



(51) International Patent Classification:

A61K 39/02 (2006.01) A61K 35/74 (2015.01)

(21) International Application Number:

PCT/US2018/056546

(22) International Filing Date:

18 October 2018 (18.10.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

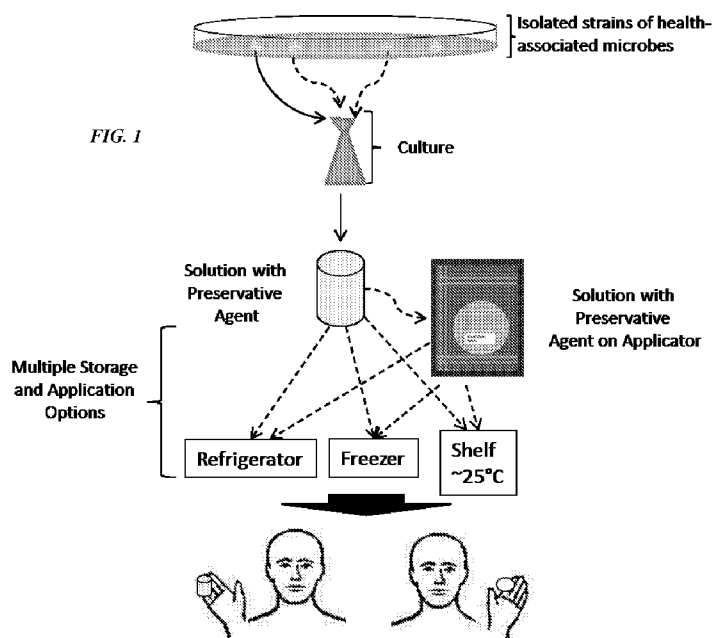
62/575,316	20 October 2017 (20.10.2017)	US
62/678,170	30 May 2018 (30.05.2018)	US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,

(54) Title: FORMULATIONS FOR TREATMENT OF SKIN CONDITIONS



(57) Abstract: Described herein are pharmaceutical composition comprising: a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and a biological stabilizer. At least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome comprising at least four different spacer sequences. Also described herein are methods of making and using such pharmaceutical compositions.



UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

- *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*
- *with sequence listing part of description (Rule 5.2(a))*

FORMULATIONS FOR TREATMENT OF SKIN CONDITIONS

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/575,316, filed October 20, 2017, and U.S. Provisional Application No. 62/678,170 filed May 30, 2018, each of which is incorporated herein by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been filed electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on October 12, 2018, is named 48236-708_601_SL.txt and is 2,301,395 bytes in size.

BACKGROUND OF THE INVENTION

[0003] The community of microorganisms living on and/or within an individual is the microbiome. The microbiome consists of many different bacterial species some of which are beneficial, neutral or deleterious to human health. Alterations in the microbiome have been connected to many disease states such as inflammatory diseases, metabolic disease, developmental diseases, psychological diseases and cancer. Determining the composition of the microbiome, and altering the microbiome from a pathological to healthy state holds great therapeutic promise for many different diseases.

SUMMARY OF THE INVENTION

[0004] Disclosed herein, in some aspects, are pharmaceutical compositions comprising: a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and a biological stabilizer, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences. In some instances, at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively. Further disclosed herein,

in some aspects, are pharmaceutical compositions comprising: a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and a biological stabilizer, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively. In some instances, at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe is selected or engineered to have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences. In some instances, the virulence gene encodes a CAMP factor. In some instances, the virulence gene encodes a CAMP2 protein. In some instances, the virulence gene encodes a hemolysin or cytotoxin. In some instances, the virulence gene is *tly*. In some instances, the virulence gene encodes a triglycerol lipase or precursor thereof. In some instances, the virulence gene is *gehA*. In some instances, the virulence gene encodes an iron acquisition protein. In some instances, the virulence gene is *htaA*. In some instances, the virulence gene encodes a heat shock protein. In some instances, the virulence gene is *hsp20*. In some instances, the virulence gene encodes an iron uptake protein. In some instances, the virulence gene comprises a *methyl transferase domain*, a *fepB* region, a *fecCD* region, a *fepC* region. In some instances, the virulence gene encodes a protein supporting host invasiveness by the first health-associated *Propionibacterium* microbe. In some instances, the virulence gene is *pap60* or *pAmce*. In some instances, the biological stabilizer comprises a cryopreservative. In some instances, the cryopreservative comprises glycerol. In some instances, the pharmaceutical composition comprises at least one of glycerol, polyethylene glycol and polypropylene glycol. In some instances, the biological stabilizer suppresses secreted lipase activity and increases propionic acid production. In some instances, the biological stabilizer increases secreted propionic acid production. In some instances, the biological stabilizer is a humectant. In some instances, the biological stabilizer is a humectant comprising glycerol. In some instances, the biological stabilizer increases propionic acid production and suppresses lipase activity. In some instances, the biological stabilizer increases propionic acid production and suppresses lipase activity and is a humectant. In some instances, the biological stabilizer increases propionic acid production and suppresses lipase activity and is a humectant. In some instances, the pharmaceutical composition comprises the pharmaceutical composition is

about 5% to about 55% glycerol by volume. In some instances, the pharmaceutical composition comprises the pharmaceutical composition is about 15% to about 40% glycerol by volume. In some instances, the pharmaceutical composition comprises the pharmaceutical composition is about 25% glycerol by volume. In some instances, the pharmaceutical composition is provided on a cotton pad, a fabric, a paper, or a combination thereof. In some instances, the pharmaceutical composition is provided on a cotton pad. In some instances, the pharmaceutical composition is vacuum sealed. In some instances, the pharmaceutical composition comprises phosphate buffered saline. In some instances, the pharmaceutical composition does not comprise a bacteria growth medium. In some instances, the first therapeutically effective amount is less than an amount that would be effective if used to treat without the second health-associated microbe. In some instances, the second therapeutically effective amount is less than an amount that would be effective if used to treat without the first health-associated microbe. In some instances, the first health-associated microbe and the second health-associated microbe have synergistic activity as a therapy for a skin disorder. In some instances, the pharmaceutical composition is lyophilized. In some instances, the pharmaceutical composition or a component thereof is freeze-dried or spray-dried. In some instances, the biological stabilizer is an oil. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type I or type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type IB. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type IB and the second health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type II and the second health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a Christie-Atkins-Much-Petersen (CAMP) gene, and wherein the mutation reduces activity of a hemolysin. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a CAMP gene that results in reduced expression of an exotoxin, reduced production of an exotoxin, reduced activity of an exotoxin, or reduced secretion of an exotoxin. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a CAMP gene that results in disruption of a STOP codon. In some instances, the CAMP gene is a CAMP2 gene. In some instances, at least the first health-associated *Propionibacterium* microbe is engineered or selected to have reduced expression of a virulence gene relative to a wildtype version of the

Propionibacterium microbe. In some instances, at least the first health-associated *Propionibacterium* microbe is engineered or selected to have reduced activity of a virulence gene encoding protein relative to a wildtype version of the *Propionibacterium* microbe. In some instances, at least the first health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex. In some instances, the first health-associated *Propionibacterium* microbe or the second health-associated *Propionibacterium* microbe comprises at least one of an HP3A11 strain, an HP4G1 strain, or an HP5G4 strain. In some instances, at least the first health-associated *Propionibacterium* microbe comprises an HP4G1 strain or an HP5G4 strain. In some instances, the first health-associated *Propionibacterium* microbe comprises an HP4G1 strain and the second health-associated *Propionibacterium* microbe comprises an HP5G4 strain. In some instances, the first health-associated microbe produces less than about one micromolar porphyrin. In some instances, the second health-associated microbe produces less than about one micromolar porphyrin. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about one micromolar porphyrin. In some instances, at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe each comprise a *Propionibacterium acnes* of a ribotype RT1. In some instances, at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT2. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe each comprise a *Propionibacterium acnes* of ribotype RT2. In some instances, at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding an ATP binding cassette transporter. In some instances, at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a deoxyribose operon repressor. In some instances, at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a type II lipase. In some instances, at least the first health-associated *Propionibacterium* microbe comprises less than about 10% pIMPLE plasmid. In some instances, at least the first health-associated *Propionibacterium* microbe comprises less than about 1% pIMPLE plasmid. In some instances, at least the first health-associated *Propionibacterium* microbe has no pIMPLE plasmid. In some instances, at least the first health-associated *Propionibacterium* microbe

lacks a gene encoding a DNA binding response regulator. In some instances, at least the first health-associated *Propionibacterium* microbe lacks a gene encoding a phosphoglycerate kinase. In some instances, the first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; and the biological stabilizer, wherein the first health-associated *Propionibacterium* microbe has a CRISPR locus in its genome, and wherein the CRISPR locus comprises at least four different spacer sequences. In some instances, the first health-associated *Propionibacterium* microbe has reduced activity of the virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe. In some instances, the pharmaceutical composition comprises the first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; and the biological stabilizer, wherein the first health-associated *Propionibacterium* microbe has reduced activity of the virulence gene encoding protein relative to a wildtype version of the first health-associated *Propionibacterium* microbe. In some instances, the first health-associated *Propionibacterium* microbe is selected or engineered to have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.

[0005] In some aspects, the instant disclosure provides methods of treating a skin disorder or condition, the methods comprising applying a therapeutically effective amount of a pharmaceutical composition disclosed herein to at least a region of skin on a subject in need thereof. In some instances, the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof. In some instances, applying is topical. In some instances, methods comprise applying the therapeutically effective amount of a pharmaceutical composition with a cotton pad. In some instances, methods comprise rubbing the cotton pad on the region of skin. In some instances, applying results in engraftment of at least one of the health-associated microbes of the pharmaceutical composition to the region of skin. In some instances, the at least one of the health-associated microbes remains present on the region of skin after at least one wash. In some instances, the wash comprises applying soap and water to the region of skin. In some instances, the wash comprises applying an antibacterial agent. In some instances, the antibacterial agent is benzoyl peroxide. In some instances, methods comprise applying the pharmaceutical composition at least once daily. In some instances, methods comprise applying the pharmaceutical composition at least once weekly. In some instances, methods comprise applying the pharmaceutical composition over a duration of at least one month. In some

instances, the region of skin is located on at least one of the subject's face, neck, chest, back, and shoulder.

[0006] Further disclosed herein, in some aspects, are methods of producing a desired preparation of a *Propionibacterium* bacteria, said method comprising: adding at least one health-associated *Propionibacterium* microbe to a preservative agent to produce a *Propionibacterium* preparation, and storing the *Propionibacterium* preparation at a temperature of about 4 ° C or less, wherein the at least one health-associated *Propionibacterium* microbe has a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.

[0007] Also disclosed herein, in some aspects, are methods of producing a desired preparation of a *Propionibacterium* bacteria, said method comprising: adding at least one health-associated *Propionibacterium* microbe to a preservative agent to produce a *Propionibacterium* preparation, and storing the *Propionibacterium* preparation at a temperature of about 4 ° C or less, wherein the at least one health-associated *Propionibacterium* microbe has reduced activity of a virulence gene encoding protein relative to a wildtype version of the at least one health-associated *Propionibacterium* microbe. In some instances, the at least one health-associated *Propionibacterium* microbe has a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences. In some instances, the at least one health-associated *Propionibacterium* microbe has reduced activity of a virulence gene encoding protein relative to a wildtype version of the at least one health-associated *Propionibacterium* microbe. In some instances, the preservative agent comprises glycerol. In some instances, the preservative agent comprises polyethylene glycol. In some instances, the preservative agent comprises glycerol and polyethylene glycol. In some instances, the portion of the preservative agent that is glycerol is less than 50%. In some instances, the portion of the preservative agent that is glycerol is less than 25%. In some instances, the pharmaceutical composition is stored at about -15 °C to about -25 °C. In some instances, more than about 10% of the *P. acnes* bacteria are viable when the pharmaceutical composition is brought to ambient temperature. In some instances, at least about 30% of the *P. acnes* bacteria are viable when the *Propionibacterium* bacteria in the glycerol solution are brought to ambient temperature. In some instances, the *Propionibacterium* preparation is brought to ambient temperature after about 90 days of storing. In some instances, more than about 10% of the sample is viable at least up to about 90 days of storing. In some instances, more than about 30% of the sample is viable at least up to about 90 days of storing. In some instances, more than 50% of the sample is viable when brought to ambient temperature after

about 20 days of storing. In some instances, the ambient temperature is between about 20 ° C and about 30 ° C. In some instances, the temperature is between about 4 ° C and about -80 ° C. In some instances, the temperature is between about 4 ° C and about -20 ° C. In some instances, the temperature is about 4 ° C. In some instances, the temperature is about -20 ° C. In some instances, methods comprise vacuum sealing the preparation of *Propionibacterium* bacteria. In some instances, methods comprise packaging the preparation of *Propionibacterium* bacteria for a single use. In some instances, methods comprise applying the preparation of *Propionibacterium* bacteria to an applicator. In some instances, the applicator is a cotton pad. In some instances, the *Propionibacterium acnes* microbe is a strain selected from HP3A11, HP4G1, and HP5G1. In some instances, methods comprise adding at least one additional health-associated microbe to the preservative agent. In some instances, methods comprise packaging the preparation of the *Propionibacterium* bacteria in plastic packaging. In some instances, methods comprise vacuum sealing the preparation of the *Propionibacterium* bacteria in plastic packaging. In some instances, methods comprise flash freezing the preparation of a *Propionibacterium* bacteria.

[0008] In some aspects, disclosed herein are pharmaceutical compositions that comprise: a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe, wherein the first health-associated *Propionibacterium* microbe produces less than about one micromolar porphyrin; a second therapeutically effective amount of a second health-associated microbe; and a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the second health-associated microbe comprises a strain of *Propionibacterium*. In some embodiments, the second health-associated microbe produces less than about one micromolar porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about one micromolar porphyrin. In some embodiments, at least one of the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe produce less than about 200 nM porphyrin. In some embodiments, at least one of the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe produce less than about 100 nM porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 100 nM porphyrin. In some embodiments, at least one of the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe produce less than about one micromolar porphyrin *in situ*. In some embodiments, at least one

of the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe produce less than about one micromolar porphyrin *in vitro*. In some embodiments, at least the first health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*, *Propionibacterium granulosum*, *Propionibacterium avidum*, or *Propionibacterium acnes* subsp. *defendens*. In some embodiments, at least the first health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*. In some embodiments, at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1 or RT2. In some embodiments, at least the first health-associated *Propionibacterium* microbe: (a) comprises at least one gene encoding an ATP binding cassette transporter; (b) comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; or (c) lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase.

[0009] In some aspects, disclosed herein are pharmaceutical compositions that comprise: (a) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe is characterized by at least one of the following: comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; comprises at least one gene encoding an ATP binding cassette transporter; or lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase, and (b) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise a *deoxyribose operon repressor* and a type II lipase. In some embodiments, a Cas5 protein is absent from the health-associated *Propionibacterium acnes* microbe. In some embodiments, the health-associated *Propionibacterium acnes* microbe expresses an ATP binding cassette transporter. In some embodiments, the health-associated *Propionibacterium acnes* microbe does not express a DNA binding response regulator or a phosphoglycerate kinase. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an RT1 or RT2 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe does not comprise an RT6 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a mixture of two or more different ribotypes of *Propionibacterium acnes*. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an HP3A11 strain, an HP3B4 strain, an HP4G1 strain, or an HP5G4 strain. In some embodiments, the pharmaceutical composition comprises

an additional strain of bacteria, wherein the additional strain comprises *Propionibacterium avidum* or *Propionibacterium granulosum*. In some embodiments, the additional strain comprises *Propionibacterium acnes* subsp. *defendens*.

[0010] In some aspects, disclosed herein are methods of treating a skin disorder or condition comprising applying a therapeutically effective amount of a pharmaceutical composition comprising: (a) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe is characterized by at least one of the following: comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; comprises at least one gene encoding an ATP binding cassette transporter; or lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase, and (b) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof. In some embodiments, the health-associated *Propionibacterium acnes* microbe has been engineered or selected to at least one gene encoding the deoxyribose operon repressor and the type II lipase. In some embodiments, a Cas5 protein is absent from the health-associated *Propionibacterium acnes* microbe. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an RT1 or RT2 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe does not comprise an RT6 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a mixture of two or more different ribotypes. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an HP3A11 strain, an HP3B4 strain, an HP4G1 strain, or an HP5G4 strain. In some embodiments, the pharmaceutical composition comprises an additional strain of bacteria, wherein the additional strain comprises *Propionibacterium avidum* or *Propionibacterium granulosum*. In some embodiments, the additional strain comprises *Propionibacterium acnes* subsp. *defendens*.

[0011] In some aspects, disclosed herein are pharmaceutical compositions that comprise: (a) a first therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the first health-associated *Propionibacterium acnes* microbe is characterized by at least one of the following: comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; comprises at least one gene encoding an ATP binding cassette transporter; or lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase;

(b) a second therapeutically effective amount of a second health-associated microbe, wherein the second health-associated microbe has been engineered or selected to comprise at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; and (c) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the second health-associated microbe is a strain of bacteria comprising *P. acnes*, *P. granulosum*, or *P. avidum*. In some embodiments, the second health-associated microbe is a strain of bacteria comprising *Propionibacterium acnes* subsp. *defendens*.

[0012] In some aspects, disclosed herein are pharmaceutical compositions that comprise: (a) a pharmaceutically acceptable excipient or biological stabilizer; and (b) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe does not express a DNA binding response regulator, a phosphoglycerate kinase, or a combination thereof. In some aspects, disclosed herein are pharmaceutical compositions that comprise: (a) a pharmaceutically acceptable excipient or biological stabilizer; and (b) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe expresses an ATP-binding cassette transporter. In some aspects, disclosed herein are pharmaceutical compositions that comprise: (a) a pharmaceutically acceptable excipient or biological stabilizer; and (b) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe: does not express a DNA binding response regulator, a phosphoglycerate kinase, or a combination thereof; and expresses an ATP-binding cassette transporter. In some embodiments, the DNA binding response regulator is encoded by a sequence of SEQ ID NO: 7. In some embodiments, the DNA binding response regulator is encoded by a sequence that is at least 50% homologous to a sequence of SEQ ID NO: 7. In some embodiments, the phosphoglycerate kinase is encoded by a sequence of SEQ ID NO: 9. In some embodiments, the phosphoglycerate kinase is encoded by a sequence that is at least 50% homologous to a sequence of SEQ ID NO: 9. In some embodiments, the ATP-binding cassette transporter is encoded by a sequence of SEQ ID NO: 6. In some embodiments, the ATP-binding cassette transporter is encoded by a sequence that is at least 50% homologous to a sequence of SEQ ID NO: 6. In some embodiments, the pharmaceutical composition comprises at least two strains of bacteria. In some embodiments, the pharmaceutical composition comprises a strain of *Propionibacterium acnes* having a ribotype of RT1, RT2 or RT3. In some embodiments, the pharmaceutical composition

comprises a strain of *Propionibacterium acnes* having a ribotype of RT1 or RT2. In some embodiments, the pharmaceutical composition does not comprise a strain of *Propionibacterium acnes* having a ribotype of RT4 or RT5 ribotype. In some embodiments, the pharmaceutical composition does not comprise a strain of *Propionibacterium acnes* having a ribotype of RT6 ribotype. In some embodiments, the pharmaceutical composition is formulated for topical administration. In some embodiments, the pharmaceutical composition is in the form of a gel, ointment, lotion, emulsion, paste, cream, foam, mousse, liquid, spray, suspension, dispersion and aerosol. In some embodiments, the pharmaceutical composition comprises a liposome or nanoparticle. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a *deoxyribose operon repressor* and a type II lipase. In some embodiments, a Cas5 protein is absent from the health-associated *Propionibacterium acnes* microbe. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 1% pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 0.3 % pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a mixture of two or more different ribotypes of *Propionibacterium acnes*. In some embodiments, the pharmaceutically acceptable excipient or biological stabilizer increases the viability of the health-associated *Propionibacterium acnes* microbe at a temperature from about -10° C to about 30° C. In some embodiments, the pharmaceutical composition comprises an additional strain of bacteria. In some embodiments, the pharmaceutical composition comprises an additional strain of bacteria, wherein the additional strain comprises *Propionibacterium avidum* and *Propionibacterium granulosum*. In some embodiments, the additional strain comprises *Propionibacterium acnes* subsp. *defendens*. In some embodiments, the health-associated *Propionibacterium acnes* microbe is selected, transformed or engineered to: (a) comprise at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; (b) comprise at least one gene encoding an ATP binding cassette transporter; or (c) lack at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase.

[0013] In some aspects, methods of treating a skin disorder or condition are provided comprising applying a therapeutically effective amount of a pharmaceutical composition disclosed herein. In some embodiments, the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof.

[0014] In some aspects, disclosed herein are pharmaceutical compositions comprising: (a)

a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; and (b) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise a *deoxyribose operon repressor* and a type II lipase. In some embodiments, a Cas 5 protein is absent from the health-associated *Propionibacterium acnes* microbe. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an RT1 or RT2 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe does not comprise an RT6 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 1% pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 0.3 % pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a mixture of two or more different ribotypes of *Propionibacterium acnes*. In some embodiments, the pharmaceutically acceptable excipient or biological stabilizer increases the viability of the health-associated *Propionibacterium acnes* microbe at a temperature from about -10° C to about 30° C. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises an HP3A11 strain, an HP3B4 strain, an HP4G1, or an HP5G4 strain. In some embodiments, the pharmaceutical composition comprises an additional strain of bacteria, wherein the additional strain comprises *Propionibacterium avidum* or *Propionibacterium granulosum*. In some embodiments, the additional strain comprises *Propionibacterium acnes* subsp. *defendens*. In some embodiments, the health-associated *Propionibacterium acnes* microbe expresses an ATP binding cassette transporter. In some embodiments, the health-associated *Propionibacterium acnes* microbe does not express a DNA binding response regulator or a phosphoglycerate kinase.

[0015] In some aspects, disclosed herein are methods of treating a skin disorder or condition comprising applying a therapeutically effective amount of a pharmaceutical composition comprising: (a) a therapeutically effective amount of a health-associated *Propionibacterium acnes* microbe, wherein the health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; and (b) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the skin disorder or condition comprises acne, eczema, seborrheic dermatitis,

psoriasis, or rosacea. In some embodiments, the health-associated *Propionibacterium acnes* microbe has been engineered or selected to at least one gene encoding the deoxyribose operon repressor and the type II lipase. In some embodiments, the Cas5 protein is absent from the health-associated *Propionibacterium acnes* microbe. In some embodiments, the pharmaceutical composition comprises a health-associated *Propionibacterium acnes* microbe having an RT1 or RT2 ribotype. In some embodiments, the pharmaceutical composition comprises a health-associated *Propionibacterium acnes* microbe having an RT3 ribotype. In some embodiments, the pharmaceutical composition does not comprise a health-associated *Propionibacterium acnes* microbe having an RT4 or RT5 ribotype. In some embodiments, the pharmaceutical composition does not comprise a health-associated *Propionibacterium acnes* microbe having an RT6 ribotype. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 1% pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises less than about 0.3% pIMPLE plasmid. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises a mixture of two or more different ribotypes. In some embodiments, the pharmaceutically acceptable excipient or biological stabilizer increases the viability of the health-associated *Propionibacterium acnes* microbe at a temperature from about -10° C to about 30° C. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises at least one of an HP3A11 strain, an HP3B4 strain, or HP4G1 strain, or an HP5G4 strain. In some embodiments, the pharmaceutical composition comprises an additional strain of bacteria, wherein the additional strain comprises *Propionibacterium avidum* or *Propionibacterium granulosum*. In some embodiments, the additional strain comprises *Propionibacterium acnes* subsp. *defendens*.

[0016] In some aspects, disclosed herein are pharmaceutical compositions comprising: (a) a first therapeutically effective amount of a first health-associated *Propionibacterium acnes* microbe, wherein the first health-associated *Propionibacterium acnes* microbe has been engineered or selected to at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; (b) a second therapeutically effective amount of a second health-associated *Propionibacterium acnes* microbe, wherein the second health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; and (c) a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments, the first or the second health-associated *Propionibacterium acnes* microbe has been engineered

or selected to comprise: (i) at least one gene encoding the deoxyribose operon repressor and the type II lipase, (ii) at least one gene encoding the deoxyribose operon repressor and less than about 10% pIMPLE plasmid, or (iii) at least one gene encoding the type II lipase and less than about 10% pIMPLE plasmid. In some embodiments, the first and the second health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise: (i) at least one gene encoding the deoxyribose operon repressor and the type II lipase, (ii) at least one gene encoding the deoxyribose operon repressor and less than about 10% pIMPLE plasmid, or (iii) at least one gene encoding the type II lipase and less than about 10% pIMPLE plasmid. In some embodiments, the first or the second health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise at least one gene encoding the deoxyribose operon repressor, the type II lipase, and less than about 10% pIMPLE plasmid. In some embodiments, the first and the second health-associated *Propionibacterium acnes* microbe has been engineered or selected to comprise at least one gene encoding the deoxyribose operon repressor, the type II lipase, and less than about 10% pIMPLE plasmid. In some embodiments, the first and the second health-associated *Propionibacterium acnes* microbes are different strains. In some embodiments, the pharmaceutical composition comprises a first or the second health-associated *Propionibacterium acnes* microbe having an RT1 or RT2 ribotype. In some embodiments, the pharmaceutical composition comprises a first or the second health-associated *Propionibacterium acnes* microbe having an RT3 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT1 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT2 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT1 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT1 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT2 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT2 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT1 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT3 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT2 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT3 ribotype. In some embodiments, the first health-associated *Propionibacterium acnes* microbe has an RT3 ribotype and the second health-associated *Propionibacterium acnes* microbe has an RT3 ribotype. In some embodiments, neither the first nor the second health-associated *Propionibacterium acnes*

microbe has an RT4 ribotype. In some embodiments, neither the first nor the second health-associated *Propionibacterium acnes* microbe has an RT5 ribotype. In some embodiments, neither the first nor the second health-associated *Propionibacterium acnes* microbe has an RT6 ribotype. In some embodiments, the pharmaceutically acceptable excipient or biological stabilizer increases the viability of the health-associated *Propionibacterium acnes* microbe at a temperature from about -10° C to about -30° C. In some embodiments, the health-associated *Propionibacterium acnes* microbe comprises at least one of an HP3A11 strain, an HP3B4 strain, or HP4G1 strain, or an HP5G4 strain. In some embodiments, the first or second health-associated *Propionibacterium acnes* microbe expresses an ATP binding cassette transporter. In some embodiments, the first or second health-associated *Propionibacterium acnes* microbe does not express a DNA binding response regulator or a phosphoglycerate kinase. In some aspects, the pharmaceutical compositions disclosed herein are for use in the treatment of a skin disorder or condition.

[0017] In some aspects, disclosed herein are methods of producing a desired preparation of a *Propionibacterium acnes* bacteria, said method comprising: (a) adding a sample of the *Propionibacterium acnes* bacteria to a glycerol solution to produce a *Propionibacterium acnes* glycerol formulation, and (b) storing the *Propionibacterium acnes* glycerol formulation at a temperature of about 4 ° C or less, wherein more than about 50% of the *P. acnes* bacteria is viable when the *Propionibacterium acnes* bacteria in the glycerol solution is brought to ambient temperature. In some embodiments, the glycerol solution is between about 25% and about 75% glycerol. In some embodiments, the glycerol solution is about 50% glycerol. In some embodiments, the temperature is between about 4 ° C and about -80 ° C. In some embodiments, the temperature is about -20 ° C. In some embodiments, at least about 70% to at least about 90% of the sample is viable after the *Propionibacterium acnes* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 90% of the sample is viable after the *Propionibacterium acnes* glycerol formulation is brought to ambient temperature. In some embodiments, the ambient temperature is between about 20 ° C and about 30 ° C. In some embodiments, the ambient temperature is about 25 ° C. In some embodiments, the *Propionibacterium acnes* glycerol formulation is brought to ambient temperature before about 90 days of initiating storing. In some embodiments, more than 50% of the sample is viable after about 20 days of storing. In some embodiments, more than about 50% of the sample is viable after about 90 days of storing. In some embodiments, more than about 50% of the sample is viable at least up to about 90 days of storing. In some embodiments, the *Propionibacterium acnes* bacteria comprise an HP3A11 strain, an HP3B4

strain, or HP4G1 strain, or an HP5G4 strain.

[0018] In some aspects, disclosed herein are methods of producing a desired preparation of a preserved *Propionibacterium acnes* sample, said method comprising: adding a sample of *Propionibacterium acnes* bacteria to a solution of glycerol in phosphate buffered saline solution (PBS). In some aspects, disclosed herein are methods of producing a desired preparation of a preserved *Propionibacterium acnes* sample, said method comprising: adding a sample of *Propionibacterium acnes* bacteria in PBS to a solution of glycerol. In some instances, the desired preparation of a preserved *Propionibacterium acnes* sample is between about 10% glycerol and about 50% glycerol. In some instances, the desired preparation of a preserved *Propionibacterium acnes* sample is between about 10% glycerol and about 40% glycerol. In some instances, the desired preparation of a preserved *Propionibacterium acnes* sample is 25% glycerol. In some instances, at least about 90% of said preserved *Propionibacterium acnes* sample is viable after sixty days of storage. In some instances, at least about 90% of said preserved *Propionibacterium acnes* sample is viable after ninety days of storage.

[0019] In some aspects, disclosed herein are methods of producing a desired preparation of a preserved *Propionibacterium acnes* sample, wherein at least about 90% of said preserved *Propionibacterium acnes* sample is viable after sixty days of storage, said method comprising: (a) adding a sample of *Propionibacterium acnes* bacteria to a solution of between about 25% and about 50% glycerol in phosphate buffered saline solution (PBS) to produce a *Propionibacterium acnes* glycerol formulation; and (b) cooling the *Propionibacterium acnes* glycerol formulation at a temperature from about -20 ° C to about 4° C, thereby forming said desired preparation wherein at least about 90% of said sample of *Propionibacterium acnes* bacteria is viable after sixty days of storage. In some aspects, disclosed herein are methods of producing a desired preparation of a preserved *Propionibacterium acnes* sample, wherein at least about 90% of said preserved *Propionibacterium acnes* sample is viable after ninety days of storage, said method comprising: adding a sample of *Propionibacterium acnes* bacteria to a solution of about 50% glycerol to produce a *Propionibacterium acnes* glycerol formulation; and freezing the *Propionibacterium acnes* glycerol formulation at -20 ° C, thereby forming said desired preparation wherein at least about 90% of said sample of *Propionibacterium acnes* bacteria is viable after a thawing of the *Propionibacterium acnes* glycerol formulation. In some embodiments, the methods comprise thawing the *Propionibacterium acnes* glycerol formulation at room temperature. In some embodiments, the solution is about 25-50% glycerol v/v in water. In some embodiments, the solution is about 25-50% glycerol v/v in a

buffered solution. In some embodiments, the buffered solution is a phosphate buffered saline. In some embodiments, the buffered solution is an acetate buffered solution. In some embodiments, the solution comprises potassium. In some embodiments, the solution comprises potassium at a concentration of about 150 mM to about 200 mM. In some embodiments, the solution comprises calcium. In some embodiments, the solution comprises calcium at a concentration of about 0.05 mM to about 0.1 mM. In some embodiments, the solution comprises a prebiotic stabilizing agent. In some embodiments, the prebiotic stabilizing agent is inulin. In some embodiments, the inulin is present in the solution at a concentration of about 0.05% v/v to about 0.2% v/v. In some embodiments, the solution comprises an anti-acne agent. In some embodiments, the anti-acne agent comprises a retinoid, a vitamin, an antioxidant, an oil, an alcohol, an extract, or an analog thereof. In some embodiments, the retinoid comprises tretinoin, tazarotene, adapalene, or retinol. In some embodiments, the vitamin or analog thereof comprises Vitamin D, Vitamin C, Vitamin E, or calcipotriene. In some embodiments, the antioxidant comprises Vitamin C or Vitamin E. In some embodiments, the alcohol comprises retinol or resveratrol. In some embodiments, the oil is tea tree oil. In some embodiments, the extract is a green tea extract. In some embodiments, the solution is incorporated in a biologic stability platform to eliminate cold chain storage (*e.g.*, uninterrupted cold storage). In some embodiments, the biologic storage platform comprises foam drying or foam formation of the solution or glycerol formulation solution. In some embodiments, the solution comprises at least one of a glyconanoparticle, a liposome, a nanoparticle, trehalose, sucrose, stachyose, hydroxyethyl starch, or a combination of glycine and mannitol. In some embodiments, the sample of *Propionibacterium acnes* bacteria comprises *Propionibacterium acnes* bacteria of ribotype RT1. In some embodiments, the sample of *Propionibacterium acnes* bacteria comprises *Propionibacterium acnes* bacteria of ribotype RT2. In some embodiments, the sample of *Propionibacterium acnes* bacteria comprises *Propionibacterium acnes* bacteria of ribotype RT1 and RT2. In some embodiments, the sample of *Propionibacterium acnes* bacteria comprises *Propionibacterium acnes* bacteria of ribotype RT3. In some embodiments, the *Propionibacterium acnes* bacteria is characterized by at least one of the following: comprises a deoR protein; comprises a type II lipase; comprises less than 10% pIMPLE plasmid; does not comprise a Cas5 protein; comprises an ATP binding cassette transporter protein; does not comprise a DNA binding response regulator; and does not comprise a phosphoglycerate kinase. In some embodiments, the sample of *Propionibacterium acnes* bacteria comprises *Propionibacterium acnes* an HP3A11 strain, an HP3B4 strain, or HP4G1 strain, or an HP5G4 strain.

[0020] In some aspects, disclosed herein are pharmaceutical compositions that comprise a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and at least one of a pharmaceutically acceptable excipient and a biological stabilizer. In some instances, the pharmaceutical compositions comprise the biological stabilizer. In some instances, the biological stabilizer comprises a cryopreservative. In some instances, the cryopreservative comprises glycerol. In some instances, the pharmaceutically acceptable excipient comprises at least one of glycerol, polyethylene glycol and polypropylene glycol. In some instances, the pharmaceutical composition is about 5% to about 55% glycerol by volume. In some instances, the pharmaceutical composition is about 15% to about 40% glycerol by volume. In some instances, the pharmaceutical composition is about 25% glycerol by volume. In some instances, the pharmaceutical composition is provided on a cotton pad, a fabric, a paper, or a combination thereof. In some instances, the pharmaceutical composition is provided on a cotton pad. In some instances, the pharmaceutical composition is vacuum sealed. In some instances, the pharmaceutical composition comprises phosphate buffered saline. In some instances, the pharmaceutical composition does not comprise a bacteria growth medium. In some instances, the first therapeutically effective amount is less than an amount that would be effective if used to treat without the second health-associated microbe. In some instances, the second therapeutically effective amount is less than an amount that would be effective if used to treat without the first health-associated microbe. In some instances, the first health-associated microbe and the second health-associated microbe have synergistic activity as a therapy for a skin disorder. In some instances, the pharmaceutical composition is lyophilized. In some instances, the pharmaceutical composition or a component thereof is freeze-dried or spray-dried. In some instances, the wherein the biological stabilizer is an oil. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type I or type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type IB. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type IB and the second health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, the first health-associated *Propionibacterium* microbe has a phylotype of type II and the second health-associated *Propionibacterium* microbe has a phylotype of type II. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a Christie-Atkins-

Much-Petersen (CAMP) gene, and wherein the mutation reduces activity of a hemolysin. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a CAMP gene that results in reduced expression of an exotoxin, reduced production of an exotoxin, reduced activity of an exotoxin, or reduced secretion of an exotoxin. In some instances, at least the first health-associated *Propionibacterium* microbe has a mutation in a CAMP gene that results in disruption of a STOP codon. In some instances, the CAMP gene is a CAMP2 gene. In some instances, at least the first health-associated *Propionibacterium* microbe is engineered or selected to have reduced expression of a virulence gene relative to a wildtype version of the *Propionibacterium* microbe. In some instances, at least the first health-associated *Propionibacterium* microbe is engineered or selected to have reduced activity of a virulence gene encoding protein relative to a wildtype version of the *Propionibacterium* microbe. In some instances, the virulence gene encodes a CAMP factor. In some instances, the virulence gene encodes a hemolysin or cytotoxin. In some instances, the virulence gene is *tly*. In some instances, the virulence gene encodes a triglycerol lipase or precursor thereof. In some instances, the virulence gene is *gehA*. In some instances, the virulence gene encodes an iron acquisition protein. In some instances, the virulence gene is *htaA*. In some instances, the virulence gene encodes a heat shock protein. In some instances, the virulence gene is *hsp20*. In some instances, the virulence gene encodes an iron uptake protein. In some instances, the virulence gene comprises a *methyl transferase domain*, a *fepB* region, a *fecCD* region, a *fepC* region. In some instances, the virulence gene encodes a protein supporting host invasiveness by the first health-associated *Propionibacterium* microbe. In some instances, the virulence gene is *pap60* or *pAmce*. In some instances, at least the first health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex. In some instances, the first health-associated *Propionibacterium* microbe or the second health-associated *Propionibacterium* microbe comprises at least one of an HP3A11 strain, an HP4G1 strain, or an HP5G4 strain. In some instances, at least the first health-associated *Propionibacterium* microbe comprises an HP4G1 strain or an HP5G4 strain. In some instances, the first health-associated *Propionibacterium* microbe comprises an HP4G1 strain and the second health-associated *Propionibacterium* microbe comprises an HP5G4 strain. In some instances, the first health-associated microbe produces less than about one micromolar porphyrin. In some instances, the second health-associated microbe produces less than about one micromolar porphyrin. In some instances, the first health-associated *Propionibacterium* microbe and the

second health-associated *Propionibacterium* microbe collectively produce less than about one micromolar porphyrin. In some instances, at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1 or RT2. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe each comprise a *Propionibacterium acnes* of a ribotype RT1 or RT2. In some instances, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe each comprise a *Propionibacterium acnes* of a ribotype RT2. In some instances, at least the first health-associated *Propionibacterium* microbe: comprises at least one gene encoding an ATP binding cassette transporter; comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; or lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase.

[0021] In some aspects, disclosed herein are methods of treating a skin disorder or condition comprising applying a therapeutically effective amount of a pharmaceutical composition disclosed herein to at least a region of skin on a subject in need thereof. In some instances, the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof. In some instances, applying is topical. In some instances, applying comprises applying the therapeutically effective amount of a pharmaceutical composition with a cotton pad. In some instances, methods comprise rubbing the cotton pad on the region of skin. In some instances, applying results in engraftment of at least one of the health-associated microbes of the pharmaceutical composition to the region of skin. In some instances, the at least one of the health-associated microbes remains present on the region of skin after at least one wash. In some instances, the wash comprises applying soap and water to the region of skin. In some instances, the wash comprises applying an antibacterial agent. In some instances, the antibacterial agent is benzoyl peroxide. In some instances, methods comprise applying the pharmaceutical composition at least once daily. In some instances, methods comprise applying the pharmaceutical composition at least once weekly. In some instances, methods comprise applying the pharmaceutical composition over a duration of at least one month. In some instances, the region of skin is located on at least one of the subject's face, neck, chest, back, and shoulder.

[0022] In some aspects, disclosed herein are methods of producing a desired preparation of a *Propionibacterium* bacteria, said method comprising: adding at least one health-associated *Propionibacterium* microbe to a preservative agent to produce a *Propionibacterium* preparation, and storing the *Propionibacterium* preparation at a

temperature of about 4 ° C or less. In some instances, the preservative agent comprises glycerol. In some instances, the preservative agent comprises polyethylene glycol. In some instances, the preservative agent comprises glycerol and polyethylene glycol. In some instances, the portion of the preservative agent that is glycerol is less than 50%. In some instances, the portion of the preservative agent that is glycerol is less than 25%. In some instances, the pharmaceutical composition is stored at about -15 °C to about -25 °C. In some instances, more than about 10% of the *P. acnes* bacteria is viable when the *Propionibacterium* bacteria in the glycerol solution is brought to ambient temperature. In some instances, at least about 30% of the *P. acnes* bacteria is viable when the *Propionibacterium* bacteria in the glycerol solution is brought to ambient temperature. In some instances, the *Propionibacterium* preparation is brought to ambient temperature after about 90 days of storing. In some instances, more than about 10% of the sample is viable at least up to about 90 days of storing. In some instances, more than about 30% of the sample is viable at least up to about 90 days of storing. In some instances, more than 50% of the sample is viable when brought to ambient temperature after about 20 days of storing. In some instances, the ambient temperature is between about 20 ° C and about 30 ° C. In some instances, the temperature is between about 4 ° C and about -80 ° C. In some instances, the temperature is between about 4 ° C and about -20 ° C. In some instances, the temperature is about 4 ° C. In some instances, the temperature is about -20 ° C. In some instances, methods comprise vacuum sealing the preparation of *Propionibacterium* bacteria. In some instances, methods comprise packaging the preparation of *Propionibacterium* bacteria for a single use. In some instances, methods comprise applying the preparation of *Propionibacterium* bacteria to an applicator. In some instances, the applicator is a cotton pad. In some instances, the at least one health-associated *Propionibacterium* microbe is a strain of *Propionibacterium acnes*. In some instances, the strain of *Propionibacterium acnes* is selected from HP3A11, HP4G1, and HP5G1. In some instances, methods comprise adding at least one additional health-associated microbe to the preservative agent.

[0023] In certain embodiments, the compositions and formulations of health-associated bacteria, described herein, comprise a biological stabilizer and suppresses lipase activity. In certain embodiments, the biological stabilizer suppresses secreted lipase activity and increases propionic acid production. In certain embodiments, the biological stabilizer increases secreted propionic acid production. In certain embodiments, the biological stabilizer is a humectant. In certain embodiments, the biological stabilizer is a humectant comprising glycerol. In certain embodiments, the biological stabilizer increases propionic acid production

and suppresses lipase activity. In certain embodiments, the biological stabilizer increases propionic acid production and suppresses lipase activity and is a humectant. In certain embodiments, the biological stabilizer increases propionic acid production and suppresses lipase activity and is a humectant.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] FIG. 1 illustrates exemplary production and packaging of compositions of health-associated microbes disclosed herein. Dashed lines indicate optional steps.

[0025] FIG. 2 shows the percentage of reads from a sample of a healthy volunteer (free of acne) that map to *P. acnes* to ribotype RT1, which are both *deoR*⁺ and type II lipase positive, versus the percentage of reads from the samples that map to *P. acnes* RT2.

[0026] FIG. 3 shows results of an assay for *P. acnes* viability with two different formulations at -20 deg C in either micro centrifuge tube or vacuum sealed cotton pads.

[0027] FIG. 4 shows a portion of a 23S, ribosomal RNA sequence from bacteria commonly found on the human face that enables characterization of a subject's skin microbiome.

Numbers listed to the left of sequences correspond to bacterial strains as follows: (1) *P. acnes*_KPA171202_RT1_2; (2) *P. acnes*_KPA171202_RT1_3; (3) *P. acnes* ATCC 11828_RT2_1; (4) *P. acnes* ATCC 11828_RT2_2; (5) *P. avidum* 44067; (6) *P. acidipropionici* ATCC 4875; (7) *S. aureus* 04-02981; (8) *S. aureus* Bmb9393; (9) *S. aureus* FDA209P; (10) *S. epidermidis* ATCC 12228; and (11) *S. epidermidis* PM221. Sequences 1-5 correspond to SEQ ID NOs: 33 to 37. Sequence 6 corresponds to SEQ ID NO: 38. Sequences 7-11 correspond to SEQ ID NOs: 39-43.

[0028] FIG. 5 shows a standard curve generated with serial dilutions of a combination of health-associated *P. acnes* and *S. epidermidis* that can be used to quantitate a percentage of health-associated *P. acnes* in a collected sample.

[0029] FIG. 6 shows qPCR of successful CRISPR editing in *P. acnes*.

[0030] FIG. 7 shows mutations in a gene encoding a *P. acnes* type I lipase that result in a gene encoding a *P. acnes* type II lipase. Type I lipase Intergenic Region corresponds to SEQ ID NO.: 44. Type I lipase Second Lipase (region) (HMPREF0675_4856) corresponds to SEQ ID NOS: 45, 46 and 47, respectively, in order of appearance. Type II lipase Second Lipase (region) (HMPREF0675_4856) corresponds to SEQ ID NOS: 50, 55 and 56, respectively, in order of appearance. Type I lipase Intergenic Region corresponds to SEQ ID NO.: 44. Type II lipase Intergenic Region corresponds to SEQ ID NO.: 49. SEQ ID NO: 57 is disclosed as the sequence extending from the Type I lipase Intergenic Region through the next 12 residues

in the Type I lipase Second Lipase (region). SEQ ID NO: 58 is disclosed as the sequence extending from the Type II lipase Intergenic Region through the next 12 residues in the Type II lipase Second Lipase (region).

[0031] **FIG. 8** shows exemplary packaging for compositions disclosed herein.

[0032] **FIG. 9** shows bacteria viability of composition disclosed herein after being packaged under several conditions.

[0033] **FIG. 10** shows fluorescence can be used to measure porphyrin levels on skin.

[0034] **FIG. 11** shows quantification of fluorescence as a measurement of porphyrin levels on skin.

[0035] **FIG. 12** shows qPCR can be used to assess the presence or engraftment of health-associated microbes to skin. **FIG. 12A** shows gene expression after treatment with a *P. acnes* strain of ribotype 1 and a *P. acnes* strain of ribotype 2. **FIG. 12B** shows gene expression after treatment with a *P. acnes* of ribotype 2. **FIG. 12C** shows gene expression after treatment with excipient control.

[0036] **FIG. 13** shows the genotyping results of three samples of lipid pillars each from a subject with acne vulgaris and a subject without.

[0037] **FIG. 14** shows strains of *P. acnes* strains of ribotype 1 (RT1) or ribotype 2 (RT2), alone or in combination are effective at displacing *P. acnes* strain of ribotype 4 (RT4). **FIG. 14A** shows RT1 against RT4. **FIG. 14B** shows RT2 against RT4. **FIG. 14C** shows a combination of RT1 and RT2 alone against RT4.

[0038] **FIG. 15** shows a representation of repetitive and spacer sequences in a CRISPR locus in various *P. acnes* and control strains.

DETAILED DESCRIPTION OF THE INVENTION

[0039] Provided herein are microbiome-based approaches to skin therapy using beneficial bacteria on the skin to eliminate or reduce harmful bacteria and restore skin to a healthy state. The methods and compositions disclosed herein may be used for a wide range of skin disorders including acne, eczema, psoriasis, rosacea and seborrheic dermatitis. Problems with current treatments for these disorders include antibiotic resistance, side effects, complicated regimens, and lack of long-term effectiveness. Treatments disclosed herein may provide alternatives to antibiotics, use healthy bacteria, present few side effects, with simple treatment regimens and long-term effectiveness.

[0040] Compositions described herein generally contain at least one health-associated microbe that conveys beneficial effects to a subject with a skin disorder. Thus, the

compositions disclosed herein are effective on the skin (*e.g.*, at skin temperature). These compositions sometimes contain a mixture of several strains that have each been isolated, purified, selected or engineered to provide a specific cocktail of bacteria that does not occur in nature. These strains can be stored or packaged with a preservative agent, such as glycerol or polyethylene glycol in a container or on an applicator such as a cotton pad, as shown in **FIG. 1**. These containers and applicators can be stored in a freezer, refrigerator or on a shelf at room temperature, both before and during use.

[0041] Many of the compositions and methods disclosed herein comprise bacteria known as *Propionibacterium acnes*, abbreviated *P. acnes*, and uses thereof, respectively. However, other bacteria, including genetically modified strains, and uses thereof are also contemplated herein. Some strains of *P. acnes* used in compositions and methods disclosed herein are referred to herein as healthy strains of *P. acnes* or, for simplicity, “healthy *P. acnes*.” Healthy strains of *P. acnes* generally promote skin health by preventing a skin disorder or reducing symptoms of a skin disorder. Healthy strains of *P. acnes* may even promote skin health by eliminating the cause of a skin disorder. Other strains of *P. acnes* are referred to herein as pathogenic strains or “pathogenic *P. acnes*.” Pathogenic *P. acnes* generally promote or cause a skin disorder or symptoms thereof. Generally, pathogenic *P. acnes* are not used in compositions and methods described herein. Instead, methods and compositions disclosed herein may be useful in reducing or preventing growth of pathogenic *P. acnes* on the skin of a subject. In some cases, an amount of *P. acnes* can be considered healthy or pathogenic, too much or too little being desirable or undesirable. In some cases, a combination of multiple *P. acnes* strains confers health. Conversely, in some cases, a different combination of multiple *P. acnes* strains can be pathogenic. Strains of *P. acnes*, combinations thereof, and amounts thereof that are healthy and pathogenic are described herein.

[0042] Compositions and methods disclosed herein may comprise bacteria with a given genetic signature and uses thereof, respectively. While *P. acnes* is the bacteria primarily exemplified herein, it is contemplated that other bacteria having a particular genetic signature that is similar to healthy *P. acnes* could likewise be useful for compositions and methods disclosed herein. For example, many *P. acnes* strains that are identified as healthy herein comprise a combination of a deoxyribose operon repressor (*deoR*), a type II lipase, and a CRISPR associated Cas endonuclease. Additionally, healthy *P. acnes* strains are generally associated with an absence or only small amounts of an extrachromosomal plasmid known in the art as pIMPLE plasmids. It has previously been reported that some strains of *P. acnes* harbor an extrachromosomal plasmid, given the term, “pIMPLE plasmid,” by those in the

field. Such plasmids are readily found in the art. pIMPLE plasmids may have multiple open reading frames (ORFs). The presence of these aforementioned genes (*e.g.*, deoR, lipase, Cas) and/or a low presence of pIMPLE plasmid may provide a healthy skin promoting genetic signature that can be used to identify bacteria other than *P. acnes* that are useful in compositions and methods of treating acne described herein.

Certain Terminologies

[0043] In the following description, certain specific details are set forth in order to provide a thorough understanding of various embodiments. However, one skilled in the art will understand that the embodiments provided may be practiced without these details. Unless the context requires otherwise, throughout the specification and claims which follow, the word “comprise” and variations thereof, such as, “comprises” and “comprising” are to be construed in an open, inclusive sense, that is, as “including, but not limited to.” As used in this specification and the appended claims, the singular forms “a,” “an,” and “the” include plural referents unless the content clearly dictates otherwise. It should also be noted that the term “or” is generally employed in its sense including “and/or” unless the content clearly dictates otherwise. Further, headings provided herein are for convenience only and do not interpret the scope or meaning of the claimed embodiments.

[0044] As used herein the term “about” refers to an amount that is near the stated amount by about 10%, 5%, or 1%.

[0045] As used herein “consisting essentially of” when used to define compositions and methods, shall mean excluding other elements of any essential significance to the combination for the stated purpose. Thus, a composition consisting essentially of the elements as defined herein would not exclude other materials or steps that do not materially affect the basic and novel characteristic(s) of the claimed disclosure, such as compositions for treating skin disorders like acne, eczema, psoriasis, and rosacea.

[0046] As used herein “health-associated” means a microbe that is more prevalent in healthy or disease free individuals than in individuals diagnosed with a given disorder. In certain embodiments, the disease may be acne, eczema, seborrheic dermatitis, psoriasis, rosacea, or any combination thereof. A health-associated microbe can be determined statistically. For example, by comparing the microbiome or the prevalence of certain microbial species or strains on the skin, in the oral cavity, or in the digestive system of a healthy non-disease afflicted individual as compared to an individual with a given disease. Genera, species, or strains that are more prevalent in/on healthy individuals are health-

associated. A health-associated strain can also be a strain that has been genetically modified or selected to express low levels of virulence factors that are associated with a given skin disease. A health-associated strain can also be a strain that has been genetically modified or selected to express high levels of beneficial genes, RNAs, or proteins that are associated with protection from a given skin disease. Health-associated strains may have or express fewer or no genes encoding proteins that promote pathogenicity. Health-associated strains may have or express repressors of pathogenic genes, pathogenic pathways or pathogenic proteins. A health-associated strain can also be a strain that has been genetically modified or selected to express, not express, or express desirable levels of markers, as described herein.

[0047] As used herein a “probiotic” is a microbe that provides health benefits when consumed or applied. In some instances, probiotics disclosed herein are microbes that inhibit the activity or growth of a disease causing bacteria associated with acne, eczema, seborrheic dermatitis, psoriasis, or rosacea. In some instances, health-associated microbes disclosed herein are considered probiotics.

[0048] As used herein, the terms "homologous," "homology," or "percent homology" when used herein to describe to an amino acid sequence or a nucleic acid sequence, relative to a reference sequence, can be determined using the formula described by Karlin and Altschul (Proc. Natl. Acad. Sci. USA 87: 2264-2268, 1990, modified as in Proc. Natl. Acad. Sci. USA 90:5873-5877, 1993). Such a formula is incorporated into the basic local alignment search tool (BLAST) programs of Altschul et al. (J. Mol. Biol. 215: 403-410, 1990). Percent homology of sequences can be determined using the most recent version of BLAST, as of the filing date of this application.

[0049] Provided throughout this application are compositions and methods for the treatment of skin disorders. It should be understood that compositions disclosed herein may be used according to methods described herein. Conversely, methods disclosed herein may appropriately employ compositions disclosed herein.

Compositions for Treatments of Skin Disorders

[0050] In some aspects, the disclosure provides compositions comprising at least one strain of bacteria. The at least one strain of bacteria is generally a strain that promotes, restores or improves skin health. Such a strain may be referred to herein as a “health-associated strain of bacteria” or a “health-associated microbe.” In some embodiments, compositions disclosed herein comprise at least one health-associated strain of bacteria. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Propionibacterium* bacteria. In some embodiments, the at least one health-associated strain of bacteria is a strain of

Staphylococcus bacteria. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Lactobacillus* bacteria. In some embodiments, the composition is formulated for application to the skin of a subject.

[0051] In some embodiments, compositions disclosed herein comprise a fungus. The fungus is generally a fungus that promotes, restores or improves skin health. In some embodiments, compositions disclosed herein comprise at least one health-associated fungus. In some embodiments, the fungus is *Malassezia*.

[0052] In some embodiments, compositions disclosed herein comprise a bacteriophage, also referred to herein as a phage for simplicity. In some embodiments, the bacteriophage is a *Propionibacterium* phage. In some embodiments, the bacteriophage is a health-associated *Propionibacterium* phage. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of a skin disorder. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of acne. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of eczema. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of psoriasis. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of seborrheic dermatitis. In some embodiments, the health-associated *Propionibacterium* phage is a phage found on skin of a subject that is free of rosacea. In some embodiments, the health-associated *Propionibacterium* phage is a phage that is more abundant or prevalent on skin free of a skin disorder than skin with a skin disorder. In some embodiments, the bacteriophage is a *Propionibacterium acnes* phage. In some embodiments, the *Propionibacterium acnes* phage targets a select strain of *P. acnes*. In some embodiments, the *Propionibacterium acnes* phage targets a pathogenic strain of *P. acnes*. Non-limiting examples of *Propionibacterium acnes* phages are described in Farrar et al. (2007) J. Bacteriol., vol. 189, pp. 4161-4167, and Liu et al. (2015) ISME J, vol. 9, pp. 2078-2093.

[0053] In some embodiments, the at least one health-associated strain of bacteria is a strain of *Propionibacterium acnes* (referred to herein as *P. acnes*). In some embodiments, the at least one health-associated strain of bacteria is not a strain of *P. acnes* subsp. *acnes*. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Propionibacterium avidum* (referred to herein as *P. avidum*). In some embodiments, the at least one health-associated strain of bacteria is a strain of *Propionibacterium granulosum* (referred to herein as *P. granulosum*). In some embodiments, the at least one health-

associated strain of bacteria is a strain of *Propionibacterium acnes* subsp. *defendens* (referred to herein as *P. acnes* subsp. *defendens*). In some embodiments, the at least one health-associated strain of bacteria is a strain of *Staphylococcus aureus*. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Staphylococcus epidermidis*. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Staphylococcus hominis*. In some embodiments, the at least one health-associated strain of bacteria is a strain of *Lactobacillus reuteri*. In some embodiments, the strain of bacteria is associated with healthy skin or normal skin, and is referred to as a probiotic (or live biologic therapeutic). In some embodiments, the health-associated microbe is associated with skin that is free of acne. In some embodiments, the health-associated microbe is associated with skin that is essentially free of acne.

[0054] Provided herein are compositions that comprise a strain of *Propionibacterium acnes*. In some instances the strain is HP3A11. In some instances, the strain is HP4G1. In some instances, the strain is HP5G4. In some instances, compositions disclosed herein comprise at least one strain selected from HP3A11, HP4G1 and HP5G4. In some instances, compositions disclosed herein comprise at least two strains selected from HP3A11, HP4G1 and HP5G4. Strains of *Propionibacterium acnes*, HP3A11, HP4G1 and HP5G4, described herein, were deposited in the American Tissue Culture Collection (10801 University Boulevard Manassas, VA 20110-2209 USA) on April 6, 2017 in accordance with and under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure. The strains were tested by the ATCC and determined to be viable. The ATCC has assigned ATCC deposit accession numbers: PTA-124010 to strain HP3A11; PTA-124011 to strain HP4G1; and PTA 124012 to HP5G4. These strains have also been deposited in the Chr. Hansen Culture Collection (CHCC) and given a CHCC number. The CHCC has assigned CHCC deposit accession numbers: 28619 to HP5G4; 28733 to HP3A11; and 28735 to HP4G1.

[0055] Provided herein are compositions that comprise at least one health-associated microbe disclosed herein. In some embodiments, a health-associated microbe disclosed herein is selected or assessed for a composition for treatment by assessing an amount of inflammation that is caused by the health-associated microbe to the skin of a subject. In some embodiments, the health-associated microbe produces or induces a low amount of pro-inflammatory mediators when applied to a subject's skin. In some embodiments, the health-associated microbe produces or induces a low amount of pro-inflammatory mediators when applied to a subject's skin. In some embodiments, the health-associated microbe does not

produce or induce pro-inflammatory mediators when applied to a subject's skin. In some embodiments, the health-associated microbe does not produce or induce pro-inflammatory mediators when applied to a subject's skin. In some embodiments, the health-associated microbe does not produce or induce an amount of pro-inflammatory mediators sufficient to cause acne of a subject when applied to a subject's skin. In some embodiments, the health-associated microbe does not produce or induce an amount of pro-inflammatory mediators sufficient to worsen acne of a subject when applied to a subject's skin. The health-associated microbe may not induce human inflammatory associated mRNAs such as interleukins, chemokine or cytokines when applied to a subject's skin. The health-associated microbe may induce only low amounts of human inflammatory associated mRNAs such as interleukins, chemokine or cytokines, when applied to a subject's skin.

[0056] In some embodiments, a health-associated microbe disclosed herein is selected or assessed by incubating a sample of keratinocytes with the health-associated microbe. In some embodiments, the health-associated microbe produces or induces a low amount of pro-inflammatory mediators when co-incubated with a subject's keratinocytes. In some embodiments, the health-associated microbe produces or induces a low amount of pro-inflammatory mediators when co-incubated with skin keratinocytes that are pooled from multiple subjects. In some embodiments, the health-associated microbe does not produce or induce pro-inflammatory mediators when co-incubated with a subject's keratinocytes. In some embodiments, the health-associated microbe does not produce or induce pro-inflammatory mediators when co-incubated with skin keratinocytes pooled from multiple subjects (*e.g.*, "pooled skin keratinocytes"). In some embodiments, the health-associated microbe comprises does not produce or induce an amount of pro-inflammatory mediators sufficient to cause acne of a subject when co-incubated with the subject's keratinocytes or pooled skin keratinocytes. In some embodiments, the health-associated microbe does not produce or induce an amount of pro-inflammatory mediators sufficient to worsen acne of a subject when co-incubated with a subject's keratinocytes or pooled skin keratinocytes. The health-associated microbe may not induce human inflammatory associated mRNAs such as interleukins, chemokine or cytokines when incubated with a subjects own keratinocytes or pooled keratinocytes from a plurality of healthy volunteers. The health-associated microbe may induce only low amounts of human inflammatory associated mRNAs such as interleukins, chemokine or cytokines, when incubated with a subjects own keratinocytes or pooled keratinocytes from a plurality of healthy volunteers. The health-associated microbe may induce only low amounts of human inflammatory associated mRNAs or proteins such as

interleukins, chemokine or cytokines, when incubated with primary human monocytes. In a certain embodiment, the inflammatory interleukin, chemokine or cytokine comprises IL-2, IL-12, or MCP-1. An exemplar assay for induction of IL-12 in monocytes by a bacterium can be found in U.S. Patent No. 9,549,905.

[0057] Compositions disclosed herein may comprise a strain that produces low levels of at least one porphyrin. In some embodiments, the strain produces undetectable levels of the at least one porphyrin. Non-limiting examples of porphyrins include coproporphyrin I, uroporphyrin III, coproporphyrin III, and protoporphyrin IX. In some embodiments, a low level of the at least one porphyrin is less than about 1 micromolar. In some embodiments, a low level of the at least one porphyrin is less than about 750 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 500 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 250 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 200 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 150 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 100 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 50 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 10 nanomolar. In some embodiments, a low level of the at least one porphyrin is less than about 1 nanomolar. In some embodiments, the low level is a level measured *in vitro*. In some embodiments, the low level is a level measured *in situ*, due to fluorescent properties of porphyrins. In some embodiments, a strain is genetically modified to delete or mutate a nucleic acid encoding an enzyme in a porphyrin production pathway to effectively create or select for strains with low porphyrin production. In some embodiments, the strain has low lipase activity as compared to a pathogenic strain of bacteria. In some embodiments, the strain has low immunogenicity as compared to a pathogenic strain of bacteria.

[0058] Disclosed herein are pharmaceutical compositions that comprise: (a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe, wherein the first health-associated *Propionibacterium* microbe produces less than about one micromolar porphyrin; (b) a second therapeutically effective amount of a second health-associated microbe; and (c) a pharmaceutically acceptable excipient or biological stabilizer. Further disclosed herein are pharmaceutical compositions that consist essentially of: (a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe, wherein the first health-associated *Propionibacterium* microbe produces less than about one

micromolar porphyrin; (b) a second therapeutically effective amount of a second health-associated microbe; (c) a pharmaceutically acceptable excipient or biological stabilizer; and (d) optionally, an additional active ingredient disclosed herein. In some embodiments, the second health-associated microbe comprises a strain of *Propionibacterium*. In some embodiments, the concentration of porphyrin is a concentration measured *in vitro*. In some embodiments, the concentration of porphyrin is a concentration measured *in situ*. For example, porphyrin concentration can be measured directly on skin of a subject using light of a wavelength around 400 nm, a camera that detects fluorescence, and digital imaging software that quantifies fluorescence. In some embodiments, excitation light of a wavelength between about 300 nm and about 900 nm is used. In some embodiments, light of a wavelength about 400 nm is used. In some embodiments, light of a wavelength between about 570 nm and about 630 nm is detected, *e.g.*, when detecting coproporphyrin III. In some embodiments, light of a wavelength greater than about 630 nm is detected, *e.g.*, when detecting protoporphyrin IX.

[0059] In some embodiments, the first health-associated microbe produces less than about one micromolar porphyrin. In some embodiments, the second health-associated microbe produces less than about one micromolar porphyrin.

[0060] In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about one micromolar porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 800 nanomolar porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 500 nanomolar porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 200 nanomolar porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 100 nM porphyrin. In some embodiments, the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about 10 nM porphyrin.

[0061] In some embodiments, the first health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*, *Propionibacterium granulosum*, *Propionibacterium avidum*, or *Propionibacterium acnes* subsp. *defendens*. In some

embodiments, the second health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*, *Propionibacterium granulosum*, *Propionibacterium avidum*, or *Propionibacterium acnes* subsp. *defendens*. In some embodiments, the first health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*. In some embodiments, the second health-associated *Propionibacterium* microbe comprises a strain of *Propionibacterium acnes*. In some embodiments, the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1 or RT2. In some embodiments, the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT3. In some embodiments, the second health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1 or RT2. In some embodiments, the second health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT3. In some embodiments, the second health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT3. In some embodiments, the first health-associated *Propionibacterium* microbe: (a) comprises at least one gene encoding an ATP binding cassette transporter; (b) comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; or (c) lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase. In some embodiments, the second health-associated *Propionibacterium* microbe: (a) comprises at least one gene encoding an ATP binding cassette transporter; (b) comprises at least one gene encoding at least one of a deoxyribose operon repressor and a type II lipase, and less than about 10% pIMPLE plasmid; or (c) lacks at least one gene encoding a DNA binding response regulator or a phosphoglycerate kinase.

[0062] Health-associated strains disclosed herein may be defined by 16S, 18S, or 23S ribosomal DNA sequences, metagenomic DNA, the presence of specific health-associated markers, the absence of disease associated markers, or a combination thereof. Health-associated strains disclosed herein may be enriched or isolated to obtain a purified strain.

[0063] Provided herein are compositions comprising not more than one isolated strain of bacteria disclosed herein. Provided herein are compositions comprising not more than two isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than three isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than four isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than five isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than six isolated

strains of bacteria disclosed herein. Provided herein are compositions comprising not more than seven isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than eight isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than nine isolated strains of bacteria disclosed herein. Provided herein are compositions comprising not more than ten isolated strains of bacteria disclosed herein.

[0064] Health-associated microbes disclosed herein may comprise at least one strain of bacteria that inhibits the activity of a pathogenic strain of *P. acnes*. In some embodiments, the health-associated microbe is bacteriostatic or bactericidal for a pathogenic strain of *P. acnes*. In some embodiments, the health-associated microbe reduces growth, re-growth or metabolism of the pathogenic strain of *P. acnes*. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 20% as compared to placebo/no health-associated microbe. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 30%. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 40%. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 50%. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 60%. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 70%. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 2-fold. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 3-fold. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 5-fold. In certain embodiments, the health-associated microbe reduces growth (or re-growth) of the pathogenic *P. acnes* by at least about 10-fold. Inhibition or reduction of growth (or re-growth) of the pathogenic *P. acnes* may be assessed in an *in vitro* assay, either in liquid culture or on solid media.

[0065] In some embodiments, the health-associated microbe comprises at least one healthy *P. acnes* strain. In some embodiments, the health-associated microbe comprises not more than one healthy *P. acnes* strain. In some embodiments, the health-associated microbe comprises at least two healthy *P. acnes* strains. In some embodiments, the at least one healthy *P. acnes* strain is not a strain of *P. acnes* subsp. *acnes*. In some embodiments, the health-associated microbe comprises at least one healthy *P. avidum* strain. In some embodiments,

the health-associated microbe comprises not more than one healthy *P. avidum* strain. In some embodiments, the health-associated microbe comprises at least two healthy *P. avidum* strains. In some embodiments, the health-associated microbe comprises at least one healthy *P. granulosum* strain. In some embodiments, the health-associated microbe comprises not more than one healthy *P. granulosum* strain. In some embodiments, the health-associated microbe comprises at least two healthy *P. granulosum* strains. In some embodiments, the health-associated microbe comprises at least one healthy *P. acnes* subsp. *defendens* strain. In some embodiments, the health-associated microbe comprises not more than one healthy *P. acnes* subsp. *defendens* strain. In some embodiments, the health-associated microbe comprises at least two healthy *P. acnes* subsp. *defendens* strains.

[0066] *P. acnes* strains may be characterized by a ribotype (RT). Ribotypes are defined, for example, as in Fitz-Gibbon *et al.*, J. Investigative Dermatology 133:2152-60 (2013). A ribotype can be determined by the nucleic acid sequence of the strain's 16S ribosomal subunit. In certain embodiments, the health-associated microbe comprises healthy *P. acnes* of a ribotype selected from at least one of the following ribotypes of RT1, RT2, RT3, RT4, RT5, RT7, RT8, RT9, or RT10. In certain embodiments, the health-associated microbe comprises healthy *P. acnes* of a ribotype selected from at least one of the following ribotypes of RT1, RT2, RT3, RT7, RT8, RT9, or RT10. In certain embodiments, the health-associated microbe comprises healthy *P. acnes* of a ribotype selected from RT1 and RT2. In certain embodiments, the health-associated microbe comprises healthy *P. acnes* of ribotype RT3. In some instances, the health-associated microbe does not comprise a *P. acnes* strain of ribotype RT6. In some instances, the health-associated microbe does not comprise a *P. acnes* strain of a ribotype selected from RT3, RT4, RT5 and RT6. In some instances, the health-associated microbe does not comprise a *P. acnes* strain of ribotype RT6. In some instances, the health-associated microbe does not comprise a *P. acnes* strain of a ribotype selected from RT3, RT4, and RT5. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT1. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT2. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT3. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT4. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT5. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT6. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT7. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT8.

In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT9. In some embodiments, compositions disclosed herein comprise a strain of *P. acnes* of ribotype RT10. In certain embodiments, the health-associated microbe comprises a strain of *P. acnes* of a ribotype selected from at least one of RT1, RT2, and RT3. In certain embodiments, the health-associated microbe comprises a *P. acnes* strain of ribotype RT1. In certain embodiments, the health-associated microbe comprises a *P. acnes* strain of ribotype RT2. In certain embodiments, the health-associated microbe comprises a *P. acnes* strain of ribotype RT3. In certain embodiments, the health-associated microbe comprises a *P. acnes* strain of ribotype RT3. In certain embodiments, the health-associated microbe does not comprise an RT6 ribotype.

[0067] In certain embodiments, health-associated microbes disclosed herein do not comprise a strain with a nucleic acid having a sequence that is 95%, 97%, 98%, 99% or 100% homologous to a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, and SEQ ID NO: 54. In certain embodiments, the health-associated microbe does not comprise a strain with a nucleic acid having a sequence that is more than 50% homologous to a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, and SEQ ID NO: 54. In certain embodiments, the health-associated microbe does not comprise a strain with a nucleic acid having a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53.

[0068] In certain embodiments, health-associated microbes disclosed herein comprise a plurality of microbes of different ribotypes. In certain embodiments, the plurality of microbes is a mixture of two or more *P. acnes* strains of different ribotypes. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* of ribotype RT2. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* of ribotype RT3. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* is not ribotype RT6. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* of ribotype RT3. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* is not ribotype RT6. In certain embodiments, the health-associated microbe comprises a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* of ribotype RT3. In certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* of ribotype RT2. In

certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* of ribotype RT3. In certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT1 and a second strain of *P. acnes* is not ribotype RT6. In certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* of ribotype RT3. In certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* is not ribotype RT6. In certain embodiments, the health-associated microbe consists essentially of a first strain of *P. acnes* of ribotype RT2 and a second strain of *P. acnes* of ribotype RT3. In some embodiments, the first strain of *P. acnes* and the second strain of *P. acnes* are provided separately. In some embodiments, the first strain of *P. acnes* and second strain of *P. acnes* are mixed.

[0069] In some embodiments, health-associated microbes disclosed herein comprise a health-associated *P. acnes* strain that is ribotype RT1, deoR-positive, type II lipase-positive, does not comprise Cas5, and has less than 5% pIMPLE plasmid. In some embodiments, deoR-positive means that the strain comprises a nucleic acid encoding deoR. In some embodiments, deoR-positive means that the strain comprises a deoR protein. In some embodiments, type II lipase-positive means that the strain comprises a nucleic acid encoding type II lipase. In some embodiments, type II lipase -positive means that the strain comprises a type II lipase protein. In some embodiments, the strain does not comprise a nucleic acid encoding a Cas 5 protein. In some embodiments, health-associated microbes disclosed herein comprise a health-associated *P. acnes* strain that is ribotype RT2, deoR-positive, type II lipase-positive, Cas5-positive and has less than 5% pIMPLE plasmid.

[0070] In certain embodiments, the health-associated microbe is a plurality of microbes of different ribotypes. In certain embodiments, the plurality of microbes comprises a mixture of three or more *P. acnes* strains of different ribotypes. In certain embodiments, the different ribotypes are RT1, RT2, and RT3. In certain embodiments, the different ribotypes are RT2, RT3, and not RT6. In certain embodiments, the different ribotypes are RT1, RT2, and not RT6. In certain embodiments, the different ribotypes are RT1, RT3, and not RT6. In certain embodiments, the mixture consists essentially of three *P. acnes* strains, wherein the three *P. acnes* strains are of ribotypes RT1, RT2, and RT3. In certain embodiments, the mixture consists essentially of three *P. acnes* strains, wherein the three *P. acnes* strains are of ribotypes RT2, RT3, and not RT6. In certain embodiments, the mixture consists essentially of three *P. acnes* strains, wherein the three *P. acnes* strains are of ribotypes RT1, RT2, and not

RT6. In certain embodiments, the mixture consists essentially of three *P. acnes* strains, wherein the three *P. acnes* strains are of ribotypes RT1, RT3, and not RT6.

[0071] In some embodiments, health-associated microbes disclosed herein comprise at least one health-associated strain of *P. acnes*, wherein the health-associated strain of *P. acnes* has a ribotype of RT1, RT2 or RT3. In some embodiments, health-associated microbes disclosed herein comprise at least two health-associated strains of *P. acnes*, wherein a first health-associated strain of *P. acnes* has a ribotype of RT1 and a second health-associated strain of *P. acnes* has a ribotype of RT2. In some embodiments, health-associated microbes disclosed herein comprise at least two health-associated strains of *P. acnes*, wherein a first health-associated strain of *P. acnes* has a ribotype of RT1 and a second health-associated strain of *P. acnes* has a ribotype of RT3. In some embodiments, health-associated microbes disclosed herein comprise at least two health-associated strains of *P. acnes*, wherein a first health-associated strain of *P. acnes* has a ribotype of RT2 and a second health-associated strain of *P. acnes* has a ribotype of RT3. In some embodiments, health-associated microbes disclosed herein do not comprise a strain of *P. acnes*, other than a health-associated strain of *P. acnes* disclosed herein that has a ribotype selected from RT1, RT2 and RT3. In some embodiments, the health-associated microbe does not comprise a strain of *P. acnes* that has a ribotype RT4 or RT5. In some embodiments, the health-associated microbe does not comprise a strain of *P. acnes* that has a ribotype RT6. In some embodiments, the health-associated microbe does not comprise a strain of *P. acnes* that comprises a nucleic acid encoding a DNA binding response regulator or a phosphoglycerate kinase, as described herein. In some embodiments, the health-associated microbe comprises a strain of *P. acnes* comprising a nucleic acid encoding an ATP binding cassette transporter, as described herein. In some embodiments, the health-associated microbe does not comprise a strain of *P. acnes* that expresses DNA binding response regulator or phosphoglycerate kinase, as described herein. In some embodiments, the health-associated microbe comprises a strain of *P. acnes* that expresses an ATP binding cassette transporter, as described herein.

[0072] In some embodiments, health-associated microbes disclosed herein comprise at least one strain of bacteria that can be identified by a genetic signature. The genetic signature can be described as one or more genes that are at least present, and optionally expressed, in a strain of bacteria. The one or more genes may comprise a gene encoding a deoxyribose operon repressor (*deoR*). The one or more genes may encode a type I lipase. The one or more genes may encode a type II lipase. The one or more genes may encode Cas 5. In some instances, the one or more genes do not comprise a gene encoding a deoxyribose operon

repressor (gene abbreviated *deoR*, protein abbreviated herein as deoR). In some instances, the one or more genes do not comprise a gene encoding a type I lipase. In some instances, the one or more genes do not comprise a gene encoding a type II lipase. In some instances, the one or more genes do not comprise a gene encoding a Cas5 protein.

[0073] In some embodiments, health-associated microbes disclosed herein comprise at least one strain of bacteria expressing a type II lipase. In some embodiments, health-associated microbes disclosed herein comprise at least one strain of bacteria expressing a deoR and a type II lipase. In some embodiments, health-associated microbes disclosed herein comprise at least one strain of bacteria expressing a Cas5 and a type II lipase. In some embodiments, health-associated microbes disclosed herein comprise at least one strain of bacteria expressing a deoR and a type II lipase and a Cas5.

[0074] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 25% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 20% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 15% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 10% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 9% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 8% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 7% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 6% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least

one strain of bacteria, wherein less than about 5% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 4% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 3% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 2% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 1% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein less than about 0.5% of a number of reads align per number of reads tested when the reads from sequencing the strain are aligned to a pIMPLE plasmid.

[0075] In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, expresses type I lipase, and does not express deoR and Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, expresses deoR and type I lipase, and does not express Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, expresses deoR and type II lipase, and does not express Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain.

[0076] In some embodiments, the composition comprises a strain of bacteria that is ribotype RT2, expresses deoR, type II lipase, and Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT4 and expresses type I lipase, but not deoR. In some embodiments, the composition comprises a strain of bacteria that is not ribotype RT6, expresses deoR, type II lipase, and Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain.

[0077] In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, comprises a nucleic acid encoding type I lipase, and does not comprises a nucleic acid encoding deoR or Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, comprises at least one nucleic acid encoding deoR and type I lipase, does not comprise a nucleic acid encoding Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT1, a nucleic acid encoding deoR and type II lipase, does not comprise a nucleic acid encoding Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT2, comprises at least one nucleic acid encoding deoR, type II lipase, and Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT4 and comprises a nucleic acid encoding type I lipase, but does not comprise a nucleic acid encoding deoR. In some embodiments, the composition comprises a strain of bacteria that is not ribotype RT6, comprises at least one nucleic acid encoding deoR, type II lipase, and Cas5, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain.

[0078] In some embodiments, the composition comprises a strain of bacteria that is ribotype RT3 and expresses type II lipase, expresses deoR, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from whole genome sequencing of the strain. In some embodiments, the strain of bacteria having ribotype RT3 expresses an ATP binding cassette transporter disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not expresses a DNA binding response regulator disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not expresses a phosphoglycerate kinase disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 expresses a Cas5 disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not expresses a Cas5 disclosed herein. In some embodiments, the composition comprises a strain of bacteria that is ribotype RT3, comprises a nucleic acid encoding type II lipase, comprises a nucleic acid encoding deoR, and wherein less than 5% of a number of reads align to pIMPLE plasmid per number of reads tested from

whole genome sequencing of the strain. In some embodiments, the strain of bacteria having ribotype RT3 comprises a nucleic acid encoding an ATP binding cassette transporter disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not comprise a nucleic acid encoding a DNA binding response regulator disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not comprise a nucleic acid encoding a phosphoglycerate kinase disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 comprises a nucleic acid encoding a Cas5 disclosed herein. In some embodiments, the strain of bacteria having ribotype RT3 does not comprise a nucleic acid encoding a Cas5 disclosed herein.

[0079] **Table 1** below provides a summary of non-limiting examples of *P. acnes* bacteria, or populations of bacteria comprising *P. acnes* bacteria, that can be distinguished by analysis of different genetic markers. The + symbol indicates the presence of deoR or Cas5 (or nucleic acids encoding deoR or Cas5) in the columns labeled deoR and Cas5, respectively. The - symbol indicates absence of deoR or Cas5 (or nucleic acids encoding deoR or Cas5) in the columns labeled deoR and Cas5, respectively. % pIMPLE plasmid refers to the number of reads aligned/number of reads tested when bacteria is sequenced for pIMPLE plasmid.

Table 1. Sequences of *P. acnes* genetic elements.

Group	RT	deo R	Lipase	Cas 5	% pIMPLE plasmid	ABC XP	DBRR	PGK	Exemplary strains
A	1	-	I	-	<5%	+	-	-	
B	1	+	I	-	<5%	+	-	-	
C	1	+	II	-	<5%	+	-	-	HP3A11
D	2	+	II	+	<5%	+	-	-	HP4G1, HP5G4
E	4	-	I	-	>1%	+	-	-	HL045PA1
F	5	-	I	-	>1%	+	-	-	HL043PA1
G	6	+	II	+	>5%	-	+	+	HL110PA3, HL110PA4

ABC XP = ATP binding cassette transporter

DBRR = DNA binding response regulator

PGK = phosphoglycerate kinase

[0080] In certain embodiments, the composition comprises at least one strain of a *P. acnes* microbe that corresponds to group A of **Table 1**. In certain embodiments, the composition comprises at least one strain of a *P. acnes* microbe that corresponds to group B of **Table 1**. In certain embodiments, the composition comprises at least one strain of a *P. acnes* microbe that corresponds to group C of **Table 1**. In certain embodiments, the composition comprises at least one strain of a *P. acnes* microbe that corresponds to group D

of **Table 1**.

[0081] In certain embodiments, the composition comprises at least one strain of a *P. acnes* microbe that corresponds to groups A, B, C or D of **Table 1**. In certain embodiments, the composition comprises at least two strains of a *P. acnes* microbe that correspond to groups A, B, C or D of **Table 1**. In certain embodiments, the composition comprises at least three strains of a *P. acnes* microbe that correspond to groups A, B, C or D of **Table 1**. In certain embodiments, the composition comprises at least four strains of a *P. acnes* microbe that correspond to groups A, B, C or D of **Table 1**. In certain embodiments, the composition comprises at least five strains of a *P. acnes* microbe that correspond to groups A, B, C, or D of **Table 1**.

[0082] In some embodiments, the composition does not comprise a strain of *P. acnes* that corresponds to group E of **Table 1**. In some embodiments, the composition does not comprise a strain of *P. acnes* that corresponds to group F of **Table 1**. In some embodiments, the composition does not comprise a strain of *P. acnes* that corresponds to group G of **Table 1**.

[0083] In some embodiments, the composition comprises at least one strain of *P. acnes* that corresponds to group A of **Table 1**, but does not comprise a strain of *P. acnes* that corresponds to groups E, F or G of **Table 1**. In some embodiments, the composition comprises at least one strain of *P. acnes* that corresponds to group B of **Table 1**, but does not comprise a strain of *P. acnes* that corresponds to groups E, F or G of **Table 1**. In some embodiments, the composition comprises at least one strain of *P. acnes* that corresponds to group C of **Table 1**, but does not comprise a strain of *P. acnes* that corresponds to groups E, F or G of **Table 1**. In some embodiments, the composition comprises at least one strain of *P. acnes* that corresponds to group D of **Table 1**, but does not comprise a strain of *P. acnes* that corresponds to groups E, F or G of **Table 1**. In some embodiments, the composition comprises at least one strain of *P. acnes* that corresponds to group C of **Table 1** and at least one strain of *P. acnes* that corresponds to group D of **Table 1**, but does not comprise a strain of *P. acnes* that corresponds to groups E, F or G of **Table 1**.

Health-Associated Microbes

[0084] Provided herein are compositions for treating and preventing skin disorders, wherein the compositions comprise a health-associated microbe. Generally, the term, “health-associated microbe,” as used herein, refers to a microbe that is more prevalent in healthy or individuals free of a skin disease than in individuals diagnosed with the skin disease. In some embodiments, health-associated microbes disclosed herein are associated with desirable or

optimal oral health. In some embodiments, health-associated microbes disclosed herein are associated with desirable or optimal gastrointestinal health.

[0085] Health-associated microbes include health-associated microbes described herein. Health-associated microbes include healthy *P. acnes* described herein. In some embodiments, health-associated microbes are microbes that can replace at least a portion of pathogenic microbes. In some embodiments, health-associated microbes are microbes that can alter a microbiome to increase a percentage of health-associated strains. In some embodiments, health-associated microbes inhibit the growth of pathogenic microbes or disease associated microbes. In some embodiments, health-associated microbes out-compete pathogenic or disease associated microbes. In certain embodiments, the skin disorder is selected from at least one of acne vulgaris (acne), eczema, seborrheic dermatitis, psoriasis, or rosacea. In some embodiments, the skin disorder is acne.

[0086] In certain embodiments, health-associated microbes disclosed herein are associated with desirable health, optimal health or improved health relative to the health of a subject with a disease, disorder or condition disclosed herein. Desirable health, optimal health or improved health may be characterized as free of a condition, disorder or disease. Desirable health, optimal health or improved health may be characterized as free of one or more symptoms of a condition, disorder or disease. Desirable health, optimal health or improved health may be characterized as free of all symptoms of a condition, disorder or disease. Desirable health, optimal health or improved health may be characterized as improved health relative to health with a disease, disorder or condition. In certain embodiments, the health-associated microbe is associated with optimal, desirable or improved skin health. In certain embodiments, the health-associated microbe is associated with optimal, desirable or improved oral health. In certain embodiments, the health-associated microbe is associated with optimal, desirable or improved digestive health. In certain embodiments, the health-associated microbe is a *P. acnes* strain associated with skin health, oral health, digestive health, or any combination thereof, that is optimal, desirable or improved relative to respective health-associated with a condition, disorder or disease.

[0087] In certain embodiments, there is a statistically significant difference in the presence of the health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 10% greater quantity of a health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 50% greater quantity of a health-associated microbe on the skin of an individual free of a

disease when compared to an individual with the disease. In certain embodiments, there is at least about a 100% greater quantity of a health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 2-fold greater presence of the health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 3-fold greater presence of the health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 5-fold greater presence of the health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease. In certain embodiments, there is at least about a 10-fold greater presence of the health-associated microbe on the skin of an individual free of a disease when compared to an individual with the disease.

[0088] In certain embodiments, the health-associated microbe is an isolated species of bacteria. In certain embodiments, the health-associated microbe is a purified species of bacteria. In certain embodiments, the health-associated microbe is an isolated and purified species of bacteria. In certain embodiments, the health-associated microbe is an isolated strain of bacteria. In certain embodiments, the health-associated microbe is a purified strain of bacteria. In certain embodiments, the health-associated microbe is an isolated and purified strain of bacteria. In certain embodiments, the health-associated microbe is an isolated species of *Propionibacterium*. In certain embodiments, the health-associated microbe is a purified species of *Propionibacterium*. In certain embodiments, the health-associated microbe is an isolated and purified species of *Propionibacterium*. In certain embodiments, the health-associated microbe is an isolated strain of *P. acnes*. In certain embodiments, the health-associated microbe is a purified strain of *P. acnes*. In certain embodiments, the health-associated microbe is an isolated and purified strain of *P. acnes*.

[0089] As described herein, some strains of *P. acnes* are associated with acne and some strains of *P. acnes* are associated with skin free of acne or disease. These *P. acnes* strains can be differentiated at the genetic level by using nucleic acid sequence determination methods known in the art such as PCR, restriction mapping, Sanger sequencing, and next-generation sequencing. In some instances, a health-associated microbe disclosed herein is beneficial for the treatment of a specific skin disorder, but not all skin disorders. In some instances, a health-associated microbe disclosed herein is beneficial for the treatment of a plurality of skin disorder, but not all skin disorders. In some instances, a health-associated microbe disclosed herein is beneficial for the treatment any skin disorder. By way of non-limiting example, a

health-associated microbe disclosed herein may be beneficial only for acne, but not for eczema, seborrheic dermatitis, or psoriasis. In another instance, a health-associated microbe disclosed herein is beneficial only for eczema, but not for acne, seborrheic dermatitis, or psoriasis. In another instance, a health-associated microbe disclosed herein is beneficial only for psoriasis, but not for acne, seborrheic dermatitis, or eczema. In another instance, a health-associated microbe disclosed herein is beneficial only for seborrheic dermatitis, but not for psoriasis, acne, or eczema. In some instances, a health-associated microbe disclosed herein is beneficial for eczema, acne and psoriasis. In some instances, a health-associated microbe disclosed herein is beneficial for acne and a condition selected from eczema, seborrheic dermatitis. In some instances, a health-associated microbe disclosed herein is beneficial for eczema, seborrheic dermatitis, acne and psoriasis.

[0090] In certain embodiments, compositions disclosed herein comprise at least one health-associated microbe, wherein the health-associated microbe is a strain of *P. acnes* or bacteria that is associated with healthy or normal skin. In certain embodiments, compositions disclosed herein comprise at least one health-associated microbe, wherein the health-associated microbe is a strain of *P. acnes* or bacteria that produces low levels of inflammatory mediators when incubated with a subject's own keratinocytes or pooled keratinocytes from multiple subjects.

[0091] In certain embodiments, compositions comprise an isolated *Propionibacterium* strain. In some embodiments the isolated *Propionibacterium* strain is a purified strain. In certain embodiments, compositions comprise a mixture of about 2 to about 10 isolated *Propionibacterium* strains. In certain embodiments, compositions comprise a mixture of about 3 to about 8 isolated *Propionibacterium* strains. In certain embodiments, compositions comprise a mixture of about 2 to about 5 isolated *Propionibacterium* strains. In certain embodiments, compositions comprise a mixture of about 3 to about 6 isolated *Propionibacterium* strains. In certain embodiments, the isolated *Propionibacterium* strain is isolated based on its phylotype or ribotype. *Propionibacterium* strains are disclosed throughout the instant specification.

[0092] In certain embodiments, compositions consist essentially of an isolated *Propionibacterium* strain and a pharmaceutically acceptable excipient or biological stabilizer. In certain embodiments, compositions consist essentially of two isolated *Propionibacterium* strains and a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments the isolated *Propionibacterium* strain is a purified strain. In certain embodiments, compositions consist essentially of about 2 to about 10 isolated

Propionibacterium strains, and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 8 isolated *Propionibacterium* strains, and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 2 to about 5 isolated *Propionibacterium* strains, and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 6 isolated *Propionibacterium* strains, and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, the isolated strain is isolated based on its phylotype or ribotype. Exemplary *Propionibacterium* strains and a pharmaceutically acceptable excipient or biological stabilizer are described throughout the instant specification.

[0093] In certain embodiments, compositions consist essentially of an isolated *Propionibacterium* strain, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of two isolated *Propionibacterium* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In some embodiments the isolated *Propionibacterium* strain is a purified strain. In certain embodiments, compositions consist essentially of about 2 to about 10 isolated *Propionibacterium* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 8 isolated *Propionibacterium* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 2 to about 5 isolated *Propionibacterium* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 6 isolated *Propionibacterium* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, the isolated strain is isolated based on its phylotype or ribotype. Exemplary *Propionibacterium* strains and a pharmaceutically acceptable excipient or biological stabilizer are described throughout the instant specification.

[0094] In certain embodiments, compositions comprise an isolated *P. acnes* strain. In some embodiments the isolated *P. acnes* strain is a purified strain. In certain embodiments, compositions comprise a mixture of about 2 to about 10 isolated *P. acnes* strains. In certain

embodiments, compositions comprise a mixture of about 3 to about 8 isolated *P. acnes* strains. In certain embodiments, compositions comprise a mixture of about 2 to about 5 isolated *P. acnes* strains. In certain embodiments, compositions comprise a mixture of about 3 to about 6 isolated *P. acnes* strains. In certain embodiments, the isolated *P. acnes* strain is isolated based on its phylotype or ribotype.

[0095] In certain embodiments, compositions consist essentially of an isolated *P. acnes* strain and a pharmaceutically acceptable excipient or biological stabilizer. In certain embodiments, compositions consist essentially of two isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer. In some embodiments the isolated *P. acnes* strain is a purified strain. In certain embodiments, compositions consist essentially of about 2 to about 10 isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 8 isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 2 to about 5 isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 6 isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein. In certain embodiments, the isolated strain is isolated based on its phylotype or ribotype. Exemplary *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer are described throughout the instant specification.

[0096] In certain embodiments, compositions consist essentially of an isolated *P. acnes* strain, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of two isolated *P. acnes* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In some embodiments the isolated *P. acnes* strain is a purified strain. In certain embodiments, compositions consist essentially of about 2 to about 10 isolated *P. acnes* strains, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 8 isolated *P. acnes* strain, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 2 to about 5 isolated *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer disclosed herein, a

pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, compositions consist essentially of about 3 to about 6 isolated *P. acnes* strain, a pharmaceutically acceptable excipient or biological stabilizer, and at least one additional active ingredient disclosed herein. In certain embodiments, the isolated strain is isolated based on its phylotype or ribotype. Exemplary *P. acnes* strains and a pharmaceutically acceptable excipient or biological stabilizer are described throughout the instant specification.

[0097] In certain embodiments, compositions disclosed herein comprise at least one *P. acnes* strain having a health-associated phylotype. In certain embodiments, the health-associated phylotype is selected from type I, type II, and type III. In certain embodiments, the health-associated phylotype is type I. In certain embodiments, the health-associated phylotype is type II. In some embodiments, compositions disclosed herein comprise at least two *P. acnes* strains having health-associated phylotypes, wherein the health-associated phylotypes are a combination of type I, type II, and type III. In certain embodiments, the type I phylotype is selected from type IA, type IB, and type IC. In certain embodiments, the type I phylotype is type IB. In certain embodiments, the type IA phylotype is selected from type IA₁ and type IA₂. Strains can be phylotyped as in McDowell et al. (PLoS ONE 8(9): e70897 (2013)). A non-limiting example of a *P. acnes* strain having a type I phylotype is *P. acnes* subsp. *acnes* (American Tissue Culture Collection accession numbers: NCTC 737T, ATCC6919T; Japanese Collection of Microorganisms accession number: JCM 6425T; Culture Collection, University of Göteborg, Sweden accession number: CCUG 1794T). A non-limiting example of a *P. acnes* strain having a type II phylotype is *P. acnes* subsp. *defendens* (Japanese Collection of Microorganisms accession number: JCM 6473, Culture Collection, University of Göteborg, Sweden accession number: CCUG 6369).

[0098] In some embodiments, compositions disclosed herein comprise a combination of health-associated microbes, wherein the health-associated microbes comprise a combination of healthy strains of *P. acnes*. In some embodiments, combinations of healthy strains of *P. acnes* comprise a combination of strains of *P. acnes* of a plurality of ribotypes. In some embodiments, the plurality of ribotypes comprises at least two ribotypes selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10. In some embodiments, the plurality of ribotypes comprises at least two ribotypes selected from RT1, RT2 and RT3. In certain embodiments, the plurality of ribotypes comprises at least two ribotypes selected from RT1, RT2, RT3 and not RT6. In certain embodiments, the plurality of ribotypes comprises ribotypes selected from RT1 and RT2. In certain embodiments, the plurality of ribotypes comprises ribotypes selected

from RT1 and RT3. In certain embodiments, the plurality of ribotypes comprises ribotypes selected from RT2 and RT3. In certain embodiments, the plurality of ribotypes comprises RT1, but not RT6. In certain embodiments, the plurality of ribotypes comprises RT2, but not RT6.

[0099] In some embodiments, compositions disclosed herein comprise a combination of health-associated microbes, wherein the health-associated microbes comprise a combination of healthy strains of *P. acnes*. In some embodiments, the combination comprises a first strain of *P. acnes* and a second strain of *P. acnes*. In some embodiments, the first strain of *P. acnes* is of a first ribotype and a second strain of *P. acnes* is of a second ribotype. In some embodiments, the first ribotype and the second ribotype are the same. In some embodiments, the first ribotype and the second ribotype are different. In some embodiments, the first ribotype is RT1 and the second ribotype is RT1. In some embodiments, the first ribotype is RT2 and the second ribotype is RT2. In some embodiments, the first ribotype is RT1 and the second ribotype is RT2. In some embodiments, the first ribotype is RT1 and the second ribotype is RT3. In some embodiments, the first ribotype is RT2 and the second ribotype is RT3. In some embodiments, the first ribotype is RT1 and the second ribotype is not RT6. In some embodiments, the first ribotype is RT2 and the second ribotype is not RT6. In some embodiments, the first ribotype is RT3 and the second ribotype is not RT6.

[00100] In some embodiments, compositions disclosed herein comprise healthy strains of *P. acnes*, and do not comprise any other type of microbe or bacteria. In some embodiments, health-associated microbes disclosed herein comprise at least one health-associated strain of *P. acnes*, wherein the health-associated strain of *P. acnes* has a ribotype of RT1 or RT2. In some embodiments, health-associated microbes disclosed herein do not comprise a strain of *P. acnes*, other than a health-associated strain of *P. acnes* disclosed herein that has a ribotype selected from RT1 and RT2. In some embodiments, the health-associated microbes do not comprise a strain of *P. acnes* that has a ribotype RT6. In some embodiments, the health-associated microbes do not comprise a strain of *P. acnes* that expresses DNA binding response regulator or phosphoglycerate kinase, as described herein. In some embodiments, the health-associated microbes comprise a strain of *P. acnes* that expresses an ATP binding cassette transporter, as described herein.

[00101] In certain embodiments, the health-associated microbe does not comprise a strain with a sequence that is 95%, 97%, 98%, 99% or 100% homologous to a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, and SEQ ID NO: 54. In certain embodiments, the health-associated microbe does not comprise a strain with a sequence that

is more than 50% homologous to a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, and SEQ ID NO: 54. In certain embodiments, the health-associated microbe does not comprise a strain with a sequence selected from SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53.

[00102] In certain embodiments, compositions disclosed herein comprise a health-associated microbe, wherein the health-associated microbe is *Lactobacillus reuteri* (referred to herein as *L. reuteri*), or a strain thereof. In certain embodiments, compositions disclosed herein comprise at least one *L. reuteri* strain selected from Korean Collection for Type Cultures (KCTC) deposited strains, such as KCTC 3679, KCTC 3594, KCTC 3678, and any combination thereof.

[00103] In certain embodiments, compositions disclosed herein comprise a health-associated microbe, wherein the health-associated microbe is *Staphylococcus epidermidis* (*S. epidermidis*). In certain embodiments, compositions disclosed herein comprise at least one *S. epidermidis* strain selected from 14.1.R1, AS1, AU 10, AU16, AU21, AU23, AU24, AU35, AU36, AU39, AU40, AU 44, AU48, AU53, AU60, AU73, AU81, FS1, G53, IS2, and a combination thereof.

Selected, transformed, or engineered bacteria

[00104] In certain embodiments, the compositions described herein comprise one or more strains of bacteria that is selected, transformed or engineered with a gene or gene mutation that is beneficial for a skin disorder. Thus, the bacteria have been transformed into a “non-pathogenic” form, or a health-associated form from a disease-associated form. In certain embodiments, a gene that contributes to pathogenesis of a skin disorder is deleted or mutated to inactivate or reduce the corresponding gene product. In certain embodiments, a gene that reduces the pathogenesis of a skin disorder is added, or mutated to activate or increase levels of the corresponding gene product. In certain embodiments, the bacteria are grown and selected from culture or selected from healthy disease free individuals.

[00105] In certain embodiments, selected, transformed, or engineered bacteria are to be delivered as a health-associated microbe via compositions and methods disclosed herein. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein comprise a gene encoding a deoxyribose operon repressor (*deoR*). In certain embodiments, selected, transformed, or engineered bacteria disclosed herein express a deoxyribose operon repressor. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein comprise a gene encoding a Type II lipase. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein express Type II lipase. By way of non-limiting example,

the Type II lipase may be a glycerol-ester hydrolase B (GehB). In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not comprise a gene encoding Type I lipase. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not express a Type I lipase. By way of non-limiting example, the type I lipase may be a glycerol-ester hydrolase A (GehA). In certain embodiments, selected, transformed, or engineered bacteria do not comprise a pIMPLE plasmid. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein comprise a gene encoding an ABC transporter. In certain embodiments, selected, transformed, or engineered bacteria express an ABC transporter. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not comprise a gene encoding a phosphoglycerate kinase. In certain embodiments, selected, transformed, or engineered bacteria do not comprise a phosphoglycerate kinase. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not comprise a gene encoding a DNA binding response regulator. In certain embodiments, selected, transformed, or engineered bacteria do not comprise a DNA binding response regulator.

[00106] In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not express a dermatan-sulfate adhesin (*e.g.*, DSA1, DSA2). In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not comprise a nucleic acid encoding a dermatan-sulfate adhesin (*e.g.*, DSA1, DSA2). The absence or deletion of dermatan-sulfate adhesins may disable adhesion of microbes to keratinocytes.

[00107] In certain embodiments, selected, transformed, or engineered bacteria disclosed herein express a hyaluronidase. In some embodiments, the hyaluronidase is a hyaluronidase expressed by a Group B *Streptococcus* strain of bacteria. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not express a hyaluronidase. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein comprise a nucleic acid encoding a hyaluronidase. In some embodiments, the nucleic acid encodes a hyaluronidase expressed by a Group B *Streptococcus* strain of bacteria. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein do not comprise a nucleic acid encoding a hyaluronidase. In certain embodiments, a strain of bacteria that is selected, transformed, or engineered bacteria is present or has increased expression of a hyaluronidase gene relative to the strain of bacteria when it is not selected, transformed, or engineered. In certain embodiments, a strain of bacteria that is selected, transformed, or engineered bacteria is present or has increased hyaluronidase activity relative to the strain of bacteria when it is not selected, transformed, or engineered. In certain embodiments, a strain

of bacteria that is selected, transformed, or engineered bacteria is present or has reduced hyaluronidase activity relative to the strain of bacteria when it is not selected, transformed, or engineered. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein lack a hyaluronidase gene.

[00108] In certain embodiments, selected, transformed, or engineered bacteria disclosed herein have reduced transposase 2 enzyme activity. In certain embodiments, the mRNA for transposase 2 is not produced or is produced in lower quantities than a wildtype transposase 2 enzyme. In certain embodiments, the genomic sequence of the transposase 2 gene has been selected or altered in such a way as to preclude translation into a functional protein. In certain embodiments, the genomic sequence of the transposase 2 gene has been selected or altered in such a way as to preclude translation into a functional protein such as the introduction of a premature stop-codon in the body of the gene sequence. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein lack transposase 2 enzyme activity. In certain embodiments, a selected, transformed, or engineered strain of bacteria disclosed herein has reduced activity relative to the strain when it is not selected, transformed, or engineered, respectively. An exemplary DNA sequence encoding transposase 2 is shown in Table 2.

[00109] In certain embodiments, selected, transformed, or engineered bacteria disclosed herein confer an antibiotic sensitivity to macrolide and tetracycline antibiotics. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein have an absence or deletion of a thiopeptide encoding island, respectively. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein have a presence or addition of a tyrosine decarboxylase island (which increases intracellular pH under stress to tolerate acidic environments), respectively. In certain embodiments, selected, transformed, or engineered bacteria disclosed herein have an ability to metabolize gelatin.

[00110] In certain embodiments, selected, transformed, or engineered bacteria comprise selected, transformed, or engineered *S. epidermis*, respectively. In certain embodiments, the selected, transformed, or engineered bacteria comprise selected, transformed, or engineered *P. acnes*.

[00111] In certain embodiments, the bacteria are transformed using recombinant DNA techniques known in the art. In certain embodiments, the bacteria are transformed by growing bacteria under selective pressure to acquire or lose a gene, gene product, or expression thereof. In a certain embodiment, the bacteria are transformed using CRISPR technology. In a certain embodiment, the bacteria are transformed using homologous recombination.

[00112] In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype selected from RT1, RT2, RT3, RT4, RT5, RT7, RT8, RT9, and RT10. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype selected from RT1, RT2, RT3, and not RT6. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype selected from RT1, RT2 and RT3. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype of RT1. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype of RT2. In certain embodiments, the selected, transformed, or engineered bacteria comprise a selected, transformed, or engineered *P. acnes* strain, wherein the selected, transformed, or engineered *P. acnes* strain has a ribotype of RT3. In certain embodiments, the selected, transformed, or engineered bacteria are an RT1 strain of *P. acnes*. In certain embodiments, the selected, transformed, or engineered bacteria are an RT2 strain of *P. acnes*. In certain embodiments, the selected, transformed, or engineered bacteria are an RT3 strain of *P. acnes*. In certain embodiments, the selected, transformed, or engineered bacteria are not an RT6 strain of *P. acnes*.

[00113] In some embodiments, compositions disclosed herein comprise health-associated microbes that are considered safe for administration to skin of a human subject. In some instances, compositions that are safe for administration to skin of a human subject comprise selected, transformed, or engineered bacteria. In some instances, compositions that are safe for administration to skin of a human subject comprise a selected, transformed, or engineered

P. acnes strain. Safety can be measured on a number of scales, including biosafety levels characterized by the United States Centers for Disease Control and Prevention (CDC). In other countries, facilities that manipulate biological agents may characterize safety of such agents according to a Pathogen or Protection Level. Generally strains disclosed herein for use in compositions and methods disclosed herein are characterized as Biosafety Level 1 (BSL1) or Pathogen Level 1 (P1) by an accredited third party. These are characterized as presenting no or low risk of causing disease or infection. Preferably, strains disclosed herein present no risk of causing disease or infection.

Markers

[00114] Disclosed herein are compositions that comprise at least one health-associated microbe. Health-associated microbes disclosed herein generally comprise at least one strain of bacteria, wherein the at least one strain of bacteria exhibits a health-associated presence, health-associated absence or health-associated expression level of at least one marker. In some instances, health-associated expression of the at least one marker is a lack of expression. In some instances, health-associated expression of the at least one marker is expression that is low as compared to expression of the at least one marker in a reference strain. In some instances, the reference strain is a pathogenic strain. In some instances, the reference strain is not a health-associated strain. In some instances, health-associated expression of the at least one marker is expression that is high as compared to expression of the at least one marker in a reference strain.

[00115] In some embodiments, the marker is a nucleic acid. In some embodiments, the nucleic acid comprises a gene encoding the marker or a portion thereof. In some embodiments, the nucleic acid is a gene encoding the marker or a portion thereof. In some embodiments, the marker is a protein. In some embodiments, the marker is a peptide (*e.g.*, less than or equal to 100 amino acids). In some embodiments, the marker is not a nucleic acid or a protein. Non-limiting examples of a marker that neither comprises a nucleic acid or protein include glycans and lipids.

[00116] Exemplary markers of health-associated microbes disclosed herein include, but are not limited to, a deoxyribose operon repressor, a CRISPR associated protein (Cas), a lipase, an ATP binding cassette transporter, a DNA binding response regulator, a phosphoglycerate kinase, dermatan-sulfate adhesin, and hyaluronidase. In some instances, the at least one strain of bacteria comprises a plasmid. In some instances, presence or absence of the plasmid is a marker. By way of non-limiting example, the plasmid may be a pIMPLE plasmid disclosed herein. As further described herein, *presence* of a *deoR*, a type II lipase, an ABC

transporter, or a Cas5, or a combination thereof, is generally associated with health-associated microbes disclosed herein. In contrast, health-associated microbes disclosed herein are generally associated with an *absence* or low expression of a pIMPLE plasmid, a type I lipase, a DNA binding response regulator, a phosphoglycerate kinase, or dermatan-sulfate adhesin, or a combination thereof. However, it would be understood to one of skill in the art that nature presents exceptions to such generalities. Therefore, expression patterns of these markers that are alternative or contrary to those described herein are contemplated as well. Compositions comprising one or more strains characterized by such markers are further characterized herein, including the description as follows.

deoR

[00117] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a nucleic acid encoding a deoxyribose operon repressor (*deoR*) protein. In some embodiments, the marker is a nucleic acid encoding a deoxyribose operon repressor (*deoR*). In some embodiments, the *deoR* is a *deoR* family transcriptional regulator expressed in *Propionibacterium acnes* subsp. *defendens* (ATCC 11828, GenBank: AER05724.1). In certain embodiments, the at least one strain of bacteria has been selected, transformed, or engineered to acquire the presence of the *deoR*. In certain embodiments, the *deoR* has a sequence that is at least 80% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is at least 90% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is at least 95% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is at least 97% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is at least 98% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is at least 99% homologous to SEQ ID NO: 1. In certain embodiments, the *deoR* has a sequence that is 100% homologous to SEQ ID NO: 1. In certain embodiments, the at least one strain of bacteria has greater expression or activity of a deoxyribose operon repressor than a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain has at least about 1.5-fold, at least about 2-fold, at least about 3-fold, at least about 5-fold or at least about 10-fold greater expression or activity of the deoxyribose operon repressor as compared to the reference strain.

pIMPLE plasmid

[00118] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria lacks a pIMPLE plasmid. In some embodiments, the at least one strain of bacteria lacks an entire pIMPLE plasmid. In some

embodiments, the at least one strain of bacteria has a low percentage of a pIMPLE plasmid (*e.g.*, <10%). In some embodiments, the low percentage of pIMPLE plasmid is less than 5%. In some embodiments, the low percentage of pIMPLE plasmid is less than 1%. In some embodiments, the low percentage of pIMPLE plasmid is less than 0.5%. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a pIMPLE plasmid. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 80% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 90% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 95% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 97% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 98% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is at least about 99% homologous to SEQ ID NO: 2. In certain embodiments, the pIMPLE plasmid has a sequence that is 100% homologous to SEQ ID NO: 2. In certain embodiments, a plasmid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 2 is partially or completely deleted from the at least one strain of bacteria. In certain embodiments, a plasmid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 2 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the a selected, transformed, or engineered strain of bacteria. In certain embodiments, the at least one strain of bacteria contains portions of a complete pIMPLE plasmid (SEQ ID NO: 2). In certain embodiments, the at least one strain of bacteria may comprise less than about 25%, 20%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6% of the complete pIMPLE sequence set forth in SEQ ID NO: 2. In certain embodiments, the at least one strain of bacteria does not comprise a specific portion of the pIMPLE plasmid that is present in an RT6 strain or any other disease associated strain. In certain embodiments, the at least one strain of bacteria comprises a low copy number of a pIMPLE plasmid (SEQ ID NO: 2).

[00119] In certain embodiments, the at least one strain of bacteria comprises less than five copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria comprises less than four copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria comprises less than three copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria comprises less than two copies of pIMPLE plasmid per bacterial genome. In certain

embodiments, the at least one strain of bacteria comprises one copy of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria comprises less than one copy of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria comprises less than a half of a copy of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria does not more than five copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria does not comprise more than four copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria does not comprise more than three copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria does not comprise more than two copies of pIMPLE plasmid per bacterial genome. In certain embodiments, the at least one strain of bacteria does not comprise more than one copy of pIMPLE plasmid per bacterial genome.

[00120] In certain embodiments, the at least one strain of bacteria comprises a low percentage of pIMPLE plasmid (SEQ ID NO: 2). In certain embodiments, the bacteria comprise less than about 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1% pIMPLE plasmid. In certain embodiments, the at least one strain of bacteria comprises less than about 1.0%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1% pIMPLE plasmid. pIMPLE plasmid percentage can be determined by next-generation sequencing of *P. acnes* bacteria, as % reads aligned. In certain embodiments, the pIMPLE percentage is percentage of total sequencing reads that align to pIMPLE from HL096PA1 (an RT5).

Lipases

[00121] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a nucleic acid encoding a lipase. In some instances, the lipase is a lipase expressed by a strain of *P. acnes*. By way of non-limiting example, a lipase expressed by a strain of *P. acnes* may be a triacylglycerol lipase, a lysophospholipase, a phospholipase, a GDSL-like protein, an esterase, acyl hydrolase or a hydrolase. In some embodiments, the marker is a nucleic acid encoding a lipase. In some embodiments, the marker is an absence of a nucleic acid encoding a lipase. In some embodiments, compositions disclosed herein comprise a strain of bacteria that expresses a lipase. In some embodiments, the lipase is Type I lipase. In some embodiments, the lipase is Type II lipase. In some embodiments, the compositions disclosed herein comprise a strain of bacteria that does not express a lipase. In some embodiments, the compositions disclosed herein comprise a strain of bacteria that does not express a Type I lipase. In some

embodiments, the compositions disclosed herein comprise a strain of bacteria that does not express a Type II lipase. In some embodiments, the strain of bacteria comprises a nucleic acid encoding a Type II lipase. Type I lipase and Type II lipase, as described herein, may be encoded by a similar nucleic acid. For example, a gene encoding Type I lipase will encode a Type II lipase upon a 6bp deletion in the intergenic region and a single base deletion, the latter causing a frameshift that creates premature STOP codon, see, *e.g.*, **FIG. 7**.

Type I lipase

[00122] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not express a Type I lipase. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a Type I lipase. In certain embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria has been selected, transformed, or engineered for an absence of Type I lipase expression or activity. In certain embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria has been selected, transformed, or engineered for the presence of Type I lipase expression or activity. In certain embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the strain has been selected, transformed, or engineered for lower expression or activity of Type I lipase relative to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, at least one strain of bacteria has at least about 1.5-fold lower expression or activity of Type I lipase compared to the reference strain. In certain embodiments, at least one strain of bacteria has at least about 2-fold lower expression or activity of Type I lipase compared to the reference strain. In certain embodiments, at least one strain of bacteria has at least about 3-fold lower expression or activity of Type I lipase compared to the reference strain. In certain embodiments, at least one strain of bacteria has at least about 5-fold lower expression or activity of Type I lipase compared to the reference strain. In certain embodiments, at least one strain of bacteria has at least about 10-fold lower expression or activity of Type I lipase compared to the reference strain.

[00123] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria expresses a Type I lipase. In certain embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria has been selected, transformed, or engineered for the presence of Type I lipase expression or activity. In certain embodiments, compositions

disclosed herein comprise at least one strain of bacteria, wherein the strain has been selected, transformed, or engineered for greater expression or activity of Type I lipase relative to the reference strain.

[00124] In some embodiments, at least a portion of the Type I lipase is encoded by a sequence of SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 80% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 90% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 95% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 97% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 98% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 99% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 80% homology to SEQ ID NO: 10. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence of SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 80% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 90% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 95% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 97% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 98% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 99% homology to SEQ ID NO: 60. In some embodiments, at least a portion of the Type I lipase is encoded by a sequence that is at least 80% homology to SEQ ID NO: 60.

[00125] In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 10 is partially or completely deleted from the at least one strain. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 3 prime end

of the nucleic acid. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 5 prime end of the nucleic acid.

[00126] In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 10 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the at least one strain. In certain embodiments, at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% of the nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 10 is disrupted.

Type II lipase

[00127] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria expresses a Type II lipase. A non-limiting example of a Type II lipase is Lipase ADE00051, HMPREF0675_4856. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a nucleic acid encoding a Type II lipase. In certain embodiments, the at least one strain of bacteria has been selected, transformed, or engineered to express a Type II lipase. In certain embodiments, the at least one strain of bacteria has at least about 1.5-fold greater expression or activity of Type II lipase compared to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain of bacteria has at least about 2-fold greater expression or activity of Type II lipase compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 3-fold greater expression or activity of Type II lipase compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 5-fold greater expression or activity of Type II lipase compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 10-fold greater expression or activity of Type II lipase compared to the reference strain.

[00128] In some embodiments, at least a portion of the type II lipase is expressed from a nucleic acid comprising SEQ ID NO.: 61. SEQ ID NO.: 61 is found in the complete circular genome of *Propionibacterium acnes* ATCC 11828 and starts at position 390,423 of ATCC 11828. The following subsequent positions are in reference to the first nucleotide of SEQ ID NO.: 61. The lipase coding sequence is bases 22-1032, referred to herein as ADE0051, HMPREF0675_4856, and SEQ ID NO.: 3. Bases 1-21 is an intergenic region. Type II Lipase has a G in position 7 and an A in position 16. In some embodiments, at least a portion of the type I lipase is expressed from a nucleic acid comprising SEQ ID NO.: 60. In contrast, relative to SEQ ID NO. 61, SEQ ID NO. 60 has a 6bp sequence TAGATA inserted between base pairs 1 and 2, an A in position 7, a G in position 16, and a G between base pairs 145 and 146. SEQ ID NO.: 60 and SEQ ID NO.: 61 are shown in **Table 2**. **FIG. 7** also illustrates the differences between sequences encoding Type I lipase and Type II lipase.

[00129] In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 90% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 95% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 97% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 97% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 99% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with 100% homology to SEQ ID NO: 3. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 90% homology to SEQ ID NO: 61. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 95% homology to SEQ ID NO: 61. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 97% homology to SEQ ID NO: 61. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 97% homology to SEQ ID NO: 61. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with at least about 99% homology to SEQ ID NO: 61. In certain embodiments, at least a portion of the Type II lipase is encoded by a nucleic acid with 100% homology to SEQ ID NO: 61.

CRISPR/Cas5

[00130] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a genetic locus of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) or at least a portion of a CRISPR locus. Generally a CRISPR locus comprises at least one spacer sequence and one repeat sequence that helps a bacteria harboring a CRISPR associated protein (Cas) recognize and cleave foreign DNA, such as that of a virus or phage. In some instances, the CRISPR locus does not comprise a Cas encoding sequence. The at least one strain of bacteria may be a strain of *P. acnes*. The CRISPR locus may be a region of DNA in *P. acnes* that is amplified by primers with sequences of SEQ ID 435 and SEQ ID 436. The CRISPR locus may comprise at least one CRISPR spacer sequence. The CRISPR locus may comprise at least about 10 nucleotides, at least about 15 nucleotides, at least about 20 nucleotides, at least about 25 nucleotides, or at least about 30 nucleotides of a CRISPR spacer sequence.

[00131] A CRISPR locus disclosed herein may comprise at least two different CRISPR spacer sequences. The CRISPR locus may comprise at least three different CRISPR spacer sequences. The CRISPR locus may comprise at least four different CRISPR spacer sequences. The CRISPR locus may comprise at least five different CRISPR spacer sequences. The CRISPR locus may comprise at least six different CRISPR spacer sequences. The CRISPR locus may comprise at least seven different CRISPR spacer sequences. The CRISPR locus may comprise at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve different CRISPR sequences. The CRISPR locus may comprise up to about 50 different CRISPR sequences. The CRISPR locus may comprise up to about 100 different CRISPR sequences. The CRISPR locus may comprise up to about 1000 different CRISPR sequences. The CRISPR locus may comprise at least one CRISPR repeat sequence. The CRISPR locus may comprise at least about 10 nucleotides, at least about 15 nucleotides, at least about 20 nucleotides, at least about 25 nucleotides, or at least about 30 nucleotides of a CRISPR repeat sequence. A larger repertoire of spacer sequences indicates the strain has acquired more phage DNA and, thus, possesses greater immunity from phages relative to a strain that has fewer spacer sequences.

[00132] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria expresses a CRISPR-associated protein (Cas). By way of non-limiting example, the CRISPR-associated proteins include Cas5, Cas9,

Cpf1, Cas3, Cas8a, Cas8b, Cas8c, Cas10d, Cse1, Cse2, Csy1, Csy2, Csy3, GSU0054, Cas10, Csm2, Cmr5, Cas10, Csx11, Csx10, Csf1, Csn2, Cas4, C2cl, C2c3, and C2c2.

[00133] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria expresses a Cas5. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a nucleic acid encoding a Cas5. In certain embodiments, the at least one strain of bacteria has been selected, transformed, or engineered to express a Cas5. In certain embodiments, the at least one strain of bacteria has at least about 1.5-fold greater expression or activity of Cas5 compared to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain of bacteria has at least about 2-fold greater expression or activity of Cas5 compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 3-fold greater expression or activity of Cas5 compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 5-fold greater expression or activity of Cas5 compared to the reference strain. In certain embodiments, the at least one strain of bacteria has at least about 10-fold greater expression or activity of Cas5 compared to the reference strain.

[00134] In some instances, the at least one strain of bacteria expresses Cas5. In some embodiments, a strain of *P. acnes* is characterized as a health-associated *P. acnes* or a disease-associated *P. acnes* based on the presence of Cas5. In some embodiments, Cas5 is found in *P. acnes* strain ATCC 11828. In some embodiments, Cas5 is encoded by a sequence as set forth in SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is at least about 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% homologous to SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is about 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is about 95% homologous to SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is about 97% homologous to SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is about 99% homologous to SEQ ID NO: 8. In some embodiments, Cas5 is encoded by a sequence that is about 100% homologous to SEQ ID NO: 8.

[00135] In some instances, the at least one strain of bacteria comprises a nucleic acid encoding Cas5, wherein the nucleic acid comprises at least about 10, at least about 20, at least about 30, at least about 40, at least about 50, at least about 60, at least about 70, at least about

80, at least about 90, at least about 100, at least about 110, at least about 120, at least about 130, at least about 140, at least about 150, at least about 160, at least about 170, at least about 180, at least about 190, at least about 200, at least about 210, at least about 220, at least about 230, at least about 240, at least about 250, at least about 260, at least about 270, at least about 280, at least about 290, at least about 300, at least about 310, at least about 320, at least about 330, at least about 340, at least about 350, at least about 360, at least about 370, at least about 380, at least about 390, at least about 400, at least about 410, at least about 420, at least about 430, at least about 440, at least about 450, at least about 460, at least about 470, at least about 480, at least about 490, at least about 500, at least about 550, at least about 650, at least about 700, or more than about 700 consecutive bases of SEQ ID NO: 8. In some instances, the at least one strain of bacteria comprises a nucleic acid encoding Cas5, wherein the nucleic acid comprises about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80, about 90, about 100, about 110, about 120, about 130, about 140, about 150, about 160, about 170, about 180, about 190, about 200, about 210, about 220, about 230, about 240, about 250, about 260, about 270, about 280, about 290, about 300, about 310, about 320, about 330, about 340, about 350, about 360, about 370, about 380, about 390, about 400, about 410, about 420, about 430, about 440, about 450, about 460, about 470, about 480, about 490, about 500, about 550, about 650, about 700, or more than about 700 consecutive bases of SEQ ID NO: 8.

ABC transporter

[00136] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises an ATP-binding cassette transporter. In certain embodiments, the at least one strain of bacteria comprises a nucleic acid encoding an ATP-binding cassette transporter (ABC transporter). In certain embodiments, the at least one strain of bacteria is selected for expression or overexpression of a nucleic acid encoding an ABC transporter. In certain embodiments, the at least one strain of bacteria is selected for increased activity of an ABC transporter. In certain embodiments, the at least one strain of bacteria is selected for the presence of a nucleic acid encoding an ABC transporter. In certain embodiments, the at least one strain of bacteria is transformed for overexpression of a nucleic acid encoding an ABC transporter. In certain embodiments, the at least one strain of bacteria is transformed for increased activity of an ABC transporter. In certain embodiments, the at least one strain of bacteria is transformed for the presence of a nucleic acid encoding an ABC transporter. In certain embodiments, the at least one strain of bacteria is engineered for overexpression of a nucleic acid encoding an ABC transporter. In

certain embodiments, the at least one strain of bacteria is engineered for increased activity of an ABC transporter. In certain embodiments, the at least one strain of bacteria is engineered for the presence of a nucleic acid encoding an ABC transporter. In some embodiments, the ABC transporter is a portion of a known ABC transporter. In some embodiments, the ABC transporter is a portion of a known ABC transporter, wherein the portion of the known ABC transporter can perform an activity of the known ABC transporter. In some embodiments, the ABC transporter is a portion of a known ABC transporter, wherein the portion of the known ABC transporter can perform an enzymatic activity of the known ABC transporter. In some embodiments, the ABC transporter is a portion of a known ABC transporter, wherein the portion of the known ABC transporter can perform a transport activity of the known ABC transporter.

[00137] In certain embodiments, the at least one strain has at least about 1.5-fold greater expression or activity of ABC transporter compared to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain has at least about 2-fold greater expression or activity of ABC transporter compared to the reference strain. In certain embodiments, the at least one strain has at least about 3-fold greater expression or activity of ABC transporter compared to the reference strain. In certain embodiments, the at least one strain has at least about 5-fold greater expression or activity of ABC transporter compared to the reference strain. In certain embodiments, the at least one strain has at least about 10-fold greater expression or activity of ABC transporter compared to the reference strain.

[00138] In some embodiments, ABC transporters disclosed herein are encoded by a sequence of SEQ ID NO.: 6 or a sequence that is homologous to SEQ ID NO.: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 80% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 90% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 95% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 96% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 97% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 98% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is at least about 99% homologous to SEQ ID NO: 6. In some embodiments, the ABC transporter is encoded by a sequence that is 100% homologous to SEQ ID NO: 6. In

certain embodiments, the at least one strain is (completely or partially) selected, transformed, or engineered with a nucleic acid that is at least about 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 6 is partially or completely present in the at least one strain.

DNA binding response regulator

[00139] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a DNA binding response regulator. In certain embodiments, the at least one strain does not comprise a nucleic acid encoding a DNA binding response regulator. In certain embodiments, the at least one strain has been selected for reduced expression or activity of a DNA binding response regulator. In certain embodiments, the at least one strain has been selected for an absence of a DNA binding response regulator. In certain embodiments, bacteria disclosed herein have been transformed for reduced expression or activity of a DNA binding response regulator. In certain embodiments, bacteria disclosed herein have been transformed for an absence of a DNA binding response regulator. In certain embodiments, bacteria disclosed herein have been engineered for reduced expression or activity of a DNA binding response regulator. In certain embodiments, bacteria disclosed herein have been engineered for an absence of a DNA binding response regulator.

[00140] In certain embodiments, the at least one strain of bacteria has at least about 1.5-fold less expression or activity of a DNA binding response regulator relative to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain has at least about 2-fold less expression or activity of a DNA binding response regulator relative to the reference strain. In certain embodiments, the at least one strain has at least about 3-fold less expression or activity of a DNA binding response regulator relative to the reference strain. In certain embodiments, the at least one strain has at least about 5-fold less expression or activity of a DNA binding response regulator relative to the reference strain. In certain embodiments, the at least one strain has at least about 10-fold less expression or activity of a DNA binding response regulator relative to the reference strain.

[00141] In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 90% homology to SEQ ID NO: 7. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 90% homology to SEQ ID NO: 7 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 95% homology to SEQ ID NO: 7. In certain embodiments, the at least one strain has been selected, transformed, or engineered to

express a nucleic acid with at least 95% homology to SEQ ID NO: 7 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 97% homology to SEQ ID NO: 7. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 97% homology to SEQ ID NO: 7 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 99% homology to SEQ ID NO: 7. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 99% homology to SEQ ID NO: 7 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with 100% homology to SEQ ID NO: 7. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with 100% homology to SEQ ID NO: 7 at a lower level relative to the reference strain.

[00142] In certain embodiments, the at least one strain comprises a nucleic acid that is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation, wherein the nucleic acid has 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 7, before being disrupted. For example, in certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 7 is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 3 prime end of the nucleic acid. In certain embodiments, the nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 7 is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 5 prime end of the nucleic acid.

Phosphoglycerate kinase

[00143] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a phosphoglycerate kinase. In certain embodiments, the at least one strain does not comprise a nucleic acid

encoding a phosphoglycerate kinase. In certain embodiments, the at least one strain has been selected for reduced expression or activity of a phosphoglycerate kinase. In certain embodiments, the at least one strain has been selected for an absence of a phosphoglycerate kinase. In certain embodiments, bacteria disclosed herein have been transformed for reduced expression or activity of a phosphoglycerate kinase. In certain embodiments, bacteria disclosed herein have been transformed for an absence of a phosphoglycerate kinase. In certain embodiments, bacteria disclosed herein have been engineered for reduced expression or activity of a phosphoglycerate kinase. In certain embodiments, bacteria disclosed herein have been engineered for an absence of a phosphoglycerate kinase.

[00144] In certain embodiments, the at least one strain of bacteria has at least about 1.5-fold less expression or activity of a phosphoglycerate kinase relative to a reference strain (*e.g.*, pathogenic strain, not a health-associated strain). In certain embodiments, the at least one strain has at least about 2-fold less expression or activity of a phosphoglycerate kinase relative to the reference strain. In certain embodiments, the at least one strain has at least about 3-fold less expression or activity of a phosphoglycerate kinase relative to the reference strain. In certain embodiments, the at least one strain has at least about 5-fold less expression or activity of a phosphoglycerate kinase relative to the reference strain. In certain embodiments, the at least one strain has at least about 10-fold less expression or activity of a phosphoglycerate kinase relative to the reference strain.

[00145] In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 90% homology to SEQ ID NO: 9. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 90% homology to SEQ ID NO: 9 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 95% homology to SEQ ID NO: 9. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 95% homology to SEQ ID NO: 9 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 97% homology to SEQ ID NO: 9. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with at least 97% homology to SEQ ID NO: 9 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with at least 99% homology to SEQ ID NO: 9. In certain embodiments, the at least one strain has been selected, transformed,

or engineered to express a nucleic acid with at least 99% homology to SEQ ID NO: 9 at a lower level relative to the reference strain. In certain embodiments, the at least one strain has been selected, transformed, or engineered to remove a nucleic acid with 100% homology to SEQ ID NO: 9. In certain embodiments, the at least one strain has been selected, transformed, or engineered to express a nucleic acid with 100% homology to SEQ ID NO: 9 at a lower level relative to the reference strain.

[00146] In certain embodiments, the at least one strain comprises a nucleic acid that is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation, wherein the nucleic acid has 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 9, before being disrupted. For example, in certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 9 is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 3 prime end of the nucleic acid. In certain embodiments, the nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 9 is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 5 prime end of the nucleic acid.

Dermatan-sulfate adhesin

[00147] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a dermatan-sulfate adhesin (DSA1 and DSA2). In certain embodiments, the at least one strain does not comprise a nucleic acid encoding a dermatan-sulfate adhesin. In certain embodiments, the at least one strain has been selected for reduced expression or activity of a dermatan-sulfate adhesin. In certain embodiments, the at least one strain has been selected for an absence of a dermatan-sulfate adhesin. In certain embodiments, bacteria disclosed herein have been transformed for reduced expression or activity of a dermatan-sulfate adhesin. In certain embodiments, bacteria disclosed herein have been transformed for an absence of a dermatan-sulfate adhesin. In certain embodiments, bacteria disclosed herein have been engineered for reduced

expression or activity of a dermatan-sulfate adhesin. In certain embodiments, bacteria disclosed herein have been engineered for an absence of a dermatan-sulfate adhesin.

[00148] In certain embodiments, the bacteria have been selected, transformed, or engineered for lower expression or activity or deletion of a dermatan-sulfate adhesin. In certain embodiments, the selected, transformed, or engineered bacteria has 1.5-fold, 2-fold, 3-fold, or 10-fold less expression or activity of the DSA 1 or DSA 2 compared to a reference strain. In certain embodiments, DSA1 or DSA2 is partially or completely deleted from the genome of the selected, transformed, or engineered, or engineered bacteria. In certain embodiments, DSA1 or DSA2 is disrupted by an insertion of one or more nucleotides or an introduction of a frameshift mutation in the genome of the selected, transformed, or engineered, or engineered bacteria.

[00149] In some embodiments, *P. acnes* is characterized as a health-associated *P. acnes* or a disease-associated *P. acnes* by detecting the absence, presence, and/or quantity of dermatan-sulfate adhesin. In some embodiments, a health-associated *P. acnes* does not comprise dermatan-sulfate adhesin. In some embodiments, dermatan-sulfate adhesin is DSA1 or DSA2.

[00150] Exemplary sequences for dermatan-sulfate adhesins are shown in Table 2. In some embodiments, the dermatan-sulfate adhesin comprises at least or about 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to at least one of the dermatan-sulfate adhesin sequences in Table 2. In some embodiments, the dermatan-sulfate adhesin comprises at least or about 95% homology to at least one of the dermatan-sulfate adhesin sequences in Table 2. In some embodiments, the dermatan-sulfate adhesin comprises at least or about 97% homology to at least one of the dermatan-sulfate adhesin sequences in Table 2. In some embodiments, the dermatan-sulfate adhesin comprises at least or about 99% homology to at least one of the dermatan-sulfate adhesin sequences in Table 2. In some embodiments, the dermatan-sulfate adhesin comprises at least or about 100% homology to at least one of the dermatan-sulfate adhesin sequences in Table 2. In some instances, the dermatan-sulfate adhesin comprises at least a portion having at least or about 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 550, 600, 650, 700, 750, 800, 850, 900 or more than 900 bases of at least one of the dermatan-sulfate adhesin sequences in Table 2.

Hyaluronidase

[00151] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a hyaluronidase.

Hyaluronidase is also known as hyaluronate lyase (locus tag PPA_RS01930). In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not have hyaluronidase activity. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a hyaluronidase. In certain embodiments, the bacteria have been selected, transformed, or engineered for lower expression or activity of hyaluronidase relative to the bacteria before selecting, transforming or engineering, respectively.

[00152] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a hyaluronidase. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria has hyaluronidase activity. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria has a nucleic acid encoding a hyaluronidase. In certain embodiments, the bacteria have been selected, transformed, or engineered for greater expression or activity of hyaluronidase relative to the bacteria before selecting, transforming or engineering, respectively.

[00153] In certain embodiments, the selected, transformed, or engineered bacteria have 1.5-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 2-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 3-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 5-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 10-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 90% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have

been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 95% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 97% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at higher level, a nucleic acid with at least 97% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a higher level, a nucleic acid with at least 99% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a higher level, a nucleic acid with 100% homology to SEQ ID NO: 4. In certain embodiments, the bacteria is a *P. acnes* bacteria. In certain embodiments, a gene with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 4 is partially or completely deleted from the genome of the synthetic bacteria. In certain embodiments, a gene with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 4 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the genome of the selected, transformed, or engineered, or engineered bacteria. In certain embodiments, the selected, transformed, or engineered or selected bacteria are deoR⁺, Type II lipase positive, pIMPLE negative, or CRISPR Cas5 positive. In certain embodiments, the selected, transformed, or engineered or selected bacteria comprise *P. acnes* of ribotype RT1 and/or RT2. In certain embodiments, the selected, transformed, or engineered or selected bacteria comprise *P. acnes* of ribotype RT3.

[00154] In certain embodiments, the bacteria have been selected, transformed, or engineered for lesser expression or absence of hyaluronate lyase. In certain embodiments, the bacteria are selected, transformed, or engineered, or engineered to acquire the presence of a hyaluronidase gene. Hyaluronidase is also known as hyaluronate lyase (locus tag PPA_RS01930). In certain embodiments, the selected, transformed, or engineered, or engineered bacteria have 1.5-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 2-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 3-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected, transformed, or engineered bacteria have 5-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the selected,

transformed, or engineered bacteria have 10-fold greater or lower expression or activity of hyaluronate lyase compared to a non-selected, transformed, or engineered strain. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 90% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 95% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a greater level, a nucleic acid with at least 97% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at higher level, a nucleic acid with at least 97% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a higher level, a nucleic acid with at least 99% homology to SEQ ID NO: 4. In certain embodiments, the bacteria have been selected, transformed, or engineered to acquire or express at a higher level, a nucleic acid with 100% homology to SEQ ID NO: 4. In certain embodiments, the bacteria is a *P. acnes* bacteria. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 4 is partially or completely deleted from the genome of the synthetic bacteria. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 4 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the genome of the selected, transformed, or engineered, or engineered bacteria. In certain embodiments, the selected, transformed, or engineered or selected bacteria are deoR⁺, Type II lipase positive, pIMPLE negative, or CRISPR Cas5 positive. In certain embodiments, the selected, transformed, or engineered or selected bacteria comprise *P. acnes* of ribotype RT1 and/or RT2. In certain embodiments, the selected, transformed, or engineered or selected bacteria comprise *P. acnes* of ribotype RT3.

Alanine dehydrogenase

[00155] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise an alanine dehydrogenase. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not have alanine dehydrogenase activity. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding an alanine dehydrogenase. In certain embodiments, the bacteria have been selected, transformed, or engineered for lower expression or activity of alanine

dehydrogenase relative to the bacteria before selection, transformation or engineering, respectively.

[00156] In certain embodiments, bacteria are selected, transformed, or engineered for the absence or deletion of a nucleic acid encoding alanine dehydrogenase or a portion thereof. In some embodiments, the alanine dehydrogenase is encoded by a sequence of SEQ ID NO: 5. In some embodiments, the alanine dehydrogenase is encoded by a sequence that is at least 80% homology to SEQ ID NO: 5. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of an alanine dehydrogenase or a portion thereof with at least 90% homology to SEQ ID NO: 5. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of an alanine dehydrogenase or a portion thereof with at least 95% homology to SEQ ID NO: 5. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of an alanine dehydrogenase or a portion thereof with at least 97% homology to SEQ ID NO: 5. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of an alanine dehydrogenase or a portion thereof with at least 98% homology to SEQ ID NO: 5. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of an alanine dehydrogenase or a portion thereof with at least 99% homology to SEQ ID NO: 5. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 5 is partially or completely deleted from the selected, transformed, or engineered, or engineered bacteria. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 5 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the selected, transformed, or engineered bacteria. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 3 prime end of the nucleic acid. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 5 prime end of the nucleic acid.

Transposase 2

[00157] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a transposase 2. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not have transposase 2 activity. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a transposase 2. In certain embodiments, the bacteria have been selected, transformed, or engineered for lower expression or activity of transposase 2 relative to the bacteria before selection, transformation or engineering, respectively. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not have transposase 2 activity, expresses deoR and is of ribotype RT1.

[00158] In certain embodiments, bacteria are selected, transformed, or engineered for the absence or deletion of a nucleic acid encoding transposase 2 or a portion thereof. In some embodiments, the transposase 2 is encoded by a sequence of SEQ ID NO: 48. In some embodiments, the transposase 2 is encoded by a sequence that is at least 80% homology to SEQ ID NO: 48. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of a transposase 2 or a portion thereof with at least 90% homology to SEQ ID NO: 48. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of a transposase 2 or a portion thereof with at least 95% homology to SEQ ID NO: 48. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of a transposase 2 or a portion thereof with at least 97% homology to SEQ ID NO: 48. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of a transposase 2 or a portion thereof with at least 98% homology to SEQ ID NO: 48. In certain embodiments, the bacteria are selected, transformed, or engineered for the absence or deletion of a transposase 2 or a portion thereof with at least 99% homology to SEQ ID NO: 48. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 48 is partially or completely deleted from the selected, transformed, or engineered, or engineered bacteria. In certain embodiments, a nucleic acid with at least 80%, 90%, 95%, 98%, 99%, or 100% homology to SEQ ID NO: 48 is disrupted by an insertion of one or more nucleotides or a introduction of a frameshift mutation in the selected, transformed, or engineered bacteria. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at

least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 3 prime end of the nucleic acid. In certain embodiments, the nucleic acid is deleted by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or more from the 5 prime end of the nucleic acid.

Additional Markers

[00159] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises at least one protein selected from a protein that mediates biosynthesis of a polysaccharide, a protein that mediates biosynthesis of cell wall, a protein that mediates biosynthesis of amino acids, a protein that mediates carbohydrate metabolism, and a protein that mediates glycerol transportation. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises at least one nucleic acid that encodes a protein, wherein the protein mediates biosynthesis of a polysaccharide, a protein that mediates biosynthesis of cell wall, a protein that mediates biosynthesis of amino acids, a protein that mediates carbohydrate metabolism, and a protein that mediates glycerol transportation. In some embodiments, the protein that mediates biosynthesis of a polysaccharide is a glycosyl transferase. In some embodiments, the protein that mediates biosynthesis of cell-wall is a D-alanin-D-alanine ligase. In some embodiments, the protein that mediates amino acid biosynthesis is a cobalamin-independent methionine synthase. In some embodiments, the protein is a glycerol uptake facilitator protein. In some embodiments, the protein is a protoporphyrinogen oxidase. In some embodiments, the protoporphyrinogen oxidase is encoded by a hemY gene.

[00160] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises at least one nucleic acid encoding a protein that is selected from a glycosyl transferase, a D-alanin-D-alanine ligase, and a cobalamin-independent methionine synthase.

[00161] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a microcin. In some embodiments, disclosed herein comprise at least one strain of bacteria, wherein the at least

one strain of bacteria does not comprise a nucleic acid encoding a microcin. By way of non-limiting example, the microcin may be a thiopeptide bacteriocin. In some embodiments, disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a protein involved in synthesis of a microcin. In some embodiments, disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a protein involved in synthesis of a microcin. In some embodiments, disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a protein involved in transport of a microcin. In some embodiments, disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a protein involved in transport of a microcin. Non-limiting examples of proteins involved in thiopeptide bacteriocin synthesis and transport are PAGK2104 and PAGK2105. Other examples of proteins involved in bacteriocin synthesis include Steptolysin S-associated genes (*sag*), or homologs thereof. A homolog may be at least about 60%, at least about 70%, at least about 80%, or at least about 90% homologous to a *sag* gene (*e.g.*, *sagB*, *sagC*, *sagD*).

[00162] In certain embodiments, the bacteria have been selected, transformed, or engineered for greater expression or activity of a protein, wherein the protein is selected from a protein that mediates biosynthesis of a polysaccharide, a protein that mediates biosynthesis of cell wall, and a protein that mediates biosynthesis of amino acids. In certain embodiments, the bacteria have been selected, transformed, or engineered for greater expression or activity of a protein selected from a glycosyl transferase, a D-alanin-D-alanine ligase, and a cobalamin-independent methionine synthase.

[00163] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a Christie-Atkins-Munch-Petersen (CAMP) protein. CAMP factors, as described herein, are likely involved in pathogenicity. In some instances, the CAMP protein is a virulence factor involved in hemolysin activity, exotoxin activity, or a combination thereof. Thus, reduction or inhibition of CAMP protein activity or expression may result in a safer strain of bacteria for compositions and methods disclosed herein. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a CAMP1 protein. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a CAMP2 protein. In some embodiments, compositions disclosed herein comprise

at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a CAMP3 protein.

[00164] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a CAMP protein. In certain embodiments, the bacteria have been selected, transformed, or engineered for less expression or activity of a CAMP protein relative to the bacteria that is not selected, transformed or engineered. In certain embodiments, the bacteria have been selected, transformed, or engineered for no expression or activity of a CAMP protein. In certain embodiments, the bacteria have been mutated to remove at least a portion of a nucleic acid encoding a CAMP protein. In some embodiments, the CAMP protein is selected from CAMP1, CAMP2, and CAMP3.

[00165] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria comprises a mutation in a CAMP protein. In certain embodiments, the bacteria have been selected, transformed, or engineered for a mutation in a CAMP protein relative to the bacteria that is not selected, transformed or engineered. In some embodiments, the mutation introduces a premature stop codon. In some embodiments, the mutation removes a stop codon. In some instances, the mutation in the stop codon results in a misfolded or misregulated CAMP protein. In some instances, the mutation in the stop codon results in lack of functional CAMP protein produced. In some instances, the mutation in the stop codon results in reduced hemolytic activity. In some instances, the mutation in the stop codon results in reduced exotoxin activity. In some instances, the mutation in the stop codon results in a safer strain for treatment of skin disorders. In some embodiments, the CAMP protein is selected from CAMP1, CAMP2, and CAMP3. In some embodiments, the CAMP protein is CAMP2.

P. acnes strain HP4G1 may have a mutation in its CAMP2 gene resulting in a missing stop codon, in particular a single nucleotide polymorphism (T to C) in position 802 of ATCC 11828's CAMP factor (see DNA encoding sequence in Table 2). CAMP-2 protein is described as having co-hemolysin and exotoxin activity. The absence of the stop codon may result in reduced co-hemolysin and exotoxin activity, making this strain safer for compositions and methods disclosed herein.

[00166] In some aspects, described herein are methods that comprise screening a strain of bacteria for a mutation in a CAMP gene. In some aspects, described herein are methods that comprise altering expression or activity of a CAMP factor in a strain of bacteria intended to

be used for treatment of skin disorders may make them safer for such use. In some instances, the strain of bacteria is a *P. acnes* strain disclosed herein.

[00167] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a sialidase. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a sialidase. In certain embodiments, the bacteria have been selected, transformed, or engineered for less expression or activity of a sialidase relative to the bacteria that is not selected, transformed or engineered. In certain embodiments, the bacteria have been selected, transformed, or engineered for no expression or activity of a sialidase. In certain embodiments, the bacteria have been mutated to remove at least a portion of a nucleic acid encoding a sialidase.

[00168] In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a neuraminidase. In some embodiments, compositions disclosed herein comprise at least one strain of bacteria, wherein the at least one strain of bacteria does not comprise a nucleic acid encoding a neuraminidase. In certain embodiments, the bacteria have been selected, transformed, or engineered for less expression or activity of a neuraminidase relative to the bacteria that is not selected, transformed or engineered. In certain embodiments, the bacteria have been selected, transformed, or engineered for no expression or activity of a neuraminidase. In certain embodiments, the bacteria have been mutated to remove at least a portion of a nucleic acid encoding a neuraminidase.

[00169] In certain embodiments, the bacteria has been selected, transformed, or engineered for higher activity or expression of any of the following proteins: Adhesion (NCBI Accession No. 50842581); CAMP factor (NCBI Accession No. 50842175, 50842711, 50842820, 50843546); Endoglycoceramidase (NCBI Accession No. 50842131); Iron transport lipoprotein (NCBI Accession No. 50841911); Lysozyme M1 (NCBI Accession No. 50843125); Protein PAGK_237 (NCBI Accession No. 482891444); Protein PPA0532 (NCBI Accession No. 50842016); Protein PPA0533 (NCBI Accession No. 50842017); or Protein PPA1498 (NCBI Accession No. 50842976). In certain embodiments, the bacteria has been selected, transformed, or engineered with a nucleic acid encoding any of the following protein any of the following proteins: Adhesion (NCBI Accession No. 50842581); CAMP factor (NCBI Accession No. 50842175, 50842711, 50842820, 50843546); Endoglycoceramidase (NCBI Accession No. 50842131); Iron transport lipoprotein (NCBI Accession No. 50841911); Lysozyme M1 (NCBI Accession No. 50843125); Protein

PAGK_237 (NCBI Accession No. 482891444); Protein PPA0532 (NCBI Accession No. 50842016); Protein PPA0533 (NCBI Accession No. 50842017); or Protein PPA1498 (NCBI Accession No. 50842976).

[00170] In certain embodiments, the bacteria has been selected, transformed, or engineered for lower activity or expression of any of the following proteins: Adhesion (NCBI Accession No. 50843565 or 50843645); Cell wall hydrolase (NCBI Accession No. 50843410); Lipase/acylhydrolase (NCBI Accession No. 50843480); NPL/P60 protein (NCBI Accession No. 50842209); Peptide ABC transporter (NCBI Accession No. 50843590); Protein PPA1197 (NCBI Accession No. 50842677); Protein PPA1281 (NCBI Accession No. 50842762); Protein PPA1715 (NCBI Accession No. 50843175); Protein PPA1939 (NCBI Accession No. 50843388); Protein PPA2239 (NCBI Accession No. 50843674); Rare lipoprotein A rlpA (NCBI Accession No. 50843612); or Triacylglycerol lipase (NCBI Accession No. 50843543).

In certain embodiments, the bacteria has been selected, transformed, or engineered with a nucleotide to delete or disrupt a gene encoding any of the following proteins: Adhesion (NCBI Accession No. 50843565 or 50843645); Cell wall hydrolase (NCBI Accession No. 50843410); Lipase/acylhydrolase (NCBI Accession No. 50843480); NPL/P60 protein (NCBI Accession No. 50842209); Peptide ABC transporter (NCBI Accession No. 50843590); Protein PPA1197 (NCBI Accession No. 50842677); Protein PPA1281 (NCBI Accession No. 50842762); Protein PPA1715 (NCBI Accession No. 50843175); Protein PPA1939 (NCBI Accession No. 50843388); Protein PPA2239 (NCBI Accession No. 50843674); Rare lipoprotein A rlpA (NCBI Accession No. 50843612); or Triacylglycerol lipase (NCBI Accession No. 50843543).

[00171] In certain embodiments, bacteria disclosed herein have been selected, transformed, or engineered for lower activity or expression of any of the following proteins:

HMPREF0675_4855; HMPREF0675_4856; HMPREF0675_4479; HMPREF0675_4480; HMPREF0675_4481; HMPREF0675_3655/3657; HMPREF0675_4816; HMPREF0675_4817; HMPREF0675_5205; HMPREF0675_5206; HMPREF0675_5014; HMPREF0675_5101; HMPREF0675_5159; HMPREF0675_4093/4094;

HMPREF0675_4163; HMPREF0675_5031; HMPREF0675_5390; HMPREF0675_3037. In certain embodiments, the bacteria have been selected, transformed, or engineered with a nucleotide to delete or disrupt a gene encoding any of the following proteins:

HMPREF0675_4855; HMPREF0675_4856; HMPREF0675_4479; HMPREF0675_4480; HMPREF0675_4481; HMPREF0675_3655/3657; HMPREF0675_4816; HMPREF0675_4817; HMPREF0675_5205; HMPREF0675_5206; HMPREF0675_5014;

HMPREF0675_5101; HMPREF0675_5159; HMPREF0675_4093/4094;
HMPREF0675_4163; HMPREF0675_5031; HMPREF0675_5390; HMPREF0675_3037.

[00172] In certain embodiments, the bacteria have been selected, transformed, or engineered for higher activity or expression of any of the following proteins HMPREF0675_4855; HMPREF0675_4856; HMPREF0675_4479; HMPREF0675_4480; HMPREF0675_4481; HMPREF0675_3655/3657; HMPREF0675_4816; HMPREF0675_4817; HMPREF0675_5205; HMPREF0675_5206; HMPREF0675_5014; HMPREF0675_5101; HMPREF0675_5159; HMPREF0675_4093/4094; HMPREF0675_4163; HMPREF0675_5031; HMPREF0675_5390; HMPREF0675_3037. In certain embodiments, the bacteria has been selected, transformed, or engineered with a nucleic acid encoding any of the following proteins: HMPREF0675_4855; HMPREF0675_4856; HMPREF0675_4479; HMPREF0675_4480; HMPREF0675_4481; HMPREF0675_3655/3657; HMPREF0675_4816; HMPREF0675_4817; HMPREF0675_5205; HMPREF0675_5206; HMPREF0675_5014; HMPREF0675_5101; HMPREF0675_5159; HMPREF0675_4093/4094; HMPREF0675_4163; HMPREF0675_5031; HMPREF0675_5390; HMPREF0675_3037.

[00173] In certain embodiments, the selected, transformed, or engineered bacteria do not comprise an antibiotic resistance gene. In certain embodiments, the selected, transformed, or engineered bacteria lack an antibiotic resistance gene to any one or more of aminoglycoside, beta-lactam, colistin, fluoroquinolone, fosfomycin, fusidic acid, macrolide, lincosamide, streptogramin B, nitroimidazole, oxazolidinone, phenicol, rifampicin, sulphonamide, tetracycline, trimethoprim, or glycopeptide. In certain embodiments, an antibiotic can be applied to halt treatment with selected, transformed, or engineered bacteria disclosed herein. In certain embodiments, the antibiotic is aminoglycoside, beta-lactam, colistin, fluoroquinolone, fosfomycin, fusidic acid, macrolide, lincosamide, streptogramin B, nitroimidazole, oxazolidinone, phenicol, rifampicin, sulphonamide, tetracycline, trimethoprim, or glycopeptide.

[00174] In certain embodiments, the bacteria are selected, transformed, or engineered in order to reduce expression or release of pro-inflammatory mediators by human cells of which the bacteria contact. Bacteria may either directly or indirectly contact human cells (*e.g.*, human skin cells). For instance, bacteria may indirectly contact human cells via factors secreted or released from the bacteria. Non-limiting example of pro-inflammatory mediators from human cells are IL-8, IL-1, IL-6, TNF-alpha, INF-alpha, and human beta defensin.

Mixtures of different microbes

[00175] Provided herein are compositions of a plurality of health-associated microbes. In some embodiments, compositions comprise a mixture of a plurality of different health-associated microbes disclosed herein. In a certain embodiment, the mixture comprises at least one selected, transformed, or engineered bacteria. In a certain embodiment, the mixture comprises at least one selected, transformed, or engineered strain of *P. acnes*. In a certain embodiment, the mixture comprises at least two selected, transformed, or engineered strains of *P. acnes*. In certain embodiments, the mixture comprises 2, 3, 4, 5, 6, 7, 8, 9, 10 or more isolated and purified species, strains, ribotypes, or phylotypes of bacteria. In some embodiments, mixtures comprise at least one strain of bacteria that normally colonizes a tissue or body area other than the skin. In some embodiments, mixtures comprise at least one strain of bacteria that normally colonizes the oral cavity. In some embodiments, the at least one bacteria that normally colonizes the oral cavity is *S. salivarius*. In some embodiments, mixtures comprise at least one strain of bacteria that normally colonizes the lumen of the gastrointestinal system.

[00176] In general, the plurality of health-associated microbes does not comprise a microbe that is detrimental to the viability, growth or activity of other health-associated microbes in the composition. In some instances, the plurality of health-associated microbes does not comprise a microbe that produces a bacteriocin that inhibits the growth of *P. acnes*. In some instances, the plurality of health-associated microbes does not comprise a microbe that produces any substances with bacteriocin-like activity that inhibits the growth of a strain of *P. acnes* disclosed herein. In some instances, the plurality of health-associated microbes comprises a health-associated microbe that does not produce a bacteriocin that inhibits the growth of a *P. acnes* strain that is also present in the composition. In some instances, the health-associated microbe is a strain of *Lactobacillus*. In some instances, the health-associated microbe is a strain of *Bifidobacterium*. In some instances, the health-associated microbe is a strain of *Streptococcus*.

[00177] In a certain embodiment, the mixture comprising at least one bacteria that normally colonizes the lumen of the gastrointestinal system comprises a *Lactobacillus* strain of bacteria or a *Bifidobacterium* strain of bacteria. In certain embodiments, the *Bifidobacterium* is *Bifidobacterium lactis* Bb-12, *Bifidobacterium animalis*, *Bifidobacterium breve*, *Bifidobacterium bifidum*, or any combination thereof. In certain embodiments, the *Lactobacillus* is *Lactobacillus acidophilus*, *Lactobacillus bacillus*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus* GG, *Lactobacillus fermentum*, *Lactobacillus Sakei*, *Lactobacillus*

casei, *Lactobacillus salivarius*, *Lactobacillus rhamnosus* LC705, *Lactobacillus F19* L, *Lactobacillus acidophilus* La-5, or any combination thereof.

[00178] In a certain embodiment, the mixture comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, or more different bacterial species. In a certain embodiment, the mixture comprises a mixture of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, or more different bacterial strains. In a certain embodiment, the mixture contains at least one non-bacterial microbe such as a fungus, virus, or bacteriophage. Any defined mixture of a plurality of health-associated microbes may be recited to “consist essentially of.” This means that the mixture includes only the specified strains plus any non-active ingredient necessary for proper administration as a topical or oral formulation, such as an excipient or diluent.

[00179] In some embodiments, compositions disclosed herein comprise a first strain of bacteria and a second strain of bacteria. In some embodiments, the amount of the first strain can be expressed as a percentage of total bacteria present in the composition. This percentage may be assessed by weight, individual microbes or colony forming units. For example, the amount of the first strain may be expressed as a percentage of total grams of bacteria per given volume of the composition. Also, by way of non-limiting example, the amount of the first strain may be expressed as a percentage of colony forming units (cfu) of bacteria per given volume of a composition disclosed herein. Regardless of how it is measured, the percentage represents the proportion or ratio of the first strain to other strains in the composition. In some embodiments, the first strain of bacteria represents about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95% or about 99% of total bacteria in the composition.

[00180] In some embodiments, compositions disclosed herein comprise a first strain of bacteria and a second strain of bacteria. In some embodiments, the first strain of bacteria represents about 1% to about 10% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 10% to about 20% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 20% to about 30% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 30% to about 40% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 40% to about 50% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 50% to about 60% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 60% to about 70% of total bacteria in the composition. In some

embodiments, the first strain of bacteria represents about 70% to about 80% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 80% to about 90% of total bacteria in the composition. In some embodiments, the first strain of bacteria represents about 90% to about 99% of total bacteria in the composition.

[00181] In some embodiments, compositions disclosed herein comprise a first strain of bacteria and a second strain of bacteria. In some embodiments, the first strain of bacteria represents at least about 1% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 10% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 20% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 30% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 40% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 50% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 60% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 70% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 80% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents at least about 90% of the total bacteria in the composition.

[00182] In some embodiments, compositions disclosed herein comprise a first strain of bacteria and a second strain of bacteria. In some embodiments, the first strain of bacteria represents not more than about 1% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 10% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 20% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 30% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 40% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 50% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 60% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 70% of the total bacteria in the composition. In some embodiments, the first strain of bacteria represents not more than about 80% of the total bacteria in the composition. In some

embodiments, the first strain of bacteria represents not more than about 90% of the total bacteria in the composition.

[00183] In some embodiments, compositions disclosed herein comprise a first strain of bacteria and a second strain of bacteria. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:2. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:3. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:4. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:5. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:6. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:7. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:8. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:9. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 1:10. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 2:3. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 2:5. In some embodiments, the first strain of bacteria and the second strain of bacteria are present in ration of about 2:7.

[00184] In some embodiments, compositions disclosed herein comprise health-associated-microbes especially useful for treating eczema. In some embodiments, compositions for treating eczema disclosed herein comprise *Staphylococcus Aureus*. In some embodiments, compositions for treating eczema disclosed herein comprise dead *Staphylococcus Aureus* bacteria. In some embodiments, compositions for treating eczema disclosed herein comprise *Staphylococcus hominis*. In other embodiments, the health-associated microbe comprises of one more of a *Dermaococcus*, *Methlyobacterium* or *Propionibacterium* as they have a negative correlation with *S. aureus*. In other embodiments, compositions disclosed herein comprise *S. mitis*, *S. sanguinis* or *S. cristatus*.

Formulations

[00185] Provided herein, in some aspects, are compositions that comprise at least one health-associated microbe disclosed herein, wherein the compositions are formulated for administration to a subject in need thereof. Generally, the subject is a human afflicted with acne, eczema, psoriasis, seborrheic dermatitis, rosacea, or any combination thereof. Generally, compositions disclosed herein are non-comedogenic, free of animal products and generally

recognized as safe (GRAS). In some embodiments, a composition is formulated for topical administration to a subject in need thereof. In some embodiments, the compositions are formulated for topical administration to the skin of the subject. In some embodiments, the compositions are formulated for topical administration to the scalp of the subject. In some embodiments, a composition is formulated for oral administration. By way of non-limiting example, compositions disclosed herein comprising strains of *Lactobacillus* may be preferentially administered by oral administration. In some embodiments, a composition is formulated for transdermal administration. In some embodiments, a composition is formulated for injectable administration. In certain embodiments, the composition is a formulation selected from a gel, ointment, lotion, emulsion, paste, cream, foam, mousse, liquid, spray, suspension, dispersion and aerosol. In certain embodiments, the formulation comprises one or more excipients to provide a desired form and a desired viscosity, flow or other physical or chemical characteristic for effective application, coverage and adhesion to skin.

[00186] Compositions disclosed herein may be presented in a formulation that includes one or more excipients to improve any one or more of shelf-life, application, and therapeutic effect. In some embodiments, the excipient is necessary to improve any one or more of shelf-life, application, skin penetration, and therapeutic effect. In some embodiments, the excipient reduces skin penetration.

[00187] Compositions disclosed herein may be presented in a formulation that includes one or more biological stabilizers to improve any one or more of shelf-life, storage viability, and freeze thawing survival. In some embodiments, the biological stabilizer is a cryopreservative. A non-limiting example of a biological stabilizer is glycerol. Other examples of biological stabilizers include, but are not limited to, glyconanoparticle, a liposome, a nanoparticle, trehalose, sucrose, stachyose, hydroxyethyl starch, glycine, mannitol, DMSO, ethylene glycol, propylene glycol (PG), polypropylene glycol (PPG), polyethylene glycol (PEG), and 2-Methyl-2,4-pentanediol (MPD). In some embodiments, the biologic stabilizer eliminates a need for temperature control, e.g., cold chain storage.

[00188] Biological stabilizers of the current disclosure can, in certain embodiments, augment the utility or engraftment of a health-associated strain of bacteria. In certain embodiments, the health-associated strain comprises *P. acnes*. In certain embodiments, the biological stabilizer comprises glycerol. Glycerol is a natural compound that is generally regarded as safe for inclusion in topical formulations. Glycerol may suppress lipase activity.

Glycerol fermentation by *P. acnes* produces short chain fatty acid, propionic acid, which suppresses the growth of MRSA and likely other *S. Aureus* strains. *P. acnes*, in the presence of glycerol may be useful as a probiotic by supporting a healthy *P. acnes* dominated community. For example, fermentation of glycerol to propionic acid may suppress MRSA growth but not growth of *P. acnes*, thereby aiding engraftment of a beneficial strain of *P. acnes* to an individual. Additionally, *P. acnes* readily metabolizes glycerol. Typically, *P. acnes* converts lipids in sebum to glycerol with secreted lipase activity. However, when glycerol is readily available, secreted lipase activity is suppressed. Much like the type II lipases found in health-associated *P. acnes*, a reduction in lipase activity reduces the anaerobic fermentation and production of short-chain fatty acids that are inflammatory to a host (*e.g.*, human).

[00189] In certain embodiments, the compositions and formulations of health-associated bacteria, described herein, comprise a health-associated *P. acnes* and glycerol at a concentration of between about 5% and about 50% w/v, between about 5% and about 40% w/v, between about 5% and about 30% w/v, between about 5% and about 20% w/v, between about 5% and about 15% w/v, between about 10% and about 50% w/v, between about 10% and about 40% w/v, between about 10% and about 30% w/v, between about 10% and about 25% w/v, between about 15% and about 50% w/v, between about 15% and about 40% w/v, between about 15% and about 30% w/v, or between about 15% and about 25% w/v. In certain embodiments, the formulations described herein comprise a health-associated *P. acnes* and glycerol at a concentration of about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, or 55%.

[00190] In certain embodiments, the compositions and formulations of health-associated bacteria, described herein, comprise a biological stabilizer that suppresses lipase activity. In certain embodiments, the biological stabilizer suppresses secreted lipase activity and increases propionic acid production. In certain embodiments, the biological stabilizer increases secreted propionic acid production. In certain embodiments, the biological stabilizer is a humectant. In certain embodiments, the biological stabilizer is a humectant comprising glycerol. In certain embodiments, the biological stabilizer increases propionic acid production and suppresses lipase activity. In certain embodiments, the biological stabilizer increases propionic acid production or suppresses lipase activity and is a humectant. In certain embodiments, the biological stabilizer increases propionic acid production and suppresses lipase activity and is a humectant.

[00191] Generally, formulations disclosed herein do not comprise a bacterial growth medium. Typical bacterial growth media (also referred to as culture media) contain a carbon source (e.g., glucose), water, salts, nitrogen, and amino acids. A common example of a bacterial growth medium is Lysogeny broth (LB), also referred to as Luria broth or Luri-Beratni medium. In contrast to traditional bacterial storage protocols that store formulations of bacteria in bacterial growth media, formulations disclosed herein comprise health-associated microbes in a buffered saline solution. In some instances the buffered saline solution is phosphate buffered saline. In some instances, the formulations comprise a biological stabilizer such as glycerol. In some instances, formulations disclosed herein comprise phosphate buffered saline and glycerol, and do not comprise a bacterial growth medium.

[00192] In some aspects, disclosed herein are formulations comprising at least one strain of *Propionibacterium acnes*, glycerol, and phosphate buffered saline solution (PBS). In some aspects, disclosed herein are formulations comprising at least one strain of *Propionibacterium acnes* and glycerol, wherein the formulations do not comprise a bacterial culture medium. In some aspects, disclosed herein are formulations comprising at least one strain of *Propionibacterium acnes*, PBS, and glycerol, wherein the formulations do not comprise a bacterial culture medium. In some instances, the formulation is between about 10% glycerol and about 50% glycerol. In some instances, the formulation is between about 10% glycerol and about 40% glycerol. In some instances, the formulation is 25% glycerol. In some instances, at least about 90% of said *Propionibacterium acnes* in the formulation is viable after sixty days of storage. In some instances, at least about 90% of said *Propionibacterium acnes* in the formulation is viable after ninety days of storage.

[00193] In certain embodiments, the health-associated microbe compositions described herein are formulated for oral ingestion. The oral ingestion form may be a pill, tablet, capsule, paste, liquid suspension, colloid, or mixed with various foods such as candies, chews, yogurt, milk, cottage cheese or non-dairy based or lactose reduced substitutes. The formulation may contain additional non-active ingredients that improve flavor, smell, or texture of the edible composition. The formulation may also include binding agents, encapsulating films, or excipients that preserve shelf-life and bioavailability.

[00194] In certain embodiments, health-associated-microbes compositions disclosed herein that are administered orally comprise a species of bacteria selected from *L. acidophilus La-5*, *Bifidobacterium animalis*, *Lactobacillus rhamnosus*, *Lactobacillus F19*, *Lactobacillus fermentum*, *Lactobacillus Sakei*, *Lactobacillus reuteri*, *Bifidobacterium breve*,

Propionibacterium freudenreichii ssp. *Shermanii* JS, *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Lactobacillus salivarius*, and combinations thereof. In some embodiments, the composition comprises *Lactobacillus salivarius* and a fructo-oligosaccharide. In some embodiments, the composition comprises *Lactobacillus rhamnosus* GG. In some embodiments, the composition comprises *Lactobacillus rhamnosus* LC705. In some embodiments, the composition comprises *Lactobacillus salivarius* and a prebiotic. In some embodiments, the composition comprises hydrolyzed whey formula with *Lactobacillus rhamnosus* GG. In some embodiments, the composition comprises hydrolyzed whey formula with *Bifidobacterium lactis* Bb-12. In certain embodiments, health-associated-microbe compositions disclosed herein that are administered orally comprise bacteria selected from *Lactobacillus rhamnosus* GG and bifidobacteria Bb-12, and a combination thereof.

[00195] An emulsion may be described as a preparation of one liquid distributed in small globules throughout the body of a second liquid. In some embodiments, the dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. The oil phase may consist at least in part of a propellant, such as an HFA propellant. Either or both of the oil phase and the aqueous phase may contain one or more surfactants, emulsifiers, emulsion stabilizers, buffers, and other excipients. Preferred excipients include surfactants, especially non-ionic surfactants; emulsifying agents, especially emulsifying waxes; and liquid non-volatile non-aqueous materials, particularly glycols such as polyethylene glycol. The oil phase may contain other oily pharmaceutically approved excipients. For example, materials such as hydroxylated castor oil or sesame oil may be used in the oil phase as surfactants or emulsifiers.

[00196] A lotion may be described as a low- to medium-viscosity liquid formulation. A lotion can contain finely powdered substances that are insoluble in the dispersion medium through the use of suspending agents and dispersing agents. Alternatively, lotions can have as the dispersed phase liquid substances that are immiscible with the vehicle and are usually dispersed by means of emulsifying agents or other suitable stabilizers. In one embodiment, the lotion is in the form of an emulsion having a viscosity of between 100 and 1000 centistokes. The fluidity of lotions permits rapid and uniform application over a wide surface area. Lotions are typically intended to dry on the skin leaving a thin coat of their medicinal components on the skin's surface.

[00197] A cream may be described as a viscous liquid or semi-solid emulsion of either the "oil-in-water" or "water-in-oil type". Creams may contain emulsifying agents and/or other stabilizing agents. In one embodiment, the formulation is in the form of a cream having a viscosity of greater than 1000 centistokes, typically in the range of 20,000-50,000 centistokes. Creams are often time preferred over ointments as they are generally easier to spread and easier to remove.

[00198] The basic difference between a cream and a lotion is the viscosity, which is dependent on the amount/use of various oils and the percentage of water used to prepare the formulations. Creams are typically thicker than lotions, may have various uses and often one uses more varied oils/butters, depending upon the desired effect upon the skin. In a cream formulation, the water-base percentage is about 60-75% and the oil-base is about 20-30% of the total, with the other percentages being the emulsifier agent, preservatives and additives for a total of 100%.

[00199] An ointment may be described as a semisolid preparation containing an ointment base and optionally one or more active agents of this disclosure. Examples of suitable ointment bases include hydrocarbon bases (*e.g.*, petrolatum, white petrolatum, yellow ointment, and mineral oil); absorption bases (hydrophilic petrolatum, anhydrous lanolin, lanolin, and cold cream); water-removable bases (*e.g.*, hydrophilic ointment), and water-soluble bases (*e.g.*, polyethylene glycol ointments). Pastes typically differ from ointments in that they contain a larger percentage of solids. Pastes are typically more absorptive and less greasy than ointments prepared with the same components.

[00200] A gel may be described as a semisolid system containing dispersions of small or large molecules in a liquid vehicle that is rendered semisolid by the action of a thickening agent or polymeric material dissolved or suspended in the liquid vehicle. The liquid may include a lipophilic component, an aqueous component or both. Some emulsions may be gels or otherwise include a gel component. Some gels, however, are not emulsions because they do not contain a homogenized blend of immiscible components. Suitable gelling agents include, but are not limited to, modified celluloses, such as hydroxypropyl cellulose and hydroxyethyl cellulose; Carbopol homopolymers and copolymers; and combinations thereof. Suitable solvents in the liquid vehicle include, but are not limited to, diglycol monoethyl ether; alkene glycols, such as propylene glycol; dimethyl isosorbide; alcohols, such as isopropyl alcohol and ethanol. The solvents are typically selected for their ability to dissolve the drug. Other additives, which improve the skin feel and/or emolliency of the formulation, may also be incorporated. Examples of such additives include, but are not limited, isopropyl

myristate, ethyl acetate, C12-C15 alkyl benzoates, mineral oil, squalane, cyclomethicone, capric/caprylic triglycerides, and combinations thereof.

[00201] Foams may be described as an emulsion in combination with a gaseous propellant. The gaseous propellant consists primarily of hydrofluoroalkanes (HFAs). Suitable propellants include HFAs such as 1,1,1,2-tetrafluoroethane (HFA 134a) and 1,1,1,2,3,3,3-heptafluoropropane (HFA 227), but mixtures and admixtures of these and other HFAs that are currently approved or may become approved for medical use are suitable. The propellants preferably are not hydrocarbon propellant gases which can produce flammable or explosive vapors during spraying. Furthermore, the compositions preferably contain no volatile alcohols, which can produce flammable or explosive vapors during use.

[00202] Emollients may be described as externally applied agents that soften or soothe skin and are generally known in the art and listed in compendia, such as the "Handbook of Pharmaceutical Excipients", 4th Ed., Pharmaceutical Press, 2003. In certain embodiments, the emollients are almond oil, castor oil, ceratonia extract, cetostearyl alcohol, cetyl alcohol, cetyl esters wax, cholesterol, cottonseed oil, cyclomethicone, ethylene glycol palmitostearate, glycerin, glycerin monostearate, glyceryl monooleate, isopropyl myristate, isopropyl palmitate, lanolin, lecithin, light mineral oil, medium-chain triglycerides, mineral oil and lanolin alcohols, petrolatum, petrolatum and lanolin alcohols, soybean oil, starch, stearyl alcohol, sunflower oil, xylitol and combinations thereof. In one embodiment, the emollients are ethylhexylstearate and ethylhexyl palmitate.

[00203] Surfactants are surface-active agents that lower surface tension and thereby increase the emulsifying, foaming, dispersing, spreading and wetting properties of a product. In certain embodiments, suitable non-ionic surfactants include emulsifying wax, glyceryl monooleate, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polysorbate, sorbitan esters, benzyl alcohol, benzyl benzoate, cyclodextrins, glycerin monostearate, poloxamer, povidone and combinations thereof. In one embodiment, the non-ionic surfactant is stearyl alcohol.

[00204] Emulsifiers are surface active substances which promote the suspension of one liquid in another and promote the formation of a stable mixture, or emulsion, of oil and water. In certain embodiments, the emulsifiers are metallic soaps, certain animal and vegetable oils, and various polar compounds. Suitable emulsifiers include acacia, anionic emulsifying wax, calcium stearate, carbomers, cetostearyl alcohol, cetyl alcohol, cholesterol, diethanolamine, ethylene glycol palmitostearate, glycerin monostearate, glyceryl monooleate, hydroxypropyl cellulose, hypromellose, lanolin, hydrous, lanolin alcohols, lecithin, medium-chain

triglycerides, methylcellulose, mineral oil and lanolin alcohols, monobasic sodium phosphate, monoethanolamine, nonionic emulsifying wax, oleic acid, poloxamer, poloxamers, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates, propylene glycol alginate, self-emulsifying glyceryl monostearate, sodium citrate dehydrate, sodium lauryl sulfate, sorbitan esters, stearic acid, sunflower oil, tragacanth, triethanolamine, xanthan gum and combinations thereof. In one embodiment, the emulsifier is glycerol stearate. In one embodiment, the emulsifier is glycerol. In one embodiment, the emulsifier is glycerin.

[00205] In some embodiments, compositions disclosed herein are formulated to be applied to a subject's scalp. In some embodiments, the composition is formulated to be used as a product selected from a shampoo, a conditioner, a mousse, a gel, and a spray. Such compositions would be useful for the treatment of seborrheic dermatitis. Treatment of seborrheic dermatitis with such compositions may result in the reduction of a symptom selected from dandruff and cradle cap. However, compositions disclosed herein may be used to treat seborrheic dermatitis at other areas of the body besides the scalp. Non-limiting examples of other areas include the chest, stomach, skin folds, arms, legs, groin area and under breasts.

[00206] In some embodiments, compositions disclosed herein comprise a buffer, wherein the buffer controls a pH of the composition. Preferably, the buffers buffer the composition from a pH of about 4 to a pH of about 7.5, from a pH of about 4 to a pH of about 7, and from a pH of about 5 to a pH of about 7. In some embodiments, the buffer comprises phosphate buffered saline. In some embodiments, the buffer is phosphate buffered saline. In some embodiments, the buffer comprises acetate buffered solution. In some embodiments, the buffer is acetate buffered solution. In some embodiments, the buffer is sodium acetate buffered solution.

[00207] In some embodiments, compositions disclosed herein are formulated to provide or maintain a desirable skin pH. In some embodiments, the desirable skin pH is between about 4.5 and about 6.5. In some embodiments, the desirable skin pH is between about 5 and about 6. In some embodiments, the desirable skin pH is about 5.5. In some embodiments, compositions disclosed herein are formulated for use with a skin pH modulating agent. In some embodiments, compositions disclosed herein are formulated for use before use of a skin pH modulating agent. In some embodiments, compositions disclosed herein are formulated for use after use of a skin pH modulating agent. Non-limiting examples of pH modulating agents include salicylic acid, glycolic acid, trichloroacetic acid, azelaic acid, lactic acid,

aspartic acid, hydrochloride, stearic acid, glyceryl stearate, cetyl palmitate, urea phosphate, and tocopheryl acetate. In some instances, compositions disclosed herein are formulated to lower pH of the skin of the subject to the desirable skin pH. In other words, compositions disclosed herein may comprise a pH lowering or pH balancing agent. Non-limiting examples of pH lowering and pH balancing agents include citric acid, lactic acid, glycolic acid, azelaic acid, retinoic acid, alpha hydroxyl acid, and ascorbic acid.

[00208] In some embodiments, compositions disclosed herein are formulated to provide more oxygen to the skin. In some embodiments, compositions disclosed herein are formulated to provide more oxygen exposure to the skin. In some embodiments, compositions disclosed herein are formulated to provide more oxygen diffusion into the skin. In some embodiments, compositions disclosed herein are formulated to provide more oxygen diffusion through the skin. In some embodiments, compositions disclosed herein are formulated with an agent that provides more oxygen to the skin. In some embodiments, compositions disclosed herein are used with an agent that provides more oxygen to the skin. In some embodiments, compositions disclosed herein are used before use of an agent that provides more oxygen to the skin. In some embodiments, compositions disclosed herein are used after use of an agent that provides more oxygen to the skin. A non-limiting example of an agent that provides oxygen to the skin is chlorophyll.

[00209] Preservatives can be used to prevent the growth of fungi and microorganisms. Suitable antifungal and antimicrobial agents include, but are not limited to, benzoic acid, butylparaben, ethyl paraben, methyl paraben, propylparaben, sodium benzoate, sodium propionate, benzalkonium chloride, benzethonium chloride, benzyl alcohol, cetylpyridinium chloride, chlorobutanol, phenol, phenylethyl alcohol, and thimerosal. In one embodiment, a concentration of a preservative that is effective to prevent fungal growth is selected, without affecting the effectiveness of the composition for its intended purposed upon topical application.

[00210] Excipients in the formulation are selected based on the type of formulation intended. In certain embodiments, the excipients include gelatin, casein, lecithin, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glyceryl monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecyl sulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose,

hydroxypropylcellulose, hydroxypropylmethycellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, sugars, and starches.

[00211] In some embodiments, compositions disclosed herein are formulated with glycerol. In some instances, a strain of bacteria in the composition ferments the glycerol, thereby producing short chain fatty acids. Non-limiting examples of short-chain fatty acids include acetic acid, lactic acid, and propionic acid. In some embodiments, the strain of bacteria is a *Propionibacterium* strain. In some embodiments, the strain of bacteria is a *P. acnes* strain.

[00212] Compositions disclosed herein are formulated to comprise health-associated microbes at a given concentration. In some instance, the concentration is sufficient to engraft skin of a subject with the health-associated microbes, as described herein. For example, the composition can comprise an amount of health-associated microbe such that the microorganisms may be delivered in effective amounts. In certain embodiments, the amount of health-associated microbe delivered is at least 1×10^3 , 1×10^4 , 1×10^5 , 1×10^6 , 1×10^7 , 1×10^8 , 1×10^9 , 1×10^{10} colony forming units per unit dose. The composition may be formulated with the health-associated microbe in a proportion of at least about 0.0001% (expressed by dry weight), from about 0.0001% to about 99%, from about 0.001% to about 90% by weight, from about 0.01% to about 80% by weight, and from about 0.1% to about 70% by weight, relative to the total weight of the composition. In general, a composition intended to be administered topically comprises at least 1×10^3 , 1×10^4 , 1×10^5 , 1×10^6 , 1×10^7 , 1×10^8 , 1×10^9 , 1×10^{10} microorganisms per gram of carrier, or at equivalent doses calculated for inactive or dead microorganisms or for bacterial fractions or for metabolites produced.

[00213] Microbes disclosed herein may be delivered in effective amounts per unit dose, of at least about 1×10^2 colony forming units (cfu) to about 1×10^{20} cfu. In the particular case of the compositions that have to be administered topically, the concentration of each bacterial strain and/or corresponding fraction and/or metabolite can be adjusted so as to correspond to doses (expressed as bacterial equivalent) ranging from about 1×10^5 to about 1×10^{12} cfu/dose.

[00214] Compositions disclosed herein for topical application generally comprise from about 1×10^2 to about 1×10^{15} cfu/g, from about 1×10^5 to about 1×10^{12} cfu/g, or from about 1×10^6 to about 10×10^{12} cfu/g of bacteria.

[00215] In certain embodiments, compositions disclosed herein are formulated in order to deliver at least 10^5 microbes per cm^2 of skin. In certain embodiments, compositions disclosed herein are formulated in order to deliver at least 10^6 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^7 microbes per cm^2

of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^8 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^9 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^9 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^8 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^7 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^6 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^7 and 10^8 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^6 microbes per cm^2 of skin and about 10^{10} microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^6 microbes per cm^2 of skin and about 10^9 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^7 microbes per cm^2 of skin and about 10^{10} microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^7 microbes per cm^2 of skin and about 10^9 microbes per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^5 microbes per cm^2 of skin and about 10^6 microbes per cm^2 of skin.

[00216] In certain embodiments, compositions disclosed herein are formulated in order to deliver at least 10^5 cfu per cm^2 of skin. In certain embodiments, compositions disclosed herein are formulated in order to deliver at least 10^6 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^7 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^8 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver at least 10^9 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^9 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^8 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^7 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver less than 10^6 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^7 and 10^8 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^6 cfu per cm^2 of skin and about 10^{10} cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^6 cfu per cm^2 of skin and about 10^9 cfu per cm^2 of skin. In certain embodiments, the composition is

formulated in order to deliver between about 10^7 cfu per cm^2 of skin and about 10^{10} cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^7 cfu per cm^2 of skin and about 10^9 cfu per cm^2 of skin. In certain embodiments, the composition is formulated in order to deliver between about 10^5 cfu per cm^2 of skin and about 10^6 cfu per cm^2 of skin.

[00217] In certain embodiments, compositions disclosed herein are formulated at a concentration of colony formulating units (cfu) per milliliter of the total composition volume. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^5 cfu per milliliter to about 10^{12} cfu per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^6 cfu per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^7 cfu per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^8 cfu per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^9 cfu per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^{10} cfu per milliliter.

[00218] In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^5 microbes per milliliter to about 10^{12} microbes per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^6 microbes per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^7 microbes per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^8 microbes per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^9 microbes per milliliter. In certain embodiments, compositions disclosed herein are formulated at a concentration of about 10^{10} microbes per milliliter.

[00219] In certain embodiments, compositions disclosed herein for topical or oral use contain biologic stability compounds including but not limited to carbohydrates such as trehalose, mannose, fructose, glucose, sucrose, lactose, raffinose, stachyose, melezitose, dextran, and sugar alcohols; and/or cryopreservatives such as glycerol, bovine-free media, (e.g., tryptic soy broth), whey protein, NaCl, phosphate buffer, MgCl, lyophilized bacteria, or other inactive/killed bacteria.

[00220] After formulation, composition disclosed herein may be packaged in a manner suitable for delivery and use by an end user. In one embodiment, the composition is placed

into an appropriate dispenser and shipped to the end user. Examples of a final container may include a pump bottle, squeeze bottle, jar, tube, capsule or vial.

[00221] In some embodiments, compositions disclosed herein can be added to an applicator before packaging. Non-limiting examples of applicators include a cotton pad, a polyester pad, a q-tip, a sponge, and a brush. In some instances, the applicator is a cotton pad.

Advantageously, a cotton pad does not bind bacteria, delivers a standardized dose, costs little, and is familiar to both clinicians and patients.

[00222] In some embodiments, pharmaceutical compositions and applicators disclosed herein are placed in a package. Non-limiting examples of a package includes bags, foil, and wax lined paper packets. In some instances, the packaging comprises plastic. In some instances, the packaging comprises a plastic bag. In some instances, the plastic comprises a material selected from polypropylene, nylon, and a combination thereof. In some instances, the plastic is thin and flexible so that it can cool, freeze, thaw or warm quickly. By way of non-limiting example, the plastic may be about 1 mil thick to about 3 mil thick (1 mil= 1/1000 of an inch). The interior of the package may be sterile. In some embodiments, air in the package is removed with a vacuum before sealing. Vacuum sealing may advantageously eliminate oxygen, increase speed of freezing (increases viability after frozen storage), ensure uniform distribution of formulation, and enable convenient compact single use container. In some embodiments, the package is heat-sealed. In some embodiments, the package is sealed with adhesive.

[00223] In another embodiment, compositions disclosed herein are lyophilized, spray-dried or freeze dried, for reconstitution before application to the skin. By way of non-limiting example, reconstitution may comprise wetting the composition before application to the skin. In some instances, the lyophilized, spray-dried or freeze dried composition is on an applicator, and the composition together with the applicator are reconstituted by wetting the applicator. In some instances, wetting occurs by applying water to the skin and then applying the applicator and/or composition to the wet skin. In one embodiment, the lyophilization, spray-drying or freeze drying is conducted with one or more excipients, such as glycerol or other sugar alcohols, to improve the shelf life of the selected, transformed, or engineered bacteria. In one embodiment, the lyophilized composition does not include trehalose (.alpha.-D-glucopyranosyl-1,1-.alpha.-D-glucopyranosyde). In some embodiments, the composition does not have to be frozen.

[00224] Compositions disclosed herein may be packaged in one or more containers. For example, a single bottle, tube, container, or capsule may be divided to two equal or unequal

parts wherein one part contains the bacteria, in their packing form (freeze dried/inactive, etc.), and the other part contains an activation material, which can be a liquid or a gel. The single bottle or container can be designed so that an end user can dispense with a single force applied to the container all or a portion of the contents in the two container parts, to dispense onto the skin or other surface the selected, transformed, or engineered bacteria and the activation material. The kit may also be of the form that comprises two or more containers, one container with the population(s) of selected, transformed, or engineered bacteria and the other with a formulation for admixture with the populations of selected, transformed, or engineered bacteria. In another example, two or more containers, one container with the population of selected, transformed, or engineered bacteria, the other container with natural nonpathogenic skin bacteria that are not selected, transformed, or engineered, and a third container with a formulation for admixture with the populations of selected, transformed, or engineered bacteria. In another example, the two or more containers composing the single bottle had one pump connected to two separate tubes, each draining from a different chamber. The kit may also include one or more complementary products, such as soaps, body washes or moisturizing lotions with certain pH, lotions or creams containing active compounds, bacteria and limiting factors etc. In another embodiment, the complementary product is a limiting factor that will enhance the growth, activity and/or expression of the compound of interest to provide a lasting or continuous expression of the compound. The complementary product may include any compound beneficial to the activity of the original product, and enhance its activity for lasting efficacy. Another contemplated packaging is one wherein the population of selected, transformed, or engineered bacteria is maintained as a layer on a bandage or film that is combined with a second layer of bandage/film that will allow activation of the bacteria, and that optionally may also limit reproduction/growth factors. In another embodiment, the final product is stored refrigerated, with the bacteria being in their active state. In another embodiment, the bacteria are stored in a small bead of water soluble cellulose. The beads can be mixed in any solution such as sunscreen/moisturizing/body wash or soap.

[00225] In yet another embodiment, this disclosure provides for compositions comprising a healthy skin microbiome transplant. Healthy skin microbiome transplants disclosed herein comprise a population of bacteria harvested from healthy or normal skin. Healthy skin microbiome transplants disclosed herein can be characterized as microbiomes that induce a low level of human inflammatory mediators (at the RNA and/or protein level) from a population of human cells when the microbiome is incubated with the population of human

cells. The population of human cells may be a subject's own keratinocytes. The population of human cells may be pooled keratinocytes. Non-limiting examples of inflammatory mediators include acne associated inflammatory markers such as IL-8, IL-6, TNF-alpha, INF-alpha, IL-1, and beta defensin. Methods of measuring levels of these mediators either at the mRNA, protein or functional level are known in the art and include, quantitative real-time PCR, northern blot, RNA-seq, microarray, ELISA, homogenous protein assays, immunoblot, or mass spectrometry.

[00226] In yet other embodiments are compositions comprising an individual's own modified microbiome. Compositions comprising an individual's own modified microbiome may be obtained by methods disclosed herein. In some embodiments, the individual's own modified microbiome is produced by harvesting or capturing the individual's own microbiome (*e.g.*, from a skin swab), culturing the microbiome, and removing at least one inflammatory strain of bacteria. In some embodiments, the individual's own modified microbiome is produced by harvesting or capturing the individual's own microbiome (*e.g.*, from a skin swab), culturing the microbiome, and removing at least one pathogenic strain of bacteria. In some embodiments, an inflammatory strain is a pathogenic strain. In some embodiments, an inflammatory strain or pathogenic strain is identified by incubating the strain with keratinocytes and detecting production of inflammatory mediators from the keratinocytes. In some embodiments, an inflammatory strain or pathogenic strain is identified by incubating the strain with keratinocytes and quantifying production of inflammatory mediators from the keratinocytes (*e.g.*, the strain produces higher levels of inflammatory mediators from the keratinocytes than a health-associated strain disclosed herein). In some embodiments, an inflammatory strain or pathogenic strain is identified by incubating the strain with keratinocytes and detecting undesirable keratinocyte gene expression or undesirable keratinocyte activity. Undesirable keratinocyte gene expression or undesirable keratinocyte activity would generally be understood by one skilled in the art to mean expression or activity in keratinocytes that promotes a skin disorder. In some instances, the keratinocytes are the subject's keratinocytes. In some instances, the keratinocytes are pooled keratinocytes. In some instances, methods comprise identifying and removing known acne associated strains such as, by way of non-limiting example, some *P. acnes* strains of ribotypes RT4 and RT5, and clade Ia bacteria. In some instances, methods comprise identifying and selecting only non-inflammatory strains identified by the method above or known to be associated with healthy skin and introducing the modified biome to the patient.

Non-limiting examples of non-inflammatory strains include *P. acnes* strains of ribotypes RT2, RT6, and clade II bacteria.

[00227] In yet another embodiment is a composition comprising a microbiome from a healthy individual's stool. These compositions may be referred to herein as a "fecal transplant." In some embodiments, the microbiome is a complete microbiome of a healthy individual's stool. In some embodiments, the microbiome is a partial microbiome of a healthy individual's stool. In some instances, the healthy individual does not have acne. In some instances, the healthy individual does not have an inflammatory condition. In some instances, the healthy individual does not have an inflammatory skin condition. Non-limiting examples of inflammatory conditions are acne, eczema, psoriasis, seborrheic dermatitis, rosacea, lupus, pemphigus, pemphigoid, scleroderma, alopecia areata, lichen sclerosis, lichen planus, pruritus, prurigo nodularis, lichen simplex chronicus, inflammatory bowel disease, colitis, irritable bowel syndrome, atherosclerosis, CAD, diabetes, HIV, and cancer. In some embodiments, the healthy individual is not a tissue transplant patient, is not taking an immunosuppressive drug, or is not currently/recently (within 12 weeks) receiving an antibiotic therapy. In some embodiments, the microbiome comprises strains of bacteria that produce no inflammatory mediators when co-incubated with colonic mucosal cells. In some embodiments, strains of bacteria that produce no inflammatory mediators when co-incubated with colonic mucosal cells are identified by 16S, 18S, or whole genome sequencing. In some embodiments, the partial microbiome is a modified microbiome, wherein the modified microbiome is derived from a fecal transplant by removing pathogenic strains or introducing health-associated strains.

Additional active ingredients

[00228] Compositions disclosed herein may comprise additional active ingredients. In certain embodiments, compositions disclosed herein comprise at least one non-living, non-microbial constituent. By way of non-limiting example, the non-living, non-microbial constituent may be selected from a small molecule, a fatty acid, an antibiotic, a metabolite, an antioxidant, and a retinoid. Non-limiting examples of antioxidants are vitamin C and vitamin E. Non-limiting examples of a retinoid are tretinoin, tazarotene, adapalene, and retinol. In some embodiments, the non-living, non-microbial constituent is vitamin D, which may be in the form of calcitriol. In some embodiments, the additional active ingredient is an agent that has anti-inflammatory activity.

[00229] In certain embodiments, the composition is intended to be used after treatment with an antibiotic. For example, an antibiotic may be used to reduce bacteria on the skin of a

subject before the subject is treated with the composition. This may allow for better growth, engraftment and/or effects of the health-associated microbes in the composition. Non-limiting examples of antibiotics include macrolide, tetracycline, β -lactam, aminoglycoside, cephalosporin, carbapenems, quinolone/fluoroquinolone, sulfonamides, salicylic acid, glycolic acid, azaleic acid, live phage therapy, synthetic phage contractile nanotubes, laser, dapsone, benzoyl peroxide, benzoyl peroxide/resveratrol combinations, and any combination thereof. In some embodiments, the antibiotic is selected from clindamycin, doxycycline, erythromycin, and tetracycline, wherein the antibiotic is formulated for topical administration. In some embodiments, the antibiotic is selected from erythromycin, tetracycline, doxycycline and minocycline, wherein the antibiotic is formulated for oral administration. In some embodiments, compositions disclosed herein comprise an antibiotic, wherein at least one *P. acnes* strain is resistant to the antibiotic.

[00230] In certain embodiments, a composition disclosed herein is used before or after a topical anti-acne medication such as benzoyl peroxide or salicylic acid. In some embodiments, the concentration of the benzoyl peroxide or salicylic acid in the anti-acne medication is between about 0.1% and about 3%. In some embodiments, the concentration of the anti-acne medication is between about 0.1% and about 2.5%. In some embodiments, the concentration of the anti-acne medication is between about 0.5% and about 2.5%. In some embodiments, the concentration of the anti-acne medication is between about 1% and about 2.5%. In some embodiments, the concentration of the anti-acne medication is less than about 2.5%. In some embodiments, the concentration of the anti-acne medication is less than about 2%. In some embodiments, the concentration of the anti-acne medication is less than about 1.5%. In some embodiments, the concentration of the anti-acne medication is less than about 1%. In some embodiments, the concentration of the anti-acne medication is less than about 0.5%. In some embodiments, the concentration of the anti-acne medication is less than about 0.1%.

[00231] In certain embodiments, compositions disclosed herein comprise a topical anti-acne medication such as a retinoid. Non-limiting examples of topical retinoid compounds include retinoic acid, tretinoin, adapalene, and tazarotene. In certain embodiments, compositions disclosed herein comprise resveratrol or trans-resveratrol. In some embodiments, the concentration of the retinoid or resveratrol in the composition is less than about 10%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is less than about 5%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is less than about 2.5%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is less than about 1%. In some embodiments, the

concentration of the retinoid or resveratrol in the composition is less than about 0.5%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is between about 0.5% and about 10%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is between about 1% and about 10%. In some embodiments, the concentration of the retinoid or resveratrol in the composition is between about 0.5% and about 2.5%.

[00232] In some embodiments, compositions disclosed herein comprise at least one omega-3 fatty acid. Non-limiting examples of omega-3 fatty acids include hexadecatrienoic acid (HTA), α -Linolenic acid (ALA), stearidonic acid (SDA), eicosatrienoic acid (ETE), eicosatetraenoic acid (ETA), eicosapentaenoic acid (EPA), heneicosapentaenoic acid (HPA), docosapentaenoic acid (DPA), clupanodonic acid, docosahexaenoic acid (DHA), tetracosapentaenoic acid, tetracosahexaenoic acid (nisinic acid), and phytosphingosine.

[00233] In some embodiments, compositions disclosed herein comprise an acid selected from glycolic acid, azelaic acid, and trichloroacetic acid. In some embodiments, compositions disclosed herein comprise a natural extract, such as tea tree oil or green tea extract.

[00234] In some embodiments, the additional active ingredient comprises a drug targeting at least one strain of *P. acnes*. In some embodiments, the drug targeting at least one strain of *P. acnes* is a small molecule drug. In some embodiments, the drug targeting at least one strain of *P. acnes* is a small molecule inhibitor of an enzyme expressed by *P. acnes*. In some embodiments, the enzyme expressed by *P. acnes* is required for *P. acnes* growth or *P. acnes* energy metabolism. In some embodiments, the drug targeting at least one strain of *P. acnes* is a biologic. In some embodiments, the biologic comprises a peptide. In some embodiments, the biologic comprises an antibody or antigen binding fragment. In some embodiments, the biologic comprises an antibody-small molecule conjugate. In some embodiments, the biologic comprises an antibody-drug conjugate. In some embodiments, the biologic comprises a nucleic acid. In some embodiments, the nucleic acid comprises an antisense nucleic acid molecule, wherein the antisense nucleic acid molecule inhibits an enzyme expressed by *P. acnes*. In some embodiments, the enzyme expressed by *P. acnes* is required for *P. acnes* growth or *P. acnes* energy metabolism. In some embodiments, the antisense nucleic acid molecule comprises siRNA. In some embodiments, the antisense nucleic acid molecule comprises a shRNA. In some embodiments, the antisense nucleic acid molecule comprises a guide RNA to be used with a CRISPR-associated endonuclease. In some embodiments, the additional active ingredient (e.g., guide RNA and CRISPR-associated endonuclease) and targets a genomic element specific for strains of *P. acnes* associated with

acne. In some embodiments, the additional active ingredient comprises an agent that will inhibit biofilm formation of *P. acnes*. In some cases the active agent is a combination of ellagic acid and tetracycline that inhibits biofilm formation and the associated virulence of *Propionibacterium acnes* *in vitro* and *in vivo*.

[00235] Compositions disclosed herein may be administered, daily, weekly, or monthly. In certain embodiments, the composition is administered twice daily. In certain embodiments, the composition is administered at least twice weekly. In certain embodiments, the composition is administered at least twice monthly.

Methods of Treating Skin Disorders

[00236] Provided herein, in some aspects, are methods for treating or preventing skin disorders disclosed herein. In some aspects, the methods comprise administering a strain of bacteria disclosed herein, wherein the strain of bacteria has been incorporated into a pharmaceutical composition. In some aspects, the methods comprise administering a pharmaceutical composition disclosed herein. In some aspects, the methods comprise administering a composition disclosed herein.

[00237] In some aspects, the disclosure provides methods for treating or preventing acne. Methods for treating or preventing acne generally comprise administering an effective amount of a strain of bacteria disclosed herein to the skin of a subject in need thereof. In some embodiments, methods comprise administering at least one composition disclosed herein. In some embodiments, methods comprise administering at least one species of bacteria disclosed herein. In some embodiments, methods comprise administering at least one strain of bacteria disclosed herein. In some embodiments, methods comprise administering at least one ribotype of bacteria disclosed herein. In some embodiments, methods comprise administering at least one health-associated microbe disclosed herein. In some embodiments, methods comprise administering at least one health-associated microbe disclosed herein. In some embodiments, methods comprise administering at least one selected species of selected bacteria disclosed herein. In some embodiments, methods comprise administering at least one selected strain of selected bacteria disclosed herein. In some embodiments, methods comprise administering at least one selected, transformed, or engineered bacteria disclosed herein. In some embodiments, methods comprise administering at least one genetically modified bacteria disclosed herein. In some embodiments, methods comprise administering at least one genetically engineered bacteria disclosed herein. In some embodiments, methods comprise administering at least one health-associated strain of bacteria described herein.

[00238] In some embodiments, methods disclosed herein comprise administering a health-associated microbe disclosed herein. In some embodiments, methods disclosed herein comprise administering a pharmaceutical composition comprising a health-associated microbe disclosed herein. In some embodiments, methods disclosed herein comprise administering daily. In some embodiments, methods disclosed herein comprise administering once daily. In some embodiments, methods disclosed herein comprise administering more than once daily. In some embodiments, methods disclosed herein comprise administering twice daily. In some embodiments, methods disclosed herein comprise administering three times daily. In some embodiments, methods disclosed herein comprise administering four times daily. In some embodiments, methods disclosed herein comprise administering once to three times daily. In some embodiments, methods disclosed herein comprise administering two to three times daily. In some embodiments, methods disclosed herein comprise administering two to four times daily. In some embodiments, methods disclosed herein comprise administering weekly. In some embodiments, methods disclosed herein comprise administering twice weekly. In some embodiments, methods disclosed herein comprise administering three times weekly. In some embodiments, methods disclosed herein comprise administering four times weekly. In some embodiments, methods disclosed herein comprise administering five times weekly. In some embodiments, methods disclosed herein comprise administering six times weekly. In some embodiments, methods disclosed herein comprise administering monthly.

[00239] In some embodiments, methods disclosed herein comprise administering a health-associated microbe disclosed herein in coordination with skin washing or cleansing. By way of non-limiting example, washing or cleansing may comprise contacting the skin with at least one of soap, benzoyl peroxide and alcohol. In some instances, cleansing is performed before administering the health-associated microbe. In some instances, cleansing is performed at least one minute before administering the health-associated microbe. In some instances, cleansing is performed at least ten minutes before administering the health-associated microbe. In some instances, cleansing is performed at least thirty minutes before administering the health-associated microbe. In some instances, cleansing is not to be performed until at least one hour after administering the health-associated microbe. In some instances, cleansing is not to be performed until at least two hours after administering the health-associated microbe. In some instances, cleansing is not to be performed until at least four hours after administering the health-associated microbe. In some instances, cleansing is not to be performed until at least six hours after administering the health-associated microbe.

In some instances, cleansing is not to be performed until at least eight hours after administering the health-associated microbe. In some instances, cleansing is not to be performed until at least twelve hours after administering the health-associated microbe.

[00240] In some embodiments, methods disclosed herein comprise administering a health-associated microbe disclosed herein in coordination with an additional treatment for the skin disorder. By way of non-limiting example, the additional treatment may comprise an extract, a clay mask, a vitamin treatment, a laser treatment, or an acid peel. In some instances, the additional treatment is performed before administering the health-associated microbe. In some instances, the additional treatment is performed at least one minute before administering the health-associated microbe. In some instances, the additional treatment is performed at least ten minutes before administering the health-associated microbe. In some instances, the additional treatment is performed at least thirty minutes before administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least one hour after administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least two hours after administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least four hours after administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least six hours after administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least eight hours after administering the health-associated microbe. In some instances, the additional treatment is not to be performed until at least twelve hours after administering the health-associated microbe.

[00241] In some embodiments, methods disclosed herein comprise administering the health-associated microbe over a duration defined by a first administering time and a last administering time. In some embodiments, the duration is about one week to about twelve weeks. In some embodiments, the duration is about one week to about ten weeks. In some embodiments, the duration is about one week to about eight weeks. In some embodiments, the duration is about one week to about six weeks. In some embodiments, the duration is about one week to about four weeks. In some embodiments, the duration is about one week to about two weeks. In some embodiments, the duration is about one week to about twelve weeks. In some embodiments, the duration is about one week to about ten weeks. In some embodiments, the duration is about one week to about eight weeks. In some embodiments, the duration is about one week to about six weeks. In some embodiments, the duration is about one week to about four weeks. In some embodiments, the duration is about two weeks

to about twelve weeks. In some embodiments, the duration is about two weeks to about ten weeks. In some embodiments, the duration is about two weeks to about eight weeks. In some embodiments, the duration is about two weeks to about six weeks. In some embodiments, the duration is about two weeks to about four weeks. In some embodiments, the duration is about four weeks to about twelve weeks. In some embodiments, the duration is about four weeks to about ten weeks. In some embodiments, the duration is about four weeks to about eight weeks. In some embodiments, the duration is about four weeks to about six weeks. In some embodiments, the duration is about six weeks to about twelve weeks. In some embodiments, the duration is about eight weeks to about twelve weeks. In some embodiments, the duration is about twelve weeks to about twenty weeks.

[00242] In some embodiments, methods disclosed herein comprise engrafting skin of a subject with a health-associated microbe disclosed herein. In some instances, engrafting comprises administering a health-associated microbe such that at least a portion of the health-associated microbe remains present on the skin for at least a sufficient amount of time to provide health benefits to the skin. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 12 hours after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 24 hours after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 48 hours after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 3 days after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 4 days after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 5 days after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 6 days after administering. In some instances, at least a portion of the health-associated microbe remains present on the skin for at least 1 week after administering. In some instances, at least a portion of the health-associated microbe is at least about 10% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 30% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 50% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 70% of total health-associated microbes administered. In some instances, at least a

portion of the health-associated microbe is at least about 90% of total health-associated microbes administered.

[00243] In some embodiments, methods disclosed herein comprise engrafting at least one pilosebaceous unit of the skin of a subject with a health-associated microbe disclosed herein. In some instances, engrafting comprises administering a health-associated microbe such that at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least a sufficient amount of time to provide health benefits to the skin. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 12 hours after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 24 hours after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 48 hours after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 3 days after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 4 days after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 5 days after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 6 days after administering. In some instances, at least a portion of the health-associated microbe remains present in the pilosebaceous unit for at least 1 week after administering. In some instances, at least a portion of the health-associated microbe is at least about 10% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 30% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 50% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 70% of total health-associated microbes administered. In some instances, at least a portion of the health-associated microbe is at least about 90% of total health-associated microbes administered.

[00244] In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin that are present in the administered health-associated microbes and not present in microbes on the skin of the subject before administering the composition. Engraftment of the health-associated bacteria may be determined by monitoring the percentage of bacteria in a sample from the treated subject comprising a genetic marker that is present in health-associated *P. acnes* and not disease-

associated *P. acnes*. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin that are present in the administered health-associated microbes at a higher level than microbes on the skin of the subject. In some instances, a higher level is at least about 2-fold more, at least about 3-fold more, at least about 5-fold more, or at least about 10-fold more. In some instances, the nucleic acid is at least one of DNA and RNA. In some instances, the nucleic acid is DNA or RNA corresponding to *deoR*. In some instances, the nucleic acid is DNA or RNA corresponding to *Cas5*. In some instances, the nucleic acid is DNA or RNA corresponding to type II lipase. In some instances, the nucleic acid is DNA or RNA corresponding to ATP binding cassette transporter. In some instances, engraftment has occurred when the presence of the nucleic acids has increased by at least about 10% over the total population of bacteria on the skin of the subject. In some instances, engraftment has occurred when the presence of the nucleic acids has increased by at least about 20% over the total population of bacteria on the skin of the subject. In some instances, engraftment has occurred when the presence of the nucleic acids has increased by at least about 30% over the total population of bacteria on the skin of the subject.

[00245] In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin that are not present in the administered health-associated microbes and present in microbes on the skin of the subject before administering the composition. Thus, a reduction in the nucleic acids would reflect engraftment. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin that are present in the administered health-associated microbes at a lower level than microbes on the skin of the subject. In some instances, a lower level is at least about 2-fold less, at least about 3-fold less, at least about 5-fold less, or at least about 10-fold less. In some instances, the nucleic acid is DNA or RNA corresponding to type I lipase. In some instances, the nucleic acid is DNA or RNA corresponding to *Cas5*. In some instances, the nucleic acid is DNA or RNA corresponding to DNA binding response regulator. In some instances, the nucleic acid is DNA or RNA corresponding to phosphoglycerate kinase. In some instances, engraftment has occurred when the presence of the nucleic acids has decreased by at least about 10% over the total population of bacteria on the skin of the subject. In some instances, engraftment has occurred when the presence of the nucleic acids has decreased by at least about 20% over the total population of bacteria on the skin of the subject. In some instances, engraftment has occurred when the presence of the

nucleic acids has decreased by at least about 30% over the total population of bacteria on the skin of the subject.

[00246] In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin after at least one face wash. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin after at least two face washes. In some instances, the face wash comprises contacting the skin with water. In some instances, the face wash comprises contacting the skin with soap and water. In some instances, the face wash comprises contacting the skin with benzoyl peroxide. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin at least one day after most recently administering the health-associated microbe. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin at least two days after most recently administering the health-associated microbe. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin at least three days after most recently administering the health-associated microbe. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin at least one week after most recently administering the health-associated microbe. In some instances, engraftment can be assessed, characterized or quantified by quantifying nucleic acids present on the skin at least one month after most recently administering the health-associated microbe.

[00247] In some embodiments, methods disclosed herein comprise administering an isolated strain of bacteria. In some embodiments, methods disclosed herein comprise administering an isolated strain of bacteria. In some embodiments, methods disclosed herein comprise administering a purified strain of bacteria. In some embodiments, methods disclosed herein comprise administering a purified and isolated strain of bacteria. In some embodiments, methods disclosed herein comprise selecting, isolating, or purifying a strain of bacteria. Selecting, isolating or purifying may comprise isolating a single clone of bacteria and propagating it to obtain a selected, isolated, or purified strain. In some embodiments, the methods comprise selecting, isolating or purifying a plurality of strains of bacteria to obtain at least a first selected, isolated, or purified strain and a second selected, isolated, or purified strain. In some embodiments, the methods further comprise combining the first selected, isolated, or purified strain and the second selected, isolated, or purified strain in a pharmaceutical composition. In some embodiments, the first selected, isolated, or purified strain or the second selected, isolated, or purified strain is selected from strains disclosed

herein. In some embodiments, the first selected, isolated, or purified strain and the second selected, isolated, or purified strain are selected from strains disclosed herein.

[00248] In some embodiments, methods comprise administering at least one health-associated strain of bacteria selected from a health-associated strain of *Propionibacterium*, *Staphylococcus* and *Lactobacillus* bacteria. In some embodiments, methods comprise administering at least one health-associated strain of *Propionibacterium* bacteria. In some embodiments, methods comprise administering at least one health-associated strain selected from a health-associated strain of *P. acnes*, a health-associated strain of *P. granulosum*, a health-associated strain of *P. avidum*, a health-associated strain of *P. acnes* subsp. *defendens*, and a health-associated *Staphylococcus*, as described herein. In some embodiments, the health-associated strain of *P. acnes* is not *P. acnes* subsp. *acnes*. In some embodiments, methods comprise administering at least one health-associated strain of *P. acnes*. In some embodiments, methods comprise administering at least one health-associated fungus. The health-associated fungus may be *Malassezia*.

[00249] In some embodiments, methods comprise administering a microbe disclosed herein. In some embodiments, the methods comprise administering a mixture of at least two microbes disclosed herein. In some embodiments, the methods comprise administering at least one health-associated microbe disclosed herein. In some embodiments, the microbe is a fungus. In some embodiments, the microbe is a protist. In some embodiments, the microbe is bacteria. In some embodiments, the bacteria comprise a strain of *Propionibacterium* bacteria. In some embodiments, the bacteria comprise a strain of *P. acnes*. In some embodiments, the bacteria comprise a strain of *P. avidum*. In some embodiments, the bacteria comprise a strain of *P. granulosum*. In some embodiments, the bacteria comprise a strain of *P. acnes* subsp. *defendens*. In some embodiments, the bacteria consist essentially of at least one strain of *P. acnes*. In some embodiments, the bacteria consist essentially of at least one strain of *P. avidum*. In some embodiments, the bacteria consist essentially of at least one strain of *P. granulosum*. In some embodiments, the bacteria consist essentially of at least one strain of *P. acnes* subsp. *defendens*.

[00250] In some embodiments, methods comprise administering a composition disclosed herein. In some embodiments, methods comprise administering a composition having a formulation disclosed herein.

[00251] In certain embodiments, methods disclosed herein comprise applying an effective amount of a composition containing a plurality of microbes of different ribotypes. In certain embodiments, the strain is a *P. acnes* strain of a ribotype selected from RT1, RT2, RT3, RT4,

RT5, RT7, RT8, RT9, and RT10. In certain embodiments, the strain is a *P. acnes* strain of a ribotype selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10. In certain embodiments, the plurality of microbes is a mixture of two or more *P. acnes* strains of different ribotypes. In certain embodiments, the different ribotypes comprise RT1 and RT2. In certain embodiments, the different ribotypes comprises RT1 and RT3. In certain embodiments, the different ribotypes comprise RT1 and not RT6. In certain embodiments, the different ribotypes comprise RT2 and RT3. In certain embodiments, the v comprises RT2 and not RT6. In certain embodiments, the different ribotypes comprise RT2 and RT3. In certain embodiments, the different ribotypes comprise RT3 and not RT6. In certain embodiments, the different ribotypes consist essentially of RT1 and RT2. In certain embodiments, the different ribotypes consist essentially of RT1 and RT3. In certain embodiments, the different ribotypes consist essentially of RT1 and not RT6. In certain embodiments, the different ribotypes consist essentially of RT2 and RT3. In certain embodiments, the different ribotypes consist essentially of RT2 and not RT6. In certain embodiments, the different ribotypes consist essentially of RT2 and RT3. In certain embodiments, the different ribotypes consist essentially of RT3 and not RT6. In certain embodiments the mixture does not comprise ribotype RT6.

[00252] In certain embodiments, methods described herein comprise applying an effective amount of a composition containing a plurality of microbes of different ribotypes. In certain embodiments, the plurality of microbes is a mixture of three or more *P. acnes* strains of different ribotypes. In certain embodiments, the mixture comprises RT1, RT2, and RT3. In certain embodiments, the mixture comprises RT2, RT3, and not RT6. In certain embodiments, the mixture comprises RT1, RT2, and RT6. In certain embodiments, the mixture comprises RT1, RT3, and not RT6. In certain embodiments, the mixture consists essentially of RT1, RT2, and RT3. In certain embodiments, the mixture consists essentially of RT2, RT3, and not RT6. In certain embodiments, the mixture consists essentially of RT1, RT2, and not RT6. In certain embodiments, the mixture consists essentially of RT1, RT3, and not RT6. In certain embodiments the mixture does not comprise RT6.

[00253] Methods described herein comprise applying health-associated microbes of various strains. Compositions described herein comprise various strains of bacteria. In certain embodiments, the strain has at least 50% homology to a strain described herein. In certain embodiments, the strain has at least 60% homology to a strain described herein. In certain embodiments, the strain has at least 70% homology to a strain described herein. In certain embodiments, the strain has at least 80% homology to a strain described herein. In certain

embodiments, the strain has at least 90% homology to a strain described herein. In certain embodiments, the strain has at least 95% homology to a strain described herein. In certain embodiments, the strain has at least 50% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 60% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 70% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 80% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 90% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 95% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has at least 99% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54. In certain embodiments, the strain has 100% homology to SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, or SEQ ID NO: 54.

[00254] In certain embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a metabolite produced by a strain of *P. acnes* to a subject in need thereof. In certain embodiments, the metabolite is selected from the group comprising bacterial culture supernatant, cell lysate, proteins, nucleic acids, lipids, and other bacterial molecules. In certain embodiments, the metabolite is selected from the group comprising bacterial culture supernatant, cell lysate, proteins, nucleic acids, lipids, and other bacterial molecules.

[00255] In some embodiments, compositions and methods disclosed herein may comprise use of bacteria that does not comprise *P. acnes* bacteria, or the application thereof, respectively. In some embodiments, the bacteria comprises a *Staphylococcus* strain. In some embodiments, compositions and methods disclosed herein may comprise use of fungus, such as *Malassezia*.

[00256] In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of bacteria associated with healthy or normal skin. Healthy or normal skin may be skin essentially free of acne. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of bacteria that produces low to absent levels of pro-inflammatory mediators when co-incubated with a subject's keratinocytes.

[00257] In some embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not induce expression

of RNA that encodes pro-inflammatory proteins. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not induce expression of pro-inflammatory proteins. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not induce activity of pro-inflammatory proteins. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not induce expression of RNA that encodes pro-inflammatory proteins.

[00258] In some embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase expression of RNA that encodes pro-inflammatory proteins. In some embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase expression of pro-inflammatory proteins. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase activity of pro-inflammatory proteins.

[00259] In some embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase expression of RNA that encodes pro-inflammatory proteins to a level that they would cause or increase acne when the bacterium is applied to a subject. In some embodiments, described herein, are methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase expression of pro-inflammatory proteins to a level that they would cause or increase acne when the bacterium is applied to a subject. In some embodiments, described herein, methods for treating or preventing acne comprising: administering an effective amount of a bacterium that does not increase activity of pro-inflammatory proteins to a level that they would cause or increase acne when the bacterium is applied to a subject. Non-limiting examples of pro-inflammatory proteins include IL-8, IL-1, IL-6, TNF-alpha, INF-alpha, and human beta defensin.

[00260] In some embodiments, described herein, are methods for treating or preventing seborrheic dermatitis comprising: administering an effective amount of a health-associated strain of *Propionibacterium* to a subject in need thereof. In some embodiments, described herein, are methods for treating or preventing seborrheic dermatitis comprising: administering an effective amount of a health-associated strain of *P. acnes* to a subject in need thereof. In some embodiments, the methods are performed after the subject has

undergone a cosmetic hair treatment (*e.g.*, hair dye). In some embodiments, the effective amount is an amount that results in greater than about 55% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results in greater than about 60% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results in greater than about 65% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results in greater than about 70% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results between about 55% *Propionibacterium* and about 75% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results between about 65% *Propionibacterium* and about 80% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results between about 70% *Propionibacterium* and about 80% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that results between about 70% *Propionibacterium* and about 85% *Propionibacterium* on an affected area of the scalp or skin of the subject. In some embodiments, the effective amount is an amount that provides a desirable ratio of *Propionibacterium* to *Staphylococcus* on the scalp or skin of the subject. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be selected from about 2:1, about 2.5:1, about 3:1, about 3.5:1 and about 4:1. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be selected from at least about 2:1, at least about 2.5:1, at least about 3:1, at least about 3.5:1 and at least about 4:1. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be between about 1.5:1 and about 4:1. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be between about 2:1 and about 4:1. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be between about 2.5:1 and about 4:1. The desirable ratio of *Propionibacterium* to *Staphylococcus* may be between about 3:1 and about 4:1. In some embodiments, an effective amount is an amount that provides a desirable amount of a *Malassezia* fungus.

[00261] In some embodiments, the methods of treating disclosed herein further comprise determining strains of bacteria on the skin of the subject that cause or promote inflammation of the skin of the subject. In some embodiments, methods comprise assessing an inflammatory mediated response in a sample of keratinocytes. In some embodiments, methods comprise assessing an inflammatory mediated response in a sample of keratinocytes

obtained from a subject. The subject may be a healthy subject. The subject may be a subject to be treated, such as a subject suffering from acne. In some embodiments, the methods comprise pooling or culturing keratinocytes from multiple subjects.

[00262] Methods disclosed herein may comprise administering a drug to the subject. In some embodiments, the drug is administered orally. In some embodiments, the drug is administered topically. In some embodiments, the drug is administered topically to the skin of the subject that is affected by acne. In certain embodiments, described herein, are methods for preventing or treating acne in a subject comprising: administering an effective amount of a drug specifically targeting *P. acnes*. In certain embodiments, described herein, are methods for preventing or treating acne in a subject comprising: administering an effective amount of a drug targeting *P. acnes* of a ribotype selected from RT1, RT2, RT3, RT4, RT5, RT7, RT8, RT9, and RT10, and combinations thereof. In certain embodiments, described herein, are methods for preventing or treating acne in a subject comprising: administering an effective amount of a drug targeting *P. acnes* of a ribotype selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10, and combinations thereof. In certain embodiments, described herein, are methods for preventing or treating acne in a subject comprising: administering an effective amount of a drug targeting a strain of bacteria or fungus that induces or promotes production of inflammatory mediators from a subject's keratinocytes when co-incubated with a subject's keratinocytes. In certain embodiments, described herein, are methods for preventing or treating acne in a subject comprising: administering an effective amount of a drug targeting a strain of bacteria or fungus that induces or promotes production of inflammatory mediators from a subject's keratinocytes when a factor produced by the bacteria or fungus is co-incubated with a subject's keratinocytes. Such drugs are disclosed herein, *e.g.*, small molecules, antisense molecules, siRNA, biologics, antibodies, and combinations thereof.

[00263] Methods disclosed herein may comprise performing laser therapy on the skin of the subject. In some embodiments, laser therapy is performed prior to administration of a drug or bacteria disclosed herein to a subject. In some embodiments, laser therapy is performed after administration of a drug or bacteria disclosed herein to a subject. In some embodiments, laser therapy is performed simultaneously with administration of a drug or bacteria disclosed herein to a subject. The laser therapy may be a blue or red-light laser targeting porphyrins.

Combination Treatments

[00264] It is envisioned that the any of the compositions, health-associated microbes disclosed herein can be used in combination with other standard treatments. For example, in some embodiments, methods comprise administering compositions disclosed herein before,

after, or simultaneously with administration of an additional therapeutic agent. In some embodiments, the methods may comprise topically administering an antibiotic. Non-limiting examples of topical antibiotics include clindamycin, doxycycline, erythromycin, and tetracycline. In some embodiments, the methods may comprise orally administering an antibiotic. Non-limiting examples of oral antibiotics include erythromycin; or a tetracycline, such as doxycycline or minocycline. Other standard treatments may comprise administering an anti-inflammatory agent, an antioxidant, an acid, light therapy, or a combination thereof. Other standard treatments may comprise administering a peroxide, an acid, or an alcohol. In some embodiments, the peroxide is benzoyl peroxide. In some embodiments, the acid is selected from salicylic acid, azelaic acid, trichloroacetic acid, and glycolic acid. In some embodiments, the alcohol is selected from cetyl alcohol, stearyl alcohol, and cetearyl alcohol.

[00265] In some embodiments, methods disclosed herein do not comprise treating the subject with an antibiotic. Methods that avoid the use of antibiotics may be desirable, as they help to prevent the ongoing problem of global antibiotic resistance.

[00266] In some embodiments, methods comprise treating the subject with a laser. In some embodiments, methods comprise treating the subject with blue light. In some embodiments, methods comprise treating the subject with red light. In some embodiments, methods comprise treating the subject with a targeted laser device and/or active ingredient directed to at least one pro-inflammatory strain of *P. acnes*. In some embodiments, methods comprise treating with a laser that targets porphyrins.

[00267] In some embodiments, standard treatments, antibiotics, laser treatment, and other treatments for the skin disorder are administered before administering a pharmaceutical composition disclosed herein, thereby reducing endogenous bacteria or pathogenic bacteria on the skin of the subject before introducing the health-associated microbe(s) of the pharmaceutical composition. By way of non-limiting example, skin is treated with benzoyl peroxide at least once before applying a pharmaceutical composition disclosed herein. In another non-limiting example, skin is treated with benzoyl peroxide daily for at least one week before applying a pharmaceutical composition disclosed herein. In yet another non-limiting example, skin is treated with benzoyl peroxide daily for at least one month before applying a pharmaceutical composition disclosed herein.

[00268] In some embodiments, methods disclosed herein comprise administering a first health-associated microbe disclosed herein at a first time point and a second health-associated microbe disclosed herein at a second time point. In some embodiments, the first time point and the second time point are separated by a sufficient amount of time such that probiotic

activity of the first health-associated microbe is not negatively impacted by the second health-associated microbe. By way of non-limiting example, the second health-associated microbe may produce a bacteriocin that is toxic to the first health-associated microbe. Applying these microbes simultaneously would result in less than optimal activity from the first health-associated microbe. However, when both are administered, but at separate time points, they may be more health-promoting than either one administered alone. In some instances, the first time point and the second time point are separated by at least 4 hours. In some instances, the first time point and the second time point are separated by at least 8 hours. In some instances, the first time point and the second time point are separated by at least 12 hours. In some instances, the first time point and the second time point are separated by at least 16 hours. In some instances, the first time point and the second time point are separated by at least 20 hours. In some instances, the first time point and the second time point are separated by at least 24 hours. In some instances, the first time point and the second time point are separated by at least 36 hours. In some instances, the first time point and the second time point are separated by at least 48 hours. In some instances, the first time point and the second time point are separated by about 4 hours to about 12 hours. In some instances, the first time point and the second time point are separated by about 12 hours to about 24 hours. In some instances, the first time point and the second time point are separated by about 24 hours to about 72 hours. In some instances, the first health-associated microbe is a strain of *P. acnes*, the second health-associated microbe is a strain of *Lactobacillus*, and the first time point and the second time point are separated by about 8 hours to about 24 hours.

Treatment of acne and other disorders with microbiome transplant

[00269] In certain embodiments, described herein, are methods to treat skin disorders comprising administering a microbiome transplant from a healthy donor or a donor unaffected by a disease to a subject in need thereof. In certain embodiments, described herein, are methods to treat skin disorders comprising administering a microbiome transplant from a healthy donor unaffected by a skin disorder. In certain embodiments, the skin disorder is acne. In certain embodiments, the skin disorder is selected from acne, eczema, psoriasis, seborrheic dermatitis, rosacea, autoimmune disease, lichen sclerosis, lichen planus, pruritus, prurigo nodularis, lichen simplex chronicus, and a combination thereof.

[00270] In a certain embodiment, the disclosure provides method for obtaining and purifying a microbiome from a stool sample of a healthy individual, wherein the healthy individual is a first subject not suffering from acne or any other skin disorder, and transplanting that to a second subject that suffers from a skin disorder. The skin disorder may

be selected from acne, eczema, psoriasis, seborrheic dermatitis, rosacea, autoimmune disease such as lupus, bullous pemphigoid, pemphigus, lichen planus, pruritus, and xerosis. In another embodiment, the disclosure provides a method for obtaining and purifying a microbiome from an oral sample of a healthy individual not suffering from an inflammatory disorder, and transplanting that to a subject that suffers from a skin disorder. Non-limiting examples of inflammatory conditions include autoimmune disease (*e.g.*, vitiligo, pernicious anemia, alopecia areata, pemphigus, pemphigoid, lupus, scleroderma, diabetes), atherosclerosis, and arthritis.

Diagnosis of acne and other diseases

[00271] Health-associated *P. acnes* can be differentiated from disease-associated *P. acnes* based on genetic differences. For example, disease-associated *P. acnes* have been shown to harbor genomic elements that encode for multiple virulence genes. Many health-associated *P. acnes*, on the other hand, carry clustered regularly interspaced short palindromic repeat (CRISPR) elements that prevent health-associated *P. acnes* from acquiring virulence genes. In addition to genetic differences, an increase in *P. acnes* derived molecules such as porphyrins, proteases, lipases, and hemolysins, may be associated with disease. Therefore, genes encoding for biosynthesis of *P. acnes* derived molecules (*e.g.*, porphyrins, proteases, lipase, and hemolysins) may be useful to distinguish between health-associated *P. acnes* and disease-associated *P. acnes*.

[00272] In one aspect, provided herein are methods of differentiating health-associated *P. acnes* bacteria from disease-associated *P. acnes* bacteria based on genetic markers. Exemplary methods comprise measuring expression of one or more genetic markers including, but not limited to, deoR, Cas5, pIMPLE, type I lipase, type II lipase, and alanine dehydrogenase. In some instances, methods for differentiating between health-associated *P. acnes* and disease-associated *P. acnes* comprise differentiation based on ribotype. Also provided herein are methods of differentiating between health-associated *P. acnes* and disease-associated *P. acnes* comprising quantitative PCR or sequencing of at least one genetic marker, such as, deoR, Cas5, pIMPLE, type I lipase, type II lipase, alanine dehydrogenase, or a combination thereof. In some cases, methods comprise differentiating between strains and/or ribotypes of *P. acnes* bacteria. As a non-limiting example, *P. acnes* RT6 comprises a DNA-binding response regulator and/or phosphoglycerate kinase, which is absent in RT1, RT2, RT3, RT4, and RT5. As another example, an ABC transporter gene is absent from RT6 and present in RT1, RT2, RT3, RT4, and RT5. In some cases, such methods are used to select for bacteria for use in a composition described herein. For example, RT6

may not be present in compositions disclosed herein. In some cases, such methods are used to monitor treatment of an individual with the health-associated microbe. Moreover, in some cases, the methods are used to distinguish between a health-associated and disease-associated bacteria of the same ribotype. For example, *P. acnes* RT1 has both a disease-associated and health-associated *P. acnes* that are distinguishable based on the presence and/or absence of genetic markers.

[00273] Methods of diagnosing and/or monitoring treatment of a disease in an individual comprising quantifying health-associated and/or disease-associated *P. acnes* in a sample from the individual are also provided. Certain methods for quantification as provided herein comprise measuring at least one of deoR, a CRISPR-associated protein, pIMPLE, type I lipase, type II lipase, alanine dehydrogenase, DNA-binding response regulator, phosphoglycerate kinase, and ABC transporter. 23S ribosomal RNA may be measured to determine quantity of total bacteria in a sample. In some embodiments, the treatment comprises administration of a health-associated microbe provided herein. As a non-limiting example, the health-associated microbe comprises a *P. acnes* strain of RT1, RT2, RT3, or a combination thereof. In some cases, the health-associated microbe does not comprise a *P. acnes* of RT6.

[00274] Further provided herein are methods for determining a microbiome profile in an individual by detecting and/or quantifying at least one of deoR, a CRISPR-associated protein, pIMPLE, type I lipase, type II lipase, alanine dehydrogenase, DNA-binding response regulator, phosphoglycerate kinase, and ABC transporter in a sample from the individual. For determining relative quantities of bacteria in a sample, 23S ribosomal RNA sequences may be used to estimate total bacteria in a sample from the individual. Determination of a microbiome profile may be useful before and/or during treatment, for example, treatment with a health-associated bacteria, such as *P. acnes*. Methods for monitoring a treatment regimen following determination of a microbiome profile are also provided.

[00275] Further provided are methods of diagnosing or characterizing acne or other skin disorders in an individual. Such methods may be combined with the health-associated microbes and bacterial compositions provided herein to assess for suitability for treatment and/or treatment monitoring. In certain embodiments, the disease is acne. In certain embodiments, the skin disorder is acne, eczema, psoriasis, seborrheic dermatitis, rosacea, autoimmune disease, lichen sclerosis, lichen planus, pruritus, prurigo nodularis, lichen simplex chronicus, or a combination thereof. In certain embodiments, an individual is diagnosed with acne if the individual is determined to possess a pathogenic strain of

Propionibacterium acnes (*P. acnes*), *Staphylococcus*, or *Malassezia* fungi. In certain embodiments, the pathogenic strain of *P. acnes* comprises a ribotype (RT) that is associated with acne. In certain embodiments, the acne associated strain of *P. acnes* is of a ribotype selected from RT1, RT2, RT3, RT7, RT8, RT9, and RT10. In certain embodiments, the acne associated strain of *P. acnes* is of a ribotype selected from RT4, RT5, and RT8. In certain embodiments, the acne associated strain of *P. acnes* is not of a ribotype selected from RT4, RT5, or RT6. In certain embodiments, the methods comprise diagnosing the individual with acne if a presence of *Staphylococcus* bacteria is detected in a sample of the subject. In certain embodiments, the methods comprise diagnosing the individual with acne if a presence of *Malassezia* fungi is detected in a sample of the subject.

[00276] In certain embodiments, the disclosure provides a method comprising: obtaining a sample from skin of a subject; optionally isolating bacterial DNA from the sample; using one or more primer sets to amplify the DNA; and analyzing the amplified DNA for the presence of a sequence having at least 95% homology with at least one of SEQ ID NOs 1-10, 29-32 and 82-434, wherein the subject is diagnosed as having acne if the presence of a sequence having at least 95% homology with at least one of SEQ ID NOs 1-10, 29-32 and 82-434 exists. For example, the amplified DNA may be analyzed for the presence of a sequence having at least 99% homology with at least one of SEQ ID NOs 1-10, 29-32 and 82-434 and wherein the subject is diagnosed as having acne if the presence of a sequence having at least 99% homology with at least one of SEQ ID NOs 1-10, 29-32 and 82-434 exists. As another example, the amplified DNA may be analyzed for the presence of at least one of SEQ ID NOs 1-10, 29-32 and 82-434 and wherein the subject is diagnosed as having acne if the presence of at least one of SEQ ID NOs 1-10, 29-32 and 82-434 exists.

[00277] In certain embodiments, methods comprise detecting or characterizing a microbe in a sample from a subject. In some embodiments, the methods comprise detecting the microbe in an *ex vivo* sample. In some embodiments, the methods comprise detecting the microbe in an *in vivo* sample. An exemplary method comprises: obtaining a stool sample from the subject; isolating bacterial DNA from the sample; amplifying DNA selected from 16S, ribosomal DNA, 18S ribosomal DNA, and/or 23S ribosomal DNA, sequencing the amplified DNA products; and typing the individual's gut bacteria. In certain embodiments, are methods for determining whether a subject has acne comprising: obtaining a stool sample from the subject; isolating bacterial DNA from the sample and whole genome shotgun sequencing DNA in the sample. Another exemplary method comprises obtaining a swab sample from the subject's skin, such as from the face, back or other affected area.

Biological samples for diagnosis

[00278] In certain embodiments, diagnosing a subject comprises obtaining a biological sample with the absence or presence of a microbe on the skin of the subject. In some instances, diagnosing determines an absence or presence of a health-associated microbe. In some instances, diagnosing determines engraftment of a health-associated microbe. In some instances, diagnosing determines absence or presence of a pathogenic microbe. In some instances, diagnosing determines a quantity of a health-associated microbe. In some instances, diagnosing quantifies engraftment of a health-associated microbe. In some instances, diagnosing determines a quantity of a pathogenic microbe.

[00279] In certain embodiments, the biological sample is a sample from the skin surface. In some embodiments, the sample is a swab sample. In some embodiments, the sample is a sample of a pilosebaceous unit. By way of non-limiting example the sample of the pilosebaceous unit can be collected by an adhesive strip or by extraction. In certain embodiments, the biological sample is a stool or fecal sample. In certain embodiments, the biological sample is an oral or oral mucosal sample. In certain embodiments, the biological sample is a swab, obtained using a cotton swab or other compatible swab. In certain embodiments, the sample contains bacteria. In certain embodiments, the sample contains a fungus. In certain embodiments, the sample contains a virus. In certain embodiments, the virus is a bacteriophage. In certain embodiments, the sample is stored after it has been collected, but before additional steps are performed. In certain embodiments, storage occurs at less than 8° C. In certain embodiments, storage occurs at less than 4° C. In certain embodiments, storage occurs at less than 0° C. In certain embodiments, storage occurs at less than -20° C. In certain embodiments, storage occurs at less than -70° C. In certain embodiments, this storage is in glycerol, glycol, dimethyl sulfoxide, growth media, nutrient broth or any combination thereof. In certain embodiments, the sample is stored for at least about 1, 2, 3, 4, 5, 6, or 7 days. In some embodiments, the sample is stored for at least about 1, 2, 3, or 4 weeks. In some embodiments, the sample is stored for at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 months. In some embodiments, the sample is stored for up to about 1, 2, 3, or 4 weeks. In some embodiments, the sample is stored for up to about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 months.

[00280] In some embodiments, a composition disclosed herein is stable at room temperature (~25°C) for at least about one day. In some embodiments, a composition disclosed herein is stable for at least about three days. In some embodiments, a composition disclosed herein is stable for at least about six days. In some embodiments, a composition disclosed herein is

stable for at least about nine days. In some embodiments, a composition disclosed herein is stable for at least about twelve days.

[00281] In some embodiments, compositions disclosed herein possess therapeutic activity when applied to skin with a skin disorder. In some embodiments, compositions disclosed herein possess an initial therapeutic activity at the time the composition is produced or packaged. In some embodiments, a composition disclosed herein maintains its initial therapeutic activity at room temperature ($\sim 25^{\circ}\text{C}$) for at least about one day. In some embodiments, a composition disclosed herein maintains its initial therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains its initial therapeutic activity for at least about twelve days.

[00282] In some embodiments, a composition disclosed herein maintains at least about 90% of its initial therapeutic activity at room temperature ($\sim 25^{\circ}\text{C}$) for at least about one day. In some embodiments, a composition disclosed herein maintains at least about 90% of its initial therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains at least about 90% of its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains at least about 90% of its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains at least about 90% of its initial therapeutic activity for at least about twelve days.

[00283] In some embodiments, a composition disclosed herein maintains at least about 80% of its initial therapeutic activity at room temperature ($\sim 25^{\circ}\text{C}$) for at least about one day. In some embodiments, a composition disclosed herein maintains at least about 80% of its initial therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains at least about 80% of its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains at least about 80% of its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains at least about 80% of its initial therapeutic activity for at least about twelve days.

[00284] In some embodiments, a composition disclosed herein maintains at least about 70% of its initial therapeutic activity at room temperature ($\sim 25^{\circ}\text{C}$) for at least about one day. In some embodiments, a composition disclosed herein maintains at least about 70% of its initial

therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains at least about 70% of its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains at least about 70% of its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains at least about 70% of its initial therapeutic activity for at least about twelve days.

[00285] In some embodiments, a composition disclosed herein maintains at least about 50% of its initial therapeutic activity at room temperature (~25°C) for at least about one day. In some embodiments, a composition disclosed herein maintains at least about 50% of its initial therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains at least about 50% of its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains at least about 50% of its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains at least about 50% of its initial therapeutic activity for at least about twelve days.

[00286] In some embodiments, a composition disclosed herein maintains at least about 30% of its initial therapeutic activity at room temperature (~25°C) for at least about one day. In some embodiments, a composition disclosed herein maintains at least about 30% of its initial therapeutic activity for at least about three days. In some embodiments, a composition disclosed herein maintains at least about 30% of its initial therapeutic activity for at least about six days. In some embodiments, a composition disclosed herein maintains at least about 30% of its initial therapeutic activity for at least about nine days. In some embodiments, a composition disclosed herein maintains at least about 30% of its initial therapeutic activity for at least about twelve days.

[00287] In some embodiments, the sample is cultured at a physiological temperature suitable for bacterial growth such as 30° C, 31° C, 32° C, 33° C, 34° C, 35° C, 36° C, 37° C, 38° C, 39° C or 40° C. In some embodiments, the sample is cultured at about 35° C to about 39° C. In some embodiments, the sample is cultured at about 36° C to about 38° C. In some embodiments, the sample is cultured in a liquid growth media. In some embodiments, the sample is cultured on a solid growth media such as an agar plate. In some embodiments, the plates are blood agar.

[00288] In certain embodiments, samples disclosed herein are processed further before analysis. In some embodiments, no extraction or processing procedures are performed on the sample. In some embodiments, nucleic acid is extracted from the sample. In some

embodiments, the nucleic acid is DNA. In some embodiments, the DNA is bacterial DNA. In some embodiments, the Bacterial DNA is 16S ribosomal DNA. In some embodiments, the Bacterial DNA is 18S ribosomal DNA. In some embodiments, the Bacterial DNA is 23S ribosomal DNA. In some embodiments, the nucleic acid is ribosomal DNA. In some embodiments, the nucleic acid is RNA. In some embodiments, the nucleic acid is ribosomal RNA. In certain embodiments, the nucleic acid is extracted using any technique that does not interfere with subsequent analysis. In certain embodiments, this technique uses alcohol precipitation using ethanol, methanol or isopropyl alcohol. In certain embodiments, this technique uses phenol, chloroform, or any combination thereof. In certain embodiments, this technique uses cesium chloride. In certain embodiments, this technique uses sodium, potassium or ammonium acetate or any other salt commonly used to precipitate DNA. In certain embodiments, this technique utilizes a column or resin based nucleic acid purification scheme such as those commonly sold commercially, one non-limiting example would be the GenElute Bacterial Genomic DNA Kit available from Sigma Aldrich. In certain embodiments, after extraction the nucleic acid is stored in water, Tris buffer, or Tris-EDTA buffer before subsequent analysis. In certain embodiments, this storage is less than 8° C. In certain embodiments, this storage is less than 4° C. In certain embodiments, this storage is less than 0° C. In certain embodiments, this storage is less than -20° C. In certain embodiments, this storage is less than -70° C. In certain embodiments, the nucleic acid is stored for 1, 2, 3, 4, 5, 6, or 7 days. In some embodiments, the nucleic acid is stored for 1, 2, 3, or 4 weeks. In some embodiments, the nucleic acid is stored for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 months.

[00289] After the samples have been obtained and the relevant nucleic acids isolated the nucleic acids are sequenced. In certain embodiments, the nucleic acid sequenced is bacterial DNA. In certain embodiments, the nucleic acid sequence is bacterial 16S ribosomal DNA. In certain embodiments, the nucleic acid sequence is bacterial 18S ribosomal DNA. In certain embodiments, the nucleic acid sequence is bacterial 23S ribosomal DNA. In certain embodiments, the nucleic acid sequenced is bacteriophage DNA. In certain embodiments, the sequence is determined using PCR. In certain embodiments, at least one primer used in the PCR has a sequence that corresponds to SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27 or SEQ ID NO: 28. In certain embodiments, the PCR used is quantitative. In certain embodiments, the PCR reaction

utilizes a TaqMan™ or a similar quantitative PCR technology. In certain embodiments, the sequencing is performed using the Sanger sequencing method. In certain embodiments, the sequencing involves the use of chain terminating dideoxynucleotides. In certain embodiments, the sequencing involves gel-electrophoresis. In certain embodiments, the sequencing is performed using a next generation sequencing method. In certain embodiments, the method is pyrosequencing. In certain embodiments, the method is ion semiconductor sequencing. In certain embodiments, the method is sequencing by synthesis. In certain embodiments, the method is sequencing by ligation. In certain embodiments, the method is single molecule real time sequencing.

[00290] After the nucleic acids are sequenced, in certain embodiments, described herein diagnosis is made. In certain, embodiments, diagnosis requires the use of a computer, statistical analysis, statistical analysis software, sequence analysis software, or any combination thereof. In certain embodiments, different organisms are identified. In certain embodiments, *Malassezia* fungi are identified. In certain embodiments, different strains of bacteria are identified during compiling of the microbiome. In certain embodiments, *Staphylococcus* bacteria are identified. In certain embodiments, different strains of *P. acnes* are identified during compiling of the microbiome. In certain embodiments, different strains of *P. acnes* are identified based upon their 16S ribosomal sequence or ribotype. In certain embodiments, *P. acnes* are identified as belonging to RT1- RT10. In certain embodiments, the *P. acnes* are identified as belonging to RT1, RT2, RT3, or any combination thereof. In further embodiments, a diagnostic report may be sent through or accessed by the internet. A diagnostic report may be sent through the mail to a health care provider, physician, or patient.

[00291] In certain embodiments, this disclosure provides a method for determining the presence of antibiotic resistant bacteria in an individual with acne comprising, obtaining a sample from skin of an individual, isolating bacterial DNA from the sample, amplifying the relevant regions of the 16S, 18S or 23S ribosomal RNA from the sample, sequencing the amplified DNA products and determining antibiotic resistance to tetracycline and erythromycin/clindamycin classes of antibiotics respectively. In certain embodiments, bacteria present on or isolated from an individual's skin is tested or determined to be resistant to antibiotics. In certain embodiments, the antibiotic is erythromycin. In certain embodiments, the antibiotic is clindamycin. In certain embodiments, antibiotic resistance is determined from the sequence of the 16S, 18S or 23S ribosomal subtype.

Methods of Preserving Preparations of *Propionibacterium*

[00292] Provided herein, in some aspects, are methods of producing desired preparations of *Propionibacterium*. In some embodiments, the methods comprise producing a desired preparation of at least one strain of *Propionibacterium*. In some embodiments, the at least one strain is a strain of *P. acnes*. In some embodiments, the at least one strain is not a strain of *P. acnes* subsp. *acnes*. In some embodiments, the at least one strain is a strain of *P. avidum*. In some embodiments, the at least one strain is a strain of *P. granulosum*. In some embodiments, the at least one strain is a strain of *P. acnes* subsp. *defendens*. In preferred embodiments, the strain of *Propionibacterium* is a health-associated strain, as described herein.

[00293] In some embodiments, methods comprise adding a sample of the *Propionibacterium* to a glycerol solution to produce a *Propionibacterium* glycerol formulation, and storing the *Propionibacterium* glycerol formulation at a temperature of about 4 ° C or less. Producing a desired preparation of *Propionibacterium* may comprise at least one of cooling, freezing, and storing a *Propionibacterium* sample, a composition thereof or a formulation thereof. In some instances, freezing comprises flash freezing. Flash freezing may freeze the preparation of *Propionibacterium* in as little as one minute. Flash freezing may freeze the preparation of *Propionibacterium* in as little as 30 seconds. Flash freezing may comprise subjecting the preparation of *Propionibacterium* to dry ice, an alcohol cooled by dry ice, or liquid nitrogen.

[00294] In some instances, methods comprise storing pharmaceutical compositions disclosed herein on an applicator. In some instances, methods comprise storing pharmaceutical compositions disclosed herein in an applicator. By way of non-limiting example, a formulation disclosed herein is applied to a cotton pad, the cotton pad with the formulation vacuum sealed in plastic to produce a vacuum sealed package, and the vacuum sealed package flash frozen for storage at -20 degrees Celsius. In another non-limiting example, a formulation disclosed herein is applied to an applicator, the applicator with the formulation added to a plastic bag, and the plastic bag stored at less than 10 degrees Celsius. In yet another non-limiting example, a lyophilized formulation disclosed herein is applied to an applicator, the applicator vacuum sealed in plastic to produce a vacuum sealed package, and the plastic bag stored at less than 10 degrees Celsius. Alternatively, a formulation disclosed herein is added to an applicator, the formulation dried after it has been applied to the applicator, the applicator vacuum sealed in plastic to produce a vacuum sealed package, and the plastic bag stored at less than 10 degrees Celsius.

[00295] By way of non-limiting example, methods are provided herein for producing a desired preparation of a *P. acnes* bacteria comprising adding a sample of the

Propionibacterium to a glycerol solution to produce a *Propionibacterium* glycerol formulation, and storing the *Propionibacterium* glycerol formulation at a temperature of about 4 ° C or less, wherein more than about 50% of the *Propionibacterium* bacteria is viable when the *Propionibacterium* bacteria in the glycerol solution is brought to ambient temperature.

[00296] Also by way of non-limited examples, methods are provided herein for producing a desired preparation of preserved *Propionibacterium*, wherein about 90% of said *Propionibacterium* is viable after sixty days of storage, said method comprising: adding a sample of *Propionibacterium* to a solution of about 50% glycerol to produce a *Propionibacterium* formulation, freezing the *Propionibacterium* glycerol formulation at -20 ° C, thereby forming said desired preparation wherein greater than about 90% of the sample of *Propionibacterium* are viable after a thawing of the *Propionibacterium* glycerol formulation.

[00297] In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 1% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 5% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 10% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 15% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 20% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 30% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 40% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, methods comprise storing the *Propionibacterium*, wherein at least about 50% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, at least about 60% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought

to ambient temperature. In some embodiments, at least about 70% of the *Propionibacterium* is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, at least about 80% of the *P. acnes* bacteria is viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature. In some embodiments, more than about 90% of the *Propionibacterium* are viable when the *Propionibacterium* in the glycerol solution is brought to ambient temperature.

[00298] In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 75% glycerol. In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 65% glycerol. In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 55% glycerol. In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 45% glycerol. In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 35% glycerol. In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 5% and about 25% glycerol. In some embodiments, a solution of 25% glycerol or less is preferable because it provides sufficient cryopreservation without having an undesirable texture on the skin (e.g., a slimy texture). In some embodiments, methods comprise adding the *Propionibacterium* to a glycerol solution, wherein the glycerol solution is between about 25% and about 75% glycerol. In some embodiments, the glycerol solution is between about 30% and about 70% glycerol. In some embodiments, the glycerol solution is between about 35% and about 65% glycerol. In some embodiments, the glycerol solution is between about 40% and about 60% glycerol. In some embodiments, the glycerol solution is between about 45% and about 50% glycerol. In some embodiments, the glycerol solution is about 25% glycerol. In some embodiments, the glycerol solution is about 30% glycerol. In some embodiments, the glycerol solution is about 35% glycerol. In some embodiments, the glycerol solution is about 40% glycerol. In some embodiments, the glycerol solution is about 45% glycerol. In some embodiments, the glycerol solution is about 50% glycerol. In some embodiments, the glycerol solution is about 55% glycerol. In some embodiments, the glycerol solution is about 60% glycerol.

[00299] In some embodiments, methods comprise storing *Propionibacterium*, or a composition thereof, disclosed herein, at a selected temperature. In some embodiments,

methods comprise storing the *Propionibacterium* glycerol formulation at a selected temperature. In some embodiments, the temperature is between about 30 ° C and about -80 ° C. In some embodiments, the temperature is between about 25 ° C and about -80 ° C. In some embodiments, the temperature is between about 25 ° C and about -20 ° C. In some embodiments, the temperature is between about 30 ° C and about 4 ° C. In some embodiments, the temperature is between about 10 ° C and about -80 ° C. In some embodiments, the temperature is between about 10 ° C and about -40 ° C. In some embodiments, the temperature is between about 10 ° C and about -30 ° C. In some embodiments, the temperature is between about 10 ° C and about -20 ° C. In some embodiments, the temperature is between about 4 ° C and about -80 ° C. In some embodiments, the temperature is between about 4 ° C and about -25 ° C. In some embodiments, the temperature is between about 4 ° C and about -20 ° C. In some embodiments, the temperature is about 22 ° C to about 28 ° C. In some embodiments, the temperature is about 25 ° C. In some embodiments, the temperature is about 4 ° C. In some embodiments, the temperature is about -20 ° C. In some embodiments, the temperature is between about -80 ° C.

[00300] In some embodiments, methods comprise thawing a composition of *Propionibacterium* disclosed herein. In some embodiments, methods comprise warming a composition of *Propionibacterium* bacteria disclosed herein. In some embodiments, methods comprise thawing a *Propionibacterium* glycerol formulation at room temperature. In some embodiments, methods comprise rapid thawing the *Propionibacterium* glycerol formulation in a bath. The bath temperature may be between about 25 ° C and about 40 ° C. In some embodiments, methods comprise rapidly thawing a composition of *Propionibacterium* bacteria disclosed herein. By way of non-limiting example, a subject may apply a composition disclosed herein, wherein the composition is frozen, directly to skin. In some embodiments, methods comprise slowly thawing a composition of *Propionibacterium* bacteria disclosed herein. By way of non-limiting example, a subject may transfer a composition disclosed herein that is frozen to a refrigerator to reach a refrigerated temperature before being brought to room temperature, before being applied to skin, or before being combined with another composition (e.g., emollient, lotion, gel). The term “frozen” includes compositions at temperatures at which the composition is in a solid form or semi-solid form. Frozen may include compositions at temperatures of less than 0 ° C, and less than -15 ° C. The term “refrigerated temperature” refers to a temperature of about 0 ° C to

about 10 ° C, *e.g.*, 4 ° C. A refrigerated temperature does not necessarily need to be achieved with a refrigerator. By non-limiting example, an ice bucket could similarly cool a sample.

[00301] In some embodiments, methods comprise storing a *Propionibacterium* glycerol formulation, wherein at least about 60% to at least about 90% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, the at least about 70% to at least about 90% of the *P. acnes* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, the at least about 80% to at least about 90% of the viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 60% of *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 70% of the *P. acnes* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 90% of the *P. acnes* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. Ambient temperature is considered an acceptable room temperature. In some embodiments, the ambient temperature is between about 25 ° C and about 35 ° C. In some embodiments, the ambient temperature is between about 20 ° C and about 30 ° C. In some embodiments, the ambient temperature is between about 22 ° C and about 28 ° C. In some embodiments, the ambient temperature is about 25 ° C.

[00302] In some embodiments, methods comprise storing a *Propionibacterium* glycerol formulation, wherein at least about 50% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 60% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 70% of the *Propionibacterium* sample is viable after at least about 20 days of storing. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 90% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 95% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 50% of the *Propionibacterium* sample is viable after at least about 60 days of storing. In some embodiments, at least about 60% of the *Propionibacterium* sample is viable after at least

[illegible]

about a year of storing. In some embodiments, at least about 70% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 90% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 95% of the *Propionibacterium* sample is viable after at least about a year of storing.

[00303] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution is between about 10% glycerol v/v and about 90% glycerol v/v in solution. In some embodiments, the solution is between about 20% glycerol v/v and about 80% glycerol v/v in solution. In some embodiments, the solution is between about 25% glycerol v/v and about 75% glycerol v/v in solution. In some embodiments, the solution is between about 30% glycerol v/v and about 70% glycerol v/v in solution. In some embodiments, the solution is between about 35% glycerol v/v and about 65% glycerol v/v in solution. In some embodiments, the solution is between about 40% glycerol v/v and about 60% glycerol v/v in solution. In some embodiments, the solution is between about 45% glycerol v/v and about 55% glycerol v/v in solution. In some embodiments, the solution is between about 15% glycerol v/v and about 35% glycerol v/v in solution. In some embodiments, the solution is between about 20% glycerol v/v and about 30% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 10% glycerol v/v in solution. In some embodiments, the solution is between about 10% glycerol v/v and about 25% glycerol v/v in solution. In some embodiments, the solution is between about 25% glycerol v/v and about 50% glycerol v/v in solution. In some embodiments, the solution is about 20% glycerol v/v in solution. In some embodiments, the solution is about 25% glycerol v/v in solution. In some embodiments, the solution is about 30% glycerol v/v in solution. In some embodiments, the solution is about 35% glycerol v/v in solution. In some embodiments, the solution is about 40% glycerol v/v in solution. In some embodiments, the solution is about 45% glycerol v/v in solution. In some embodiments, the solution is about 50% glycerol v/v in solution. In some embodiments, the solution is about 55% glycerol v/v in solution. In some embodiments, the solution is about 60% glycerol v/v in solution. In some embodiments, the solution is about 65% glycerol v/v in solution. In some embodiments, the solution is about 75% glycerol v/v in solution.

[00304] In some embodiments, methods comprise storing *Propionibacterium* bacteria in a solution, wherein the solution comprises glycerol and water. In some embodiments, the solution consists essentially of glycerol and water. In some embodiments, methods comprise

storing *Propionibacterium* in a solution, wherein the solution comprises glycerol and a saline solution. In some embodiments, the solution consists essentially of glycerol and a saline solution. In some embodiments, the solution comprises glycerol and a buffered saline solution. In some embodiments, the solution consists essentially of glycerol and a buffered saline solution. In some embodiments, the solution comprises glycerol and a buffered solution. In some embodiments, the buffered solution comprises sodium bicarbonate, citric acid or triethanolamine. In some embodiments, the solution comprises glycerol and a phosphate buffered saline solution. In some embodiments, the solution consists essentially of glycerol and a phosphate buffered saline solution. In some embodiments, the solution comprises an acetate buffer (*e.g.*, sodium acetate buffer).

[00305] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution has a pH of between about 3.5 and about 7. In some embodiments, the solution has a pH of between about 4 and about 6.5. In some embodiments, the solution has a pH of between about 4 and about 6. In some embodiments, the solution has a pH of between about 4 and about 5.5. In some embodiments, the solution has a pH of between about 4.5 and about 5.5. In some embodiments, the solution has a pH of between about 4.8 and about 5. In some embodiments, the solution has a pH of about 4. In some embodiments, the solution has a pH of about 4.2. In some embodiments, the solution has a pH of about 4.4. In some embodiments, the solution has a pH of about 4.6. In some embodiments, the solution has a pH of about 4.8. In some embodiments, the solution has a pH of about 5. In some embodiments, the solution has a pH of about 5.2. In some embodiments, the solution has a pH of about 5.4. In some embodiments, the solution has a pH of about 5.6. In some embodiments, the solution has a pH of about 5.8. In some embodiments, the solution has a pH of about 6.

[00306] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution comprises a salt or ion thereof. In some embodiments, the solution comprises an ion selected from potassium, calcium, magnesium, sodium, and boron. In some embodiments, the solution comprises potassium. In some embodiments, the solution comprises potassium. In some embodiments, the concentration of the salt or ion thereof is between about 0.001 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.001 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.01 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.05 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between

about 0.01 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.1 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 100 mM and about 250 mM. In some embodiments, the concentration of the salt or ion thereof is between about 125 mM and about 225 mM. In some embodiments, the concentration of the salt or ion thereof is between about 150 mM and about 200 mM. In some embodiments, the concentration of potassium is between about 100 mM and about 250 mM. In some embodiments, the concentration of potassium is between about 125 mM and about 225 mM. In some embodiments, the concentration of potassium is between about 150 mM and about 200 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.001 mM to about 1 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.01 mM to about 0.5 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.05 mM to about 0.1 mM.

[00307] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution comprises a prebiotic stabilizing agent. In some embodiments, the prebiotic stabilizing agent is selected from a polysaccharide or oligosaccharide. In some embodiments, the prebiotic stabilizing agent is inulin. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.01% v/v to about 1% v/v. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.01% v/v to about 0.5% v/v. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.05% v/v to about 0.2% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.01% v/v to about 1% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.01% v/v to about 0.5% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.05% v/v to about 0.2% v/v. For clarity, the term % v/v, as used herein, represent the percentage of a total volume of a solution that is represented by a volume of a component of the solution.

[00308] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution comprises an anti-acne agent, wherein the anti-acne agent is an agent that prevents, reduces or abolishes acne. In some embodiments, the anti-acne agent is selected from a retinoid, a vitamin, an antioxidant, an oil, an alcohol, an extract, and analogs thereof. For clarity, the term, “analog,” as used herein, refers to a compound having a structure similar to that of another one, but differing from it by less than about 10% of the total structure. In some embodiments, the retinoid is selected from tretinoin, tazarotene, adapalene,

and retinol. In some embodiments, the vitamin or analog thereof is selected from a Vitamin A, Vitamin C, Vitamin D, Vitamin E, and calciptotriene. In some embodiments, the antioxidant is selected from Vitamin C and Vitamin E. In some embodiments, the vitamin is Vitamin B₁₂. In some embodiments, the alcohol is selected from retinol (also known as Vitamin A₁) and resveratrol. In some embodiments, the oil is selected from lavender oil, clary sage oil, juniper berry oil, bergamot oil, jojoba oil, rosemary oil, coconut oil, avocado oil, peppermint oil, and tea tree oil. In some embodiments, the oil is tea tree oil. In some embodiments, the extract is selected from an extract of aloe, garlic, amaranth, neem, coriander, lemon, basil, grapefruit, cucumber, grape, beet, green tea or a combination thereof. In some embodiments, the extract is a green tea extract.

[00309] In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution is incorporated in a biologic stability platform. In some embodiments, the biologic stability platform eliminates a need for temperature control, *e.g.*, cold chain storage. In some embodiments, the biologic storage platform comprises foam drying or foam formation of the solution or glycerol formulation solution. In some embodiments, the biologic stability platform comprises at least one of a glyconanoparticle, a liposome, a nanoparticle, trehalose, sucrose, stachyose, hydroxyethyl starch, and a combination of glycine and mannitol.

[00310] In some embodiments, methods comprise storing or preserving a sample of *P. acnes* of at least one selected ribotype. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotype RT1. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotype RT2. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotype RT3. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotypes RT1 and RT2. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotypes RT1 and RT3. In some embodiments, the sample of *P. acnes* bacteria comprises *P. acnes* bacteria of ribotypes RT2 and RT3. In some embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotype RT1. In some embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotype RT2. In some embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotype RT3. In some embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotypes RT1 and RT2. In some embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotypes RT1 and RT3. In some

embodiments, the sample of *P. acnes* bacteria consists essentially of *P. acnes* bacteria of ribotypes RT3 and RT2.

[00311] In some embodiments, methods may comprise culturing an initial culture of the sample of *P. acnes* bacteria. The initial culture may be a smaller aliquot of the *Propionibacterium* and the method may comprise proliferating the *Propionibacterium* to obtain a desired amount. In some embodiments, methods may comprise culturing the initial culture in a culture medium. In some embodiments, the cell culture medium comprises reinforced clostridial medium. In some embodiments, the cell culture medium consists essentially of reinforced clostridial medium. In some embodiments, the cell culture medium comprises Luria broth. In some embodiments, the cell culture medium comprises tryptone broth. In some embodiments, methods comprise at least one step of splitting, diluting or passaging the initial culture or product thereof in the culture medium. In some embodiments, the methods comprise at least one step of washing the sample of the initial culture or product thereof. In some embodiments, the methods comprise at least one step of centrifuging or pelleting the initial culture or product thereof. In some embodiments, the culture is centrifuged at about 3500 rcf to about 4500 rcf. In some embodiments, the culture is centrifuged at about 3800 rcf to about 4200 rcf. In some embodiments, the culture is centrifuged at about 4000 rcf. In some embodiments, the methods comprise at least one step of vortexing the initial culture or product thereof. In some embodiments, the methods comprise at least one step of pipetting the initial culture or product thereof. Any one of the steps described herein may be performed at least one time. Any one of the steps described herein may be performed two times. Any one of the steps described herein may be performed three times. In some embodiments, methods comprise adding a sachet to a culture comprising the sample of *Propionibacterium* or an initial culture thereof. In some embodiments the sachet reduces oxygen exposure to the *Propionibacterium*.

Compositions of Preserved *Propionibacterium*

[00312] Provided herein, in some aspects, are compositions that comprise a preserved sample of bacteria, wherein the bacteria comprises *Propionibacterium*. In some embodiments, compositions disclosed herein comprise *P. acnes* bacteria of ribotype RT1. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT2. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT3. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT1 and RT2. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT2 and RT3. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT1 and

RT3. In some embodiments, the bacteria of the compositions consist essentially of *P. acnes* bacteria of ribotype RT1. In some embodiments, the bacteria of the compositions consist essentially of *P. acnes* bacteria of ribotype RT2. In some embodiments, the bacteria of the compositions consist essentially of *P. acnes* bacteria of ribotype RT3. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT1 and RT2. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT1 and RT3. In some embodiments, the compositions comprise *P. acnes* bacteria of ribotype RT2 and RT3.

[00313] In some embodiments, compositions disclosed herein comprise a sample of bacteria preserved in at least one cryopreservative agent. In some embodiments, the cryopreservative agent is a polyol. Non-limiting examples of polyols include DMSO, ethylene glycol, glycerol, polyethylene (PEG) glycol, polypropylene glycol (PPG), sucrose, trehalose, and 2-Methyl-2,4-pentanediol (MPD). In various embodiments, the PEG may have a molecular weight between about 10 g/mol and about 10,000 g/mol. In various embodiments, the PEG may have a molecular weight between about 10 g/mol and about 5,000 g/mol. In various embodiments, the PEG may have a molecular weight between about 10 g/mol and about 1,000 g/mol. In various embodiments, the PEG may have a molecular weight between about 10 g/mol and about 500 g/mol.

[00314] In some embodiments, compositions disclosed herein comprise polyethylene glycol. In some embodiments, a composition comprising polyethylene glycol allows for a reduced amount of glycerol, whilst maintaining viability of bacteria in the composition that is similar to viability of bacteria in compositions without polyethylene glycol and a greater amount of glycerol. In some embodiments, reducing or minimizing the amount of glycerol in a composition disclosed herein results in a formulation that has a texture that is more preferable to a subject. In some embodiments, reducing or minimizing the amount of glycerol in a composition disclosed herein results in a formulation that is less comedogenic relative to a composition with a greater amount of glycerol.

[00315] In some embodiments, compositions disclosed herein comprise a sample of bacteria preserved in a mixture of a first polyol and a second polyol. In some embodiments, the first polyol or the second polyol is glycerol. In some embodiments, the first polyol or the second polyol is a polyethylene glycol. In some embodiments, compositions disclosed herein comprise a sample of bacteria preserved in a mixture of glycerol and polyethylene glycol. In some embodiments, the mixture is between about 1% glycerol v/v and about 50% glycerol v/v, and between about 1% polyethylene glycol w/v and about 50% w/v polyethylene glycol. In some embodiments, the mixture is between about 5% glycerol v/v and about 50% glycerol

v/v, and between about 5% polyethylene glycol w/v and about 50% w/v polyethylene glycol. In some embodiments, the mixture is between about 5% glycerol v/v and about 30% glycerol v/v, and between about 5% polyethylene glycol w/v and about 40% w/v polyethylene glycol. In some embodiments, the mixture is between about 10% glycerol v/v and about 35% glycerol v/v, and between about 10% polyethylene glycol w/v and about 35% w/v polyethylene glycol.

[00316] In some embodiments, compositions disclose herein comprise a solution, wherein the solution is between about 1% glycerol v/v and about 75% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 50% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 40% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 35% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 30% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 25% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 20% glycerol v/v in solution. In some embodiments, the solution is between about 1% glycerol v/v and about 15% glycerol v/v in solution. In some embodiments, the solution is between about 5% glycerol v/v and about 50% glycerol v/v in solution. In some embodiments, the solution is between about 5% glycerol v/v and about 40% glycerol v/v in solution. In some embodiments, the solution is between about 5% glycerol v/v and about 35% glycerol v/v in solution. In some embodiments, the solution is between about 5% glycerol v/v and about 30% glycerol v/v in solution. In some embodiments, the solution is between about 5% glycerol v/v and about 25% glycerol v/v in solution. In some embodiments, the solution is between about 10% glycerol v/v and about 40% glycerol v/v in solution. In some embodiments, the solution is between about 10% glycerol v/v and about 35% glycerol v/v in solution. In some embodiments, the solution is between about 10% glycerol v/v and about 30% glycerol v/v in solution. In some embodiments, the solution is between about 10% glycerol v/v and about 25% glycerol v/v in solution. In some embodiments, the solution is between about 15% glycerol v/v and about 40% glycerol v/v in solution. In some embodiments, the solution is between about 15% glycerol v/v and about 35% glycerol v/v in solution. In some embodiments, the solution is between about 15% glycerol v/v and about 30% glycerol v/v in solution. In some embodiments, the solution is between about 15% glycerol v/v and about 25% glycerol v/v in solution. In some embodiments, the solution is between about 20% glycerol v/v and about 50% glycerol v/v in solution. In some embodiments, the solution is

between about 20% glycerol v/v and about 40% glycerol v/v in solution. In some embodiments, the solution is between about 20% glycerol v/v and about 30% glycerol v/v in solution.

[00317] In some embodiments, compositions disclose herein comprise a solution, wherein the solution is between about 1% polyethylene glycol w/v and about 75% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 50% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 40% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 35% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 30% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 25% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 20% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 1% polyethylene glycol w/v and about 15% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 5% polyethylene glycol w/v and about 50% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 5% polyethylene glycol w/v and about 40% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 5% polyethylene glycol w/v and about 35% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 5% polyethylene glycol w/v and about 30% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 5% polyethylene glycol w/v and about 25% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 10% polyethylene glycol w/v and about 40% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 10% polyethylene glycol w/v and about 35% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 10% polyethylene glycol w/v and about 30% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 10% polyethylene glycol w/v and about 25% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 15% polyethylene glycol w/v and about 40% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 15% polyethylene glycol w/v and about 35% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 15% polyethylene glycol w/v and about 30% polyethylene glycol w/v in solution. In some embodiments, the solution is

between about 15% polyethylene glycol w/v and about 25% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 20% polyethylene glycol w/v and about 50% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 20% polyethylene glycol w/v and about 40% polyethylene glycol w/v in solution. In some embodiments, the solution is between about 20% polyethylene glycol w/v and about 30% polyethylene glycol w/v in solution.

[00318] In some embodiments, the solution is about 5% glycerol v/v in solution. In some embodiments, the solution is about 10% glycerol v/v in solution. In some embodiments, the solution is about 15% glycerol v/v in solution. In some embodiments, the solution is about 20% glycerol v/v in solution. In some embodiments, the solution is about 25% glycerol v/v in solution. In some embodiments, the solution is about 30% glycerol v/v in solution. In some embodiments, the solution is about 35% glycerol v/v in solution. In some embodiments, the solution is about 40% glycerol v/v in solution. In some embodiments, the solution is about 45% glycerol v/v in solution. In some embodiments, the solution is about 50% glycerol v/v in solution. In some embodiments, the solution is about 55% glycerol v/v in solution. In some embodiments, the solution is about 60% glycerol v/v in solution. In some embodiments, the solution is about 70% glycerol v/v in solution.

[00319] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution comprises glycerol and water. In some embodiments, the solution consists essentially of glycerol and water. In some embodiments, methods comprise storing *Propionibacterium* in a solution, wherein the solution comprises glycerol and a saline solution. In some embodiments, the solution consists essentially of glycerol and a saline solution. In some embodiments, the solution comprises glycerol and a buffered saline solution. In some embodiments, the solution consists essentially of glycerol and a buffered saline solution. In some embodiments, the solution comprises glycerol and a buffered solution. In some embodiments, the buffered solution comprises sodium bicarbonate, citric acid or triethanolamine. In some embodiments, the solution comprises glycerol and a phosphate buffered saline solution. In some embodiments, the solution consists essentially of glycerol and a phosphate buffered saline solution.

[00320] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution has a pH of between about 3.5 and about 7. In some embodiments, the solution has a pH of between about 4 and about 6.5. In some embodiments, the solution has a pH of between about 4 and about 6. In some embodiments, the solution has a pH of between about 4 and about 5.5. In some embodiments, the solution has a pH of between about 4.5 and about

5.5. In some embodiments, the solution has a pH of between about 4.8 and about 5. In some embodiments, the solution has a pH of about 4. In some embodiments, the solution has a pH of about 4.2. In some embodiments, the solution has a pH of about 4.4. In some embodiments, the solution has a pH of about 4.6. In some embodiments, the solution has a pH of about 4.8. In some embodiments, the solution has a pH of about 5. In some embodiments, the solution has a pH of about 5.2. In some embodiments, the solution has a pH of about 5.4. In some embodiments, the solution has a pH of about 5.6. In some embodiments, the solution has a pH of about 5.8. In some embodiments, the solution has a pH of about 6.

[00321] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution comprises a salt or ion thereof. In some embodiments, the solution comprises an ion selected from potassium, calcium, magnesium, sodium, and boron. In some embodiments, the solution comprises potassium. In some embodiments, the solution comprises potassium. In some embodiments, the concentration of the salt or ion thereof is between about 0.001 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.001 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.01 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.05 mM and about 0.1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.01 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 0.1 mM and about 1 mM. In some embodiments, the concentration of the salt or ion thereof is between about 100 mM and about 250 mM. In some embodiments, the concentration of the salt or ion thereof is between about 125 mM and about 225 mM. In some embodiments, the concentration of the salt or ion thereof is between about 150 mM and about 200 mM. In some embodiments, the concentration of potassium is between about 100 mM and about 250 mM. In some embodiments, the concentration of potassium is between about 125 mM and about 225 mM. In some embodiments, the concentration of potassium is between about 150 mM and about 200 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.001 mM to about 1 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.01 mM to about 0.5 mM. In some embodiments, the solution comprises calcium at a concentration of about 0.05 mM to about 0.1 mM.

[00322] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution comprises at least one stabilizing agent. In some embodiments, the stabilizing

agent is selected from inulin, sucrose, trehalose, cornstarch, maltodextrin, guar gum, locust bean gum, and xanthan gum. In some embodiments, trehalose or sucrose stabilizes bacteria for cold-chain free stability. In some embodiments, the stabilizing agent is inulin. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.01% v/v to about 1% v/v. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.01% v/v to about 0.5% v/v. In some embodiments, the stabilizing agent is present in the solution at a concentration of about 0.05% v/v to about 0.2% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.01% v/v to about 1% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.01% v/v to about 0.5% v/v. In some embodiments, the solution comprises inulin at a concentration of about 0.05% v/v to about 0.2% v/v.

[00323] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution comprises an anti-acne agent, wherein the anti-acne agent is an agent that prevents, reduces or abolishes acne. In some embodiments, the anti-acne agent is selected from a retinoid, a vitamin, an antioxidant, an oil, an alcohol, an extract, and analogs thereof. In some embodiments, the retinoid is selected from tretinoin, tazarotene, adapalene, and retinol. In some embodiments, the vitamin or analog thereof is selected from Vitamin D, Vitamin C, Vitamin E, and calcipotriene. In some embodiments, the vitamin or analog thereof is selected from Vitamin B₁₂. In some embodiments, the antioxidant is selected from Vitamin C and Vitamin E. In some embodiments, the alcohol is selected from retinol and resveratrol. In some embodiments, the oil is tea tree oil. In some embodiments, the extract is a green tea extract.

[00324] In some embodiments, compositions disclosed herein comprise a solution, wherein the solution is incorporated in a biologic stability platform. In some embodiments, the biologic stability platform eliminates a need for temperature control, *e.g.*, cold chain storage. In some embodiments, the biologic storage platform comprises foam drying or foam formation of the solution or glycerol formulation solution. In some embodiments, the biologic stability platform comprises at least one of a glyconanoparticle, a liposome, a nanoparticle, trehalose, sucrose, stachyose, hydroxyethyl starch, and a combination of glycine and mannitol.

[00325] In some embodiments, compositions disclosed herein have a temperature of about -80 ° C to about 10 ° C. In some embodiments, the composition is at a temperature of about -80 ° C to about 4 ° C. In some embodiments, the composition is at a temperature of about -40 ° C to about 10 ° C. In some embodiments, the composition is at a temperature of about -25 °

C to about 10 ° C. In some embodiments, the composition is at a temperature of about -20 ° C to about 4 ° C. In some embodiments, the composition is at a temperature of about -90 ° C to about -70 ° C. In some embodiments, the composition is at a temperature of about -30 ° C to about -10 ° C. In some embodiments, the composition is at a temperature of about -80 ° C. In some embodiments, the composition is at a temperature of about -20 ° C. In some embodiments, the composition is at a temperature of about 4 ° C.

[00326] In some embodiments, compositions disclosed herein comprise a *Propionibacterium* glycerol formulation, wherein at least about 60% to at least about 90% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, the at least about 70% to at least about 90% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, the at least about 80% to at least about 90% of the viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 60% of the *P. acnes* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 70% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. In some embodiments, at least about 90% of the *Propionibacterium* sample is viable after the *Propionibacterium* glycerol formulation is brought to ambient temperature. Ambient temperature is considered an acceptable room temperature. In some embodiments, the ambient temperature is between about 25 ° C and about 35 ° C. In some embodiments, the ambient temperature is between about 20 ° C and about 30 ° C. In some embodiments, the ambient temperature is between about 22 ° C and about 28 ° C. In some embodiments, the ambient temperature is about 25 ° C.

[00327] In some embodiments, compositions disclosed herein comprise a *Propionibacterium* glycerol formulation, wherein at least about 50% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 60% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 70% of the *P. acnes* sample is viable after at least about 20 days of storing. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some embodiments, at least about 90% of the *Propionibacterium* sample is viable after at least about 30 days of storing. In some

[illegible]

embodiments, at least about 95% of the *Propionibacterium* sample is viable after at least about 180 days of storing. In some embodiments, at least about 50% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 60% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 70% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 80% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 90% of the *Propionibacterium* sample is viable after at least about a year of storing. In some embodiments, at least about 95% of the *Propionibacterium* sample is viable after at least about a year of storing.

[00328] In some embodiments, compositions disclosed herein have a storage life of at least about thirty days to at least about ninety days. In some embodiments, the compositions disclosed herein have a storage life of at least about 30 days to at least about 120 days. In some embodiments, the compositions disclosed herein have a storage life of at least about 30 days to at least about 180 days. In some embodiments, the compositions disclosed herein have a storage life of at least about thirty days to about ninety days. In some embodiments, the compositions disclosed herein have a storage life of at least about 30 days to about 120 days. In some embodiments, the compositions disclosed herein have a storage life of at least about 30 days to about 180 days. In some embodiments, the compositions disclosed herein have a storage life of at least about thirty days. In some embodiments, the compositions disclosed herein have a storage life of at least about sixty days. In some embodiments, the compositions disclosed herein have a storage life of at least about ninety days. In some embodiments, the compositions disclosed herein have a storage life of at least about 120 days. In some embodiments, the compositions disclosed herein have a storage life of at least about 180 days. In some embodiments, the compositions disclosed herein have a storage life of at least about 240 days. In some embodiments, the compositions disclosed herein have a storage life of at least about one year. In some embodiments, the compositions disclosed herein have a storage life of up to about one year.

[00329] In some embodiments, the compositions disclosed herein are capable of being thawed and subsequently applied to a subject in need thereof. In some embodiments, the compositions disclosed herein are capable of being warmed and subsequently applied to a subject in need thereof. In some embodiments, the compositions disclosed herein are capable of being refrigerated and subsequently applied to a subject in need thereof. In some embodiments, subsequently applied to the subject comprises applying the composition

directly to the skin of the subject. In some embodiments, subsequently applied to the subject comprises applying the composition to an application composition before being applied to the skin. The application composition may be selected from a liquid, gel, lotion, emollient, paste, mask, and virtually any solution that can be applied to the skin of a subject. In some embodiments, the application composition is free of any anti-acne agent. In some embodiments, the application composition comprises an anti-acne agent. In some embodiments, the compositions disclosed herein are capable of being applied directly from a frozen formulation to skin of a subject without thawing or warming.

Table 2. Exemplary Sequences (Additional SEQ IDs provided in sequence listing filed herewith). Bold, double underlined characters highlight differences between Type I lipase and Type II lipase.

Type I lipase:

GTAGATACAGAT**AC**ATCTGAG**G**AGATCCATGAAGAAAACTGGTTACTCACAACC
CTCCTTGCCACAATGATGATCGCCATGGGCACGACGACCACCGCCTTCGCCAGCCC
GCCTACCGACATCACTCCCGAACATCCAGGCGGGGTAC**CG**CGCCTCACAGCCCCG
ACGGAATCCCCTCGAATATTGAGGGGGCCAAGTATGCCCAGCTGGACCTCTGCAATC
AGGTTTCGAATGAAGAACCCCGGCACGAAAGTCCCGGGCACCAACGACTTCACCT
GCAAACCGAGGAAAGGCACCCATCCCGTCGTGCTCATCCCGGGCACATCCGAGGA
CGCCTTCATCACGTGGTTCGTACTACGGTCCCCGCCAGGATTCTGCGCCTACACGTTC
AACTACAACCCGGAAACACATCCGCTTGTGGAAGCCGCTGAGACCAGCGGCAACA
TCTACTCCACGGCAGCTTTCATGGCCCACTTCGTTGACAGAGTGCTCAAGGCAACC
GGTGCTCAGAAGGTCAACCTCGTCGGCCATTCTCAGGGCGGCGGCCCCCTGCCGCG
CGCGTACATCAAATATTACGGGGCGCCAAGAAAGTCCTCATCTCGTCGGTTTGGTT
CCTTCCAACAGGGGAACACGCATGCTCGGCCTGGAGAAGTTCCTCAATGCCAGCGG
AAACCCGCTCAGCACTATCTTCAATGCTGCAGCACAGTTTCGAAAGCTGGAATCCC
TGCCCCAACAGTTGCAAGACTCCACATTTCTCAGGGAACCTAACGCGGATGGAATG
ACCGTCCCCGGCATCACATACACCGTCATCGCCACCCAGTTCGACAACCGAGTATT
TCCGTGGACTAATACTTCATCAATGAGCCCGGGGTCAAGAACATCGTCATCCAAG
ACGTCGTGCCCTTGGACCACAGCGCCACACGGATATCCCTAGGACCCGATGACCC
TTCAGATTGTCATCAACGCCTTGGACCCCGAGCGGGCCGCCCCGGTACCTGCACC
ATTCGCCCATTCAGGCCCAAGTTAG (SEQ ID NO. 60)

Type II lipase:

GCAGATGCATCTGAGAAGATCCATGAAGAAAACTGGTTACTCACAACCCTCCTTG
CCACAATGATGATCGCCATGGGCACGACGACCACCGCCTTCGCCAGCCCGCCTACC
GACATCACTCCCGAACATCCAGGCGGGGTACCCGCCTCACAGCCCCGACGGAATC
CCCTCGAATATTGAGGGGGCCAAGTATGCCCAGCTGGACCTCTGCAATCAGGTTTCG
AATGAAGAACCCCGGCACGAAAGTCCCGGGCACCAACGACTTCACCTGCAAACCG
AGGAAAGGCACCCATCCCGTCGTGCTCATCCCGGGCACATCCGAGGACGCCTTCAT
CACGTGGTTCGTACTACGGTCCCCGCCAGGATTCTGCGCCTACACGTTCAACTACAA
CCCGGAAACACATCCGCTTGTGGAAGCCGCTGAGACCAGCGGCAACATCTACTCCA
CGGCAGCTTTCATGGCCCACTTCGTTGACAGAGTGCTCAAGGCAACCGGTGCTCAG
AAGGTCAACCTCGTCGGCCATTCTCAGGGCGGCGGCCCCCTGCCGCGCGCGTACAT
CAAATATTACGGGGCGCCAAGAAAGTCCTCATCTCGTCGGTTTGGTTCTTCCAAC
AGGGGAACACGCATGCTCGGCCTGGAGAAGTTCCTCAATGCCAGCGGAAACCCGC

TCAGCACTATCTTCAATGCTGCAGCACAGTTTCGAAAGCTGGAATCCCTGCCCCAA
CAGTTGCAAGACTCCACATTTCTCAGGGAACCTCAACGCGGATGGAATGACCGTCCC
CGGCATCACATACACCGTCATCGCCACCCAGTTCGACAACCGAGTATTTCCGTGGA
CTAATACCTTCATCAATGAGCCCCGGGTCAAGAACATCGTCATCCAAGACGTCTGT
CCCTTGGACCACAGCGCCCACACGGATATCCCTAGGACCCGATGACCCTTCAGATT
GTCATCAACGCCTTGGACCCCCGAGCGGGCCGCCCGGTCACCTGCACCATTGCCCC
ATTCAGGCCCAGTTAG (SEQ ID NO. 61)

dermatan-sulfate adhesin (example 1):

ATACGTCGGTCAAGAATTGCTGTGCTGCTGCGACGGCTACTGCGCTGGTCGGATC
AATCGCAGCAATCACCCCTCCCCCCCCCCCCCAGGCAGAAGCTAGCTCCAATAGG
CCACGCTCGGTAGCTCAAGCCGCTATCGCCACGGATGGAAAGGGGATAATCGACA
AGGACTGCCGTGATGCAGTCATCAACGATGCAAAGCTACGTGCCGCGATTGCCGGT
GCGTTGGTTAAGGCTGGATTTAGTTCCGCCGACGCGGTGGCTCTAGCGCCGCGTAT
TGCCAAAGAAATGGCAAAGAGGGCGTCTCTCATCAACCACCACAAGCTAAAG
GCTCTCATCGGAGCCCAGCTGGGTCTGCTCACTGATGCGAAGATCCAGCGTGCTGC
CGCTGCAGTGGACCTCGGCATCAAAGCCACTCTAGCTGCGACAATCATTCCCAACG
CGCTGCATTCAGCGGCATTCAAGGATGCGGTGGTTCGAAACCTTGTCGCCGCCGGC
GTTGACAAGAAGTTGGCAAAGGCTACGGCTGTCGCCATTGCCGCAACTGCGCTCAA
TCCCGCTCTCGGGCCGATCGCAAAGACTGAGGCTATTAAGGCCGAGATCGCTGCCC
AGGCAGCTCTCCTGGTGGGCAGGGGCGTGCACCTCAAGAAAGCAGCCATCGAACA
TATCATCGGTGCGAGTTTCGACGCTGCCGTTGCCACGGCAATCGTCAGTTCTCCCAT
CCTAAATGCGCGTATCGTCACCCACTTGGTTAGGGCTGGGATAGACAAGTCCCTTG
CAGTCCAGATCGCACCTCGCATTATCGATCGGCTGGCCAAGGAGCCGCTTCTTGCG
CTCAACACCGCCAAGCTCATGAAGAACATCACTCGACAGATTGTTGACGTTATCAC
CGCCGACAAAGCTATCAAGACTGCTGAGCAGCTCGAGAAAGAACTGCCGGCTCTG
GACGACCTTGTGAAGAAGGCTTGCTCCTGCCCGAAGCCGACTCCTACTCCGACTCC
CACTCCTACTCCAACACCAAAAACCAACCCCAACTCCAACACCAAAAACCAACCCCAA
CACCGAAGCCAAAGCCAACCCCGGCTCCGGCTCCGACTAGTGGGGCGACCTCTGAT
GAGTCGACCAGCCGCTCGGGAGGCCATTGCGAGGGTGGCTCCGGGACTCATTACAT
CCATCACGGTGTTGCCCTGTGCTGACCCACTCAAGTGATCTTCCGTCAACGGGATT
CTGA (SEQ ID NO. 437)

dermatan-sulfate adhesin (example 2)

ATGCGTCGAACAAGAATCACTGTGGCAGCTGTGACAGCAACTGCCTTAATCGGCTC
ACTATCAGCTATCACCCCTCCCCGCGAATGCTGCTTCTAACGGGAACAGCTCCAT
AACCCAGTCAGCTGCCTTCAGCCCCCGCGCCACGACAAAGATCAGCGAGGACTGCC
GCAAAGCCATCATCAACGACCTGAAACTGCGCGGCGCGATCGTCGGAGCACTCGTC
AAGGCTGGACTCAGCGCAGCCGACGCGAGCCGCCCTGGCCCCCGTATCGCCGCCGA
AATGGCAGCGGAGGGTACCCTTACCATCAACCATCACCGACTGAAGGTCCTCGTCG
CTTCCCAGCTGGGCCTCGTAGCAGACGCTGCGGTCCAACACGCAGCTGCAGCCATC
GACCTCAGCTTCAAGGCCATCCTAGGCGCGTCGATCATCCCCAACGCACTAGGATC
AGCCGCGTTCAAGAACGCGGTCATCGCAAACCTCGTCGCTGCTGGTATCGACAAGC
ACCTGGCACGAGCCACCGCCGTGGCGATCGTCGCCACCGCACTGAACCCCGCCCTC
GGGCCCATCGCGAAGTTCGAACTCATCAAAGCTGAGATCGCCGCCAAGCAGCTCT
TCTCATCCGAAGGGGCGTCCATCTCCAGAAGGCAGCCATCGAGCACGTCATCGGCC
GCGCCTTCGACGCCGCTGTCGCGACCGCGATTATCAGCTCTCCGATCCTGAGTGCA
CGCATCGTCACTCACCTGGTCAGGGCTGGAATAGACAAGTCCATTGCCATCAGCCT
TGCACCGCATATCGTCAAGCGCCTGGCCAAGGAGCCGCTACTGGCGTTCAACACCG
CCAAGCTCGTCAAGGACATCGCCCGGCAAATCGTCGACATCCGCAACACCCAGGA
AGCCATAGCAGTCTACAAGCAACTCAAGGCTGAACTACCAACCCTGGACGGACTC
GTGCAGAAGGCCTGCACCCCCGAGCCGACTCCTACGCCGACCCCGACTCCTACGCC

GACACCGACACCGGCTCCGACACCGACACCGGCTCCGACACCGACACCGGCTCCG
ACACCGGCTCCGACACCGACACCGGCTCCGACACCGACACCAACGCCCACTCCAAC
ACCGACCCCAACCCCAACCCACGGGGCCACAACCACCGCCGATCAGCCGGACA
ACGGACCGCCACAACCTCGGGTCTCATCACACCCGCATCGCGGCCCCCGCACTGAT
CCACGCGAAGGCCCTCCCAGCAACAGGAACGGGAGCCTGA (SEQ ID NO. 438)

deoR:

GGGACAGCGACCGGTGAAGGGTCCGCTGGGAGCAAGGGGATCGTCAGTCGGTGTC
TGCAGGCTGAAGGGGCGCTTGGATGACGTGGTGTCCGCTCCGGCGGAAGGCACCG
AGCTTCTCGCTCAGCTCACTGTTTCGACGACTGGACGGTGACGATCCCCGTCCGGGG
CGGTATCGATGCCCAATATGGTTCGCTACCGGTGGTGAGGATCTTGGTGGGATCAG
CGAGGATCCACGACGTGCGAGCCCCGCGTCATCGCTTCGTGTTTGAACTCGACGGAC
TCCAGGAGTGGGCAGTTGAGCCCCGTGCGTCGCAGAGACTGCGTCGCAGCCGATGA
ACGCGACATCAGGGGTGATGCTGCGCAGGTTTGATGACGCCACGGTCCCAGAAG
GCTTCCGCTGTGCTGCCTTAACGCCCCGCCGAGCACCATGACGTTGGCGGTGCCTTC
GGCCACGGCCTGGAGCACGGACAGGCCCGCTACGAGGATGGTGATGTCGTTACGA
GTCGACAGAAGGCGGCCCAAGTGTGCTGCGGTGGACGTTCCGGAATCGAGCAGAACTA
GGTCACTCTCGTTCACGAGGTGTTTGGCGGCATATGTGGCCATTGCTGCCTTGGAG
ACGTGCTCGCATTGTTCTTCTCGTGCCAGGTAGGCTCGTGTCGTGCGGATCATGACG
TCTCCCCCGGAAATCTTCCAGATCTTGGATTCTATCCGAGAGGGCATCGACATCGCG
GCGAATCGTCGATGTAGAGACACCGAACAGTTGGGAAAGATCTCCGATGGACTCC
GAGTGCCCCAAAGAACGCAGATGGTTCGACAATGTGTGCGCGTCGGGCAGCTGTGCG
CCGTGCGCGGCTGTTTGGGTGTTGTGCTCATGGTGTCTTGATCGGTGACGTGGTTTG
GCTGATCCAATTTGAGGACCGCCTCTAAGGATAACCCAGCGGCATCACTGCTGGAC
TCGGTCTGTTTGGGTGGTCGGTCCAAGAATTTCTCAGGTACAGGCTAATAAGGTT
ACCTCGTCGGTGCCT (SEQ ID NO. 439)

Transposase 2:

ATGACAGACAGGTCCTATCCGGCGATGATCCGGCTTCGGCGCAACGCCTGGACCGA
GTTCTGTCCTTCTGGATTACGACGTCGAGATCCGCAAGATCCTCTGCTCGACGA
ACGCGATCAAGTCGTTGAACACCCGCTTCCGCACGGTCATGCGGGCGCAGGGTCAT
TTCCCGACGCGCTGA (SEQ ID NO. 440)

CAMP2 (ATCC 11828):

ATGAAGAAGACCCATCTTGTAGCTCCTCTCCTTGTCGGCGCAATGCTCGTGCCAGC
GGCGCTGTCAGTCCCAGTGCTCATGCTGTGCGAGCCGACGACGACCATCTCGGCGA
CCAGCACCCACGAGCTCTCGGCCAATGAAGCTCGCAATAGTATGCAGCTTCTGAAC
GCACGTATTGCGACCCTTCAGTCAGTACAGAAATCCGTCCCCGGTTCTGACTACTCT
GACCAGATCCGAGATCTTCTCAAGGCTGCCTTCGACCTGCGTGGCCTCATCGAGAC
CCTCGCTCATGGGGGGATCCCGTTCTACAACCCGTCGACGATCATGCCGAGGATCA
AGTTGGTCGCCACCACTGTTGACACCAATTCACACTGCTACGACCACTCTCCAAAAC
AAGGTCCGCCCCGCCACGTCGAACTCGGTCTCGAAGTCACCAAGGCCGTCTGCT
GACCGCTAACCCAGCGTCCACCGCCAAGGAACTCGACGCCGAGGGCGCCGCCCTC
AAGGCTCGCCTGGAAAAGGTCTCGCAATACCCCGACCTACCCCGAATGACGTTGC
CACTGTGTACGTACGCACCAACTTCAGCAAGACAATCTGGCAGGTGCGCGCCGACC
GTGACCGGTACATCCTTGGTCACAAGAGCGCCGCAAGTGTACAAGACGCTCAATCAC
GCCATACCAAGGCCGTCGGCGTTGACTGGACCCAAAGACGACCGTCGGGAACA
TCCAGGCTGCACGCACCGAGCTCCTTGCGGCCTATCAGACCGCATTTAATCCCTG
ATGTCAAGAAGGCTGCCTGA (SEQ ID NO. 441)

[00330] The following examples are given for the purpose of illustrating various embodiments of the disclosure and are not meant to limit the present disclosure in any

fashion. The present examples, along with the methods described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the disclosure. Changes therein and other uses which are encompassed within the spirit of the disclosure as defined by the scope of the claims will occur to those skilled in the art.

The following numbered embodiments are contemplated implementations of the current disclosure

1. A pharmaceutical composition comprising:

- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
- b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
- c) a biological stabilizer,

wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.

2. The pharmaceutical composition of embodiment 1, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.

3. A pharmaceutical composition comprising:

- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
- b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
- c) a biological stabilizer,

wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.

4. The pharmaceutical composition of embodiment 3, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe is selected or engineered to have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.
5. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes a CAMP factor.
6. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes a CAMP2 protein.
7. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes a hemolysin or cytotoxin.
8. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes a triglycerol lipase or precursor thereof.
9. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes an iron acquisition protein.
10. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes a heat shock protein.
11. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene encodes an iron uptake protein.
12. The pharmaceutical composition of embodiment 2 or 3, wherein the virulence gene is selected from *pap60* and *pAmce*.
13. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the biological stabilizer comprises glycerol.
14. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the pharmaceutical composition is about 5% to about 55% glycerol by volume.
15. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the pharmaceutical composition is about 15% to about 40% glycerol by volume.
16. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the pharmaceutical composition is provided on a cotton pad, a fabric, a paper, or a combination thereof.
17. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first therapeutically effective amount is less than an amount that would be effective if used to treat without the second health-associated microbe.
18. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the second therapeutically effective amount is less than an amount that would be effective if used to treat without the first health-associated microbe.

19. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated microbe and the second health-associated microbe have synergistic activity as a therapy for a skin disorder.
20. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the pharmaceutical composition is lyophilized.
21. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the pharmaceutical composition or a component thereof is freeze-dried or spray-dried.
22. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the wherein the biological stabilizer is an oil.
23. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated *Propionibacterium* microbe has a phylotype of type I or type II.
24. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated *Propionibacterium* microbe has a phylotype of type IB.
25. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe has a mutation in a Christie-Atkins-Much-Petersen (CAMP) gene.
26. The pharmaceutical composition of embodiment 25, wherein the CAMP gene is a CAMP2 gene.
27. The pharmaceutical composition of embodiment 25, wherein the mutation results in reduced expression of an exotoxin, reduced production of an exotoxin, reduced activity of a hemolysin, reduced activity of an exotoxin, or reduced secretion of an exotoxin.
28. The pharmaceutical composition of embodiment 25, wherein the mutation in the CAMP gene results in disruption of a STOP codon.
29. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex.
30. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated *Propionibacterium* microbe or the second health-associated *Propionibacterium* microbe comprises at least one of an HP3A11 strain, an HP4G1 strain, or an HP5G4 strain.
31. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated microbe produces less than about one micromolar porphyrin.
32. The pharmaceutical composition of embodiment 1, 2, or 3, wherein the first health-associated *Propionibacterium* microbe and the second health-associated

Propionibacterium microbe collectively produce less than about one micromolar porphyrin.

33. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1.
34. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT2.
35. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding an ATP binding cassette transporter.
36. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a deoxyribose operon repressor.
37. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a type II lipase.
38. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe lacks a gene encoding a DNA binding response regulator.
39. The pharmaceutical composition of embodiment 1, 2, or 3, wherein at least the first health-associated *Propionibacterium* microbe lacks a gene encoding a phosphoglycerate kinase.
40. The pharmaceutical composition of embodiment 1, 2, or 3, comprising the first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; and the biological stabilizer, wherein the first health-associated *Propionibacterium* microbe has a CRISPR locus in its genome, and wherein the CRISPR locus comprises at least four different spacer sequences.
41. The pharmaceutical composition of claim of embodiment 43, wherein the first health-associated *Propionibacterium* microbe has reduced activity of the virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe.

42. A method of treating a skin disorder or condition comprising applying a therapeutically effective amount of a pharmaceutical composition of embodiment 1, 2, or 3 to at least a region of skin on a subject in need thereof.
43. The method of embodiment 42, wherein the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof.
44. The method of embodiment 42, wherein applying is topical.
45. The method of embodiment 42, wherein applying comprises applying the therapeutically effective amount of a pharmaceutical composition with a cotton pad.
46. The method of embodiment 45, comprising rubbing the cotton pad on the region of skin.
47. The method of embodiment 42, wherein the at least one of the health-associated microbes remains present on the region of skin after at least one wash.
48. The method of embodiment 47, wherein the wash comprises applying soap and water to the region of skin.
49. The method of embodiment 47, wherein the wash comprises applying an antibacterial agent.
50. The method of embodiment 49, wherein the antibacterial agent is benzoyl peroxide.
51. The method of embodiment 42, comprising applying the pharmaceutical composition at least once daily.
52. A pharmaceutical composition comprising:
- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
 - b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a metabolic enhancing compound,
- wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.
53. The pharmaceutical composition of embodiment 52, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
54. A pharmaceutical composition comprising:

- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
 - b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a metabolic enhancing compound,
- wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
55. The pharmaceutical composition of embodiment 52, 53, or 54, wherein the metabolic enhancing compound suppresses lipase activity and/or increases propionic acid production.
56. The pharmaceutical composition of embodiment 52, 53, or 54, wherein the metabolic enhancing compound suppresses secreted lipase activity and/or increases secreted propionic acid production.
57. The pharmaceutical composition of any one of embodiments 52 to 56, wherein the metabolic enhancing compound suppresses *S. aureus*.
58. The pharmaceutical composition of any one of embodiments 52 to 56, wherein the metabolic enhancing compound comprises a humectant.
59. The pharmaceutical composition of any one of embodiments 52 to 56, wherein the metabolic enhancing compound comprises glycerol.
60. The pharmaceutical composition of any one of embodiments 52 to 56, wherein the metabolic enhancing compound consists essentially of glycerol.

EXAMPLES

Example 1: Identification of health-associated strains

[00331] Characteristics that may predispose a particular microbe to be a health-associated microbe can be determined using samples from healthy and disease afflicted individuals, culturing the microbes from each, and performing a comparative genomic analysis. In the present example, samples were collected from individuals afflicted with acne vulgaris in order to determine health-associated *P. acnes* strains.

[00332] Microcomedone or swab samples were collected from consented adult subjects. Clonal samples were isolated by limiting dilution on plates, and then grown in 200 μ L of

liquid culture. Microbial DNA was isolated from 96 individual cultures. DNA was isolated using QIAGEN's DNeasy Blood & Tissue kit, following the manufacturer's instructions. QIAGEN's DNeasy Blood & Tissue kit, following the manufacturer's instructions. Paired-end DNA sequencing (2 x 300bp) was done on an Illumina MiSeq using reagent kit v3, following the manufacturer's instructions, yielding 200,000 to 600,000 reads for each of the 96 samples. Initial analysis was performed in Illumina's BaseSpace Sequence Hub, all reads from each sample are aligned with a BWA Aligner to:

- a. *deoR*;
- b. *Propionibacterium acnes* ATCC 11828 (accession CP003084); or
- c. pIMPLE and other reference genomes.

[00333] Alignments were interrogated with the Broad Institute's Integrative Genomics Viewer and confirmed using Biomatter's Geneious version 9.1. All 96 clones were analyzed for the presence or absence of the *deoR* sequence, type I lipase or type II lipase sequence, and presence or absence of pIMPLE plasmid. Sequence alignments were performed between sequences of *P. Acnes* from healthy volunteers and the *deoR* gene. Analysis revealed that approximately half of all healthy clones were positive for *deoR* (greater than 0.4% of reads mapping to *deoR* locus). Sequence alignments were also performed between *P. acnes* of healthy volunteers and the lipase gene locus *P. acnes* were positive for type I Lipase and for type II Lipase. With regard to the pIMPLE plasmid sequence alignments of reads from healthy volunteers performed against pIMPLE-HL096PA1 (GenBank: CP003294.1), revealed *P. acnes* from healthy volunteers are free of pIMPLE plasmid. Number of clones from healthy volunteers map *P. acnes* to ribotype RT1. Results are summarized in **Table 3**.

Table 3. summary of sequencing data for the *P. acnes* isolated from healthy volunteers

	RT1; <i>deoR</i> -	RT1; <i>deoR</i> +; LP1	RT1; <i>deoR</i> +; LP2	RT2	Staph.	Other	sum
# of clones	112	160	42	1	7	48	370
% of total	30.3%	43.2%	11.4%	0.3%	1.9%	13.0%	
RT1=ribotype 1; RT2=ribotype 2; <i>deoR</i> =no <i>deoR</i> ; <i>deoR</i> + = <i>deoR</i> ; LP1=type I; Lipase; LP2 =type II lipase; Staph= <i>Staphylococcus</i> ; other <i>P. avidum</i> , <i>P. acidipropionici</i> , or <i>Staphylococcus</i>							

[00334] **FIG. 2** shows that a greater percentage of the total reads from healthy volunteers align to RT1 than align to RT2, as indicated by the position of each data point above the diagonal where RT1=RT2. As shown in Table 3, the distribution of genotypes of 370 *P. acnes* clones collected from healthy subjects indicates that some RT1 strains are *deoR*

positive and Type II lipase positive. This data collectively shows that some RT1 strains may be considered a health-associated *P. acnes*.

Example 2: Identification of health-associated strains with Hyaluronidase genes

[00335] Health-associated *P. acnes* clones that were RT1 or RT2 positive were further examined for presence of a gene encoding hyaluronidase. Unexpectedly most health-associated strains that were positive for Type II lipase also possessed a hyaluronidase gene. See Table 4.

Table 4. Hyaluronidase presence in health-associated *P. acnes* strains also positive for type II lipase

Clone	Ribotype	Hyaluronidase
1	RT1; deoR+; L2	Yes
2	RT1; deoR+; L2	Yes
3	RT1; deoR+; L2	Yes
4	RT1; deoR+; L2	Yes
5	RT1; deoR+; L2	Yes
6	RT1; deoR+; L1	No
7	RT1; deoR+; L2	Yes
8	RT1; deoR+; L2	Yes
9	RT1; deoR+; L2	Yes
10	RT1; deoR+; L2	Yes
11	RT1; deoR+; L2	Yes
12	RT2	Yes
13	RT2	Yes
14	RT2	Yes
15	RT2	Yes
RT1=Ribotype 1; RT2=Ribotype 2; L1 –Lipase type I; L2=Lipase type 2; Deor+=DeoRepressor positive		

Example 3: P. Acnes Viability Assay

[00336] Viability of *P. acnes* was assessed over three months of storage as shown in Table 5. At least three samples were tested at each time point.

Table 5. Assessed *P. acnes* storage conditions

Solution	Temperature
25% glycerol in PBS	-20 ° C
50% glycerol in water	-20 ° C

[00337] Samples were prepared according to the following:

[00338] 1. *P. acnes* of ribotypes RT2 (HP4G1) were started at 0.10 OD₆₀₀ and grown to ~ 1.0 OD₆₀₀ in exponential phase in reinforced clostridial medium (RCM).

[00339] 2. Three days later, cultures displayed a dense turbidity, and they were split 1:5 with RCM to produce two liquid cultures (LC).

[00340] 3. One day later, one liquid culture was chosen to be split 1:5 with RCM.

[00341] 4. One day later, the liquid cultures were spun down at 4,300 rcf for 5 minutes. Media was discarded and pellets washed with 10 ml 25% v/v glycerol/water to wash the cells.

[00342] 5. The 10ml of resuspended culture from all LCs were transferred into one 50ml tube to form a combined LC, gently inverted 5 times.

[00343] 6. The combined LC was evenly aliquoted to two 50 ml tubes and spun down at 4,300 rcf. The media was discarded.

[00344] 7. The cells were resuspended in either 25% glycerol in PBS and 50% glycerol in water, as separate treatments.

[00345] 8. 2ml of resuspended bacteria in either 25% glycerol in PBS and 50% glycerol was placed onto a pad, as separate treatments.

[00346] 9. The pad was vacuum sealed inside a bag.

[00347] 10. The bag was flash frozen by being covered with dry ice and then stored in a -20C freezer.

[00348] 11. Small aliquots of resuspended bacteria in both treatments were stored in multiple microcentrifuge tubes.

[00349] 12. Small aliquots of resuspended bacteria in either 25% glycerol in PBS or 50% glycerol were flash frozen by being covered with dry ice and then stored in a -20C freezer.

[00350] 13. For every sampling time point, a microcentrifuge and frozen bag and pad with resuspended bacteria in either 25% glycerol in PBS or 50% glycerol was thawed at room temperature and diluted. Both treatments were tested at every time point.

[00351] 14. 20 microliters of the thawed bacteria were serially diluted in 96 well plates with RCM and the dilution series was spotted on Brucella plates.

[00352] 15. Plates were imaged with a digital camera, and colonies counted with 95% Confidence Interval.

[00353] **FIG. 3** shows the viability of a HP4G1 *P. acnes* preparations after 6 days, 43 days, 73 days and 98 days of preservation at – 20 degrees Celsius.

Example 4. Identification of *P. acnes* RT6

[00354] In an effort to isolate and purify health-associated strains of *P. acnes*, (e.g., strains associated with acne) it may be useful to identify undesirable strains of *P. acnes* in a sample (e.g., strains found on skin of subjects with acne). For instance, in some cases, *P. acnes* of ribotype RT6 is undesirable. To this end, genes can be identified that are specific to strains of interest. The following example demonstrates how this can be performed.

[00355] Identities of genes that distinguish *P. acnes* of ribotype RT6 from healthy strains were confirmed. Genes encoding DNA binding response regulator and phosphoglycerate kinase were identified in *P. acnes* of ribotype RT6, but not RT1, RT2, RT3, RT4 and RT5. In addition a gene encoding ABC transporter is absent in RT6, but present in RT1, RT2, RT3, RT4 and RT5. Sequences for these genes are provided as SEQ ID NOS: 6 (ABC transporter), 7 (DNA binding response regulator), and 9 (phosphoglycerate kinase)

[00356] The presence or absence of these genes was confirmed by sequence alignment using BLAST, Megablast, (a registered trademark of the National Library of Medicine) either the whole complete genome or all of the scaffolds of a completed genome against each of these three gene sequences; the results are shown in **Table 6**. “Y” is a perfect match for the entire sequence OR > 60bp continuous perfect sequence alignment. “N” means there is < 60bp perfect alignment. The best match of a “N” was 26bp.

Table 6. Characterization of exemplary *P. acnes* strains

Strain Name	Ribotype	recA type	ABC transporter	DNA binding response regulator	Phosphoglycerate kinase
HL002PA2	1	IA	Y	N	N
HL025PA1	1	IB	Y	N	N
HL030PA1	1	IB	Y	N	N
HL050PA2	1	II	Y	N	N
HL096PA3	1	IA	Y	N	N
HP3A11	1	IB	Y	N	N
HP3B4	1		Y	N	N
KPA171202	1	IB	Y	N	N
ATCC 11828	2	II	Y	N	N
HL001PA1	2	II	Y	N	N
HL103PA1	2	II	Y	N	N
HP4G1	2	II	Y	N	N
HP5G4	2	II	Y	N	N
HL002PA1	3	IB	Y	N	N
HL005PA1	4	IA	Y	N	N
HL007PA1	4	IA	Y	N	N
HL038PA1	4	IA	Y	N	N

Strain Name	Ribotype	recA type	ABC transporter	DNA binding response regulator	Phosphoglycerate kinase
HL045PA1	4	IA	Y	N	N
HL053PA1	4	IA	Y	N	N
HL056PA1	4	IA	Y	N	N
HL074PA1	4	IA	Y	N	N
HL099PA1	4	IA	Y	N	N
HL043PA1	5	IA	Y	N	N
HL043PA2	5	IA	Y	N	N
HL072PA1	5	IA	Y	N	N
HL072PA2	5	IA	Y	N	N
HL096PA1	5	IA	Y	N	N
HL096PA2	5	IA	Y	N	N
HL097PA1	5	IC	Y	N	N
PRP-38	5	IC	Y	N	N
HL110PA3	6	II	N	Y	Y
HL110PA4	6	II	N	Y	Y

Example 5. Pan bacterial assay to characterize skin microbiome

[00357] Robust pan-sampling of the skin microbiome is demonstrated in the following example. This can be performed with or without the use of preservatives. This method is compatible with qPCR analysis and does not require DNA purification. TaqMan qPCR assays were used to quantitate most bacteria collected from the face. Performance was confirmed with two different bacterial phyla, all *Propionibacterium* and *Staphylococcus*. This method required the assessment of only a single locus to recognize most bacteria commonly found on the face (*P. acnes* strains and *Staphylococcus*), whereas current methods in the field use multiple primer pairs to achieve similar coverage. The majority of the bacteria on the skin of a subject's face is described in the following **Table 7**.

Table 7. Bacteria on Human Facial Skin

	<i>P. acnes</i>	<i>P. avidum</i>	<i>S. epidermidis</i>	<i>S. aureus</i>
Kingdom	Bacteria	Bacteria	Bacteria	Bacteria
Phylum	Actinobacteria	Actinobacteria	Firmicutes	Firmicutes
			Bacilli	Bacilli
Order	Actinomycetales	Actinomycetales	Bacillales	Bacillales
Family	Propionibacteriaceae	Propionibacteