Janthinobacterium lividum nucleic acid sequence at the 16s rRNA gene sequence; is at least 90% identical; or at least 93% identical, or at least 95%, or at least 97%, or at least 98%, or at least 99%, or 100% identical to human-derived Janthinobacterium lividum nucleic acid sequence at the 16s rRNA gene sequence.

[0010a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising Janthinobacterium lividum, wherein the Janthinobacterium lividum comprises a nucleic acid sequence at least 98% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7 at the 16s rRNA gene sequence in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.

[0010b] In one aspect, the present disclosure refers to the use of a pharmaceutical composition that comprises a bacterium of the genus *Janthinobacterium,* wherein the bacterium comprises a nucleic acid sequence at least 95%, 98%, or 99% identical to the 16s rRNA gene sequence of SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7, or a metabolite of probiotic Janthinobacterium bacteria, postbiotic of probiotic Janthinobacterium bacteria, and/or cell lysate of probiotic Janthinobacterium bacteria, in the manufacture of a medicament for treating a skin condition in a subject in need thereof, wherein the medicament is for administration topically.

[0011] In some examples, the pharmaceutical composition is used to treat a yeast pathogenic microorganism, such as Candida albicans, C. glabrata, C. parapsilosis, C. tropicalis, C. krusei or C. kefyr. In some examples, the pharmaceutical composition is

used to treat a fungal pathogenic microorganism, such as a Trichophyton or a Malassezia species. In some examples the pharmaceutical composition is used to treat a fungal pathogenic microorganism such as T. rubrum, T. verrucosum, T. tonsurans, T. terrestre, T. interdigitale. In some examples, the pharmaceutical composition is used to treat a bacterium pathogenic microorganism, such as Staphylococcus, Pseudomonas, Enterococcus and *S.* aureus. In some examples, the pharmaceutical composition is used to treat a virus pathogenic microorganism, such as poliovirus, herpes simplex virus, hepatitis A virus, rotavirus, adenovirus, SARS-CoV-2 and influenza type A virus. In some examples, the pharmaceutical composition is used to treat the pathogenic microorganism selected from the group consisting of Gardnerella vaginalis, Candida albicans, Atopobium vaginae, Staphylococcus aureus, Escherichia coli, Pseudomonas, and Salmonella.

[0012] In some examples, the metabolite of human-derived Janthinobacterium lividum is soluble in the formulation for topical administration. In some examples, the pharmaceutical composition comprises a metabolite selected from violacein, indole-3-carboxaldehyde, prodigiosin, salicylate, 2,4-diamabutyrate and one or more lantibiotics. In some examples, the human-derived Janthinobacterium lividum produces an antimicrobial metabolite, selected from violacein, indole-3-carboxaldehyde, prodigiosin, salicylate, 2,4-diamabutyrate and one or more lantibiotics, at a level higher than an other non-human Janthinobacterium lividum reference strain.

[0013] In some examples, the pharmaceutical composition comprising the human-derived Janthinobacterium lividum is anhydrous, frozen at –20 °C, or frozen at –80 °C, before reconstitution with a separately-stored sterile liquid. In some examples, the liquid for reconstitution is selected from eye lubricant, glycerol, sucrose, mannitol, 2-Hydroxyethylstarch (HES), Noveon AA-1 polycarbophil, Methocel F4M (HPMC), carboxymethyl cellulose, and/or including λ-Carrageenan.

[0014] In some examples, the human-derived Janthinobacterium lividum compositions described herein are used in a method to inhibit, treat or prevent a pathogenic microorganism, method comprising administering an effective amount of a human-derived Janthinobacterium lividum, metabolite and/or cell lysate of human-derived Janthinobacterium lividum to a subject in need thereof, wherein human-derived Janthinobacterium lividum, metabolite and/or cell lysate of human-derived Janthinobacterium lividum is present in an amount effective for inhibiting, treating or preventing at least one pathogenic microorganism. In some examples, the human-derived Janthinobacterium lividum is applied in conjunction with

an additional antifungal or antibacterial agent. In some examples the compositions have an additional probiotic or non-pathogenic microorganism.

[0015] In some examples, the pharmaceutical, synthetic, cosmetic and probiotic compositions of this disclosure contain at least 10, 10^2, 10^3, 10^4, 10^5, 10^{10}, 10^{20} colonizing forming units (CFUs) per a milliliter or milligram of human-derived Janthinobacterium lividum .

[0016] Disclosed herein are methods of manufacturing a pharmaceutical composition comprising an effective amount of probiotic human-derived Janthinobacterium lividum, an optional metabolite, cell lysate, and/or prebiotic, and a pharmaceutically acceptable excipient, the method comprising preserving a human-derived Janthinobacterium lividum by spray drying or lyophilization in the presence of a drug substance formulation containing an excipient which enhances preservation and packaging the preserved human-derived Janthinobacterium lividum for reconstitution with a second excipient formulation to generate the formulation immediately prior to administration. In some examples, the excipient is chosen from the group consisting of amino acid, complex carbohydrate, simple carbohydrate, DMSO, mannitol, natural tears, eye lubricant, trehalose, and glycerol.

[0017] Described herein is a kit comprising at least one vial of stabilized human-derived Janthinobacterium lividum and at least one optional vial of liquid for reconstitution of stabilized human-derived Janthinobacterium lividum , instructions for mixing and application, and optionally one or more implements of mixing and application. In some examples, implements of mixing and application are included and comprise one or more elements selected from a syringe, an empty sterile container, and an atomizer or mister. In some examples, the kit contains multiple vials of stabilized human-derived Janthinobacterium lividum and at least one vial of liquid for reconstitution of stabilized human-derived Janthinobacterium lividum , for multiple applications to one or more subjects in need thereof. In some examples, the kit is prepared for application by a medical professional. In some examples, the kit is prepared for application by a patient.

5. BRIEF DESCRIPTION OF FIGURES

[0018] **Figure 1** shows representative examples of Janthinobacterium lividum isolated from a human heel, a human forehead, and a radish, all grown on petri dishes.

[0019] **Figure 2** shows Janthinobacterium lividum prevalence and abundance on healthy skins, estimated using next-generation sequencing reads as part of the 16s rRNA gene.

What is claimed is:

1. A composition comprising human-derived *Janthinobacterium lividum,* formulated for topical application to a human subject.

2. The composition of claim 1, formulated for topical application to prevent, treat, or reduce a symptom of a disease of a mammalian subject arising from an infection with a pathogenic microorganism, and optionally further comprising an additional isolated microbe, and/or an anti-fungal.

3. A cosmetic formulation comprising the composition of claim 1, further comprising a sunscreen, moisturizer, anti-aging, probiotic, or health promoting composition.

4. The composition of claim 1, wherein the *Janthinobacterium lividum* comprises a nucleic acid sequence at least 95% or 99% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7.

5. The composition of claim 1, wherein the disease, disorder, or condition is: a. associated with a dermatophyte, and selected from tinea barbae, tinea capitis, tinea corporis, tinea curis, tinea pedis, or onychomycosis; or b. associated with gram positive bacteria or *Staphylococcus*, and selected from atopic dermatitis, impetigo, skin infections and soft tissue infections.

6. The composition of claim 1, further comprising a postbiotic or a prebiotic selected from one or more of an amino acid, biotin, glycerol, a polysaccharide, an oligosaccharide, fructooligosaccharide, galactooligosaccharide, inulin, lactulose, mannan oligosaccharide, oligofructose-enriched inulin, oligofructose, oligodextrose, tagatose, trans-galactooligosaccharide, and xylooligosaccharide.

7. A pharmaceutical formulation comprising the composition of claim 1 in an amount effective to treat, inhibit, reduce a symptom of, or prevent a skin disease, disorder, or condition in a human subject, wherein the pharmaceutical composition is to be administered in an amount effective to inhibit the growth of a topical pathogenic microorganism present on or in a tissue of the human subject.

8. The pharmaceutical formulation of claim 7, wherein the topical pathogenic microorganism is a Dermatophyte selected from Trichophyton mentagrophytes and Trichophyton rubrum, or a bacterium comprising Staphylococcus aureus.

9. The composition of claim 1, wherein the formulation of *Janthinobacterium lividum* is a dehydrated formulation, and wherein the *Janthinobacterium lividum* are at least 20% viable upon rehydration, or are at least 30 % viable at room temperature for at least thirty days.

10. The composition of claim 1, wherein the composition comprises a dried formulation of human-derived *Janthinobacterium lividum,* formulated for topical administration to a human or non-human subject as a cream, gel, foam, ointment, powder or lotion.

11. The composition of claim 1, formulated for topical administration to human skin or human mucosa as a liquid, tincture, spray, mister, or inhaler.

12. A pharmaceutical composition comprising *Janthinobacterium lividum*, wherein the *Janthinobacterium lividum* comprises a nucleic acid sequence at least 98% identical to SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7 at the 16s rRNA gene sequence in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.

13. A pharmaceutical composition comprising an excipient suitable for formulation with at least one human-derived *Janthinobacterium lividum* in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.

14. Use of a human-derived *Janthinobacterium lividum* in the manufacture of a medicament for inhibiting or preventing growth of a pathogenic microorganism in a human subject in need thereof.

15. Use of a pharmaceutical composition that comprises a bacterium of the genus *Janthinobacterium,* wherein the bacterium comprises a nucleic acid sequence at least 95%, 98%, or 99% identical to the 16s rRNA gene sequence of SEQ ID NO: 5, SEQ

ID NO: 6, or SEQ ID NO: 7, or a metabolite of probiotic Janthinobacterium bacteria, postbiotic of probiotic Janthinobacterium bacteria, and/or cell lysate of probiotic Janthinobacterium bacteria, in the manufacture of a medicament for treating a skin condition in a subject in need thereof, wherein the medicament is for administration topically.

16. An isolated human-derived *Janthinobacterium lividum* that over-produces 2-(alpha-D-mannosyl)-D-glyceric acid, 2-ketogluconate, 2-O-ethyl ascorbic acid, anthramycin, Aprobarbital, bendiocarb, Bis(2-ethylhexyl) phthalate, cis-5- Tetradecenoylcarnitine, Dibutyl phthalate, imidazole propionate, indole-3-carboxaldehyde, indolin-2-one, N-Acetyl-L-aspartic acid, Phosphoric acid, Phthalic acid, Pimilprost, trimethadione, or Vernolate, wherein the *Janthinobacterium lividum* is present in a composition in an amount effective to treat, inhibit or prevent a disease, disorder, or condition associated with a pathogenic microorganism.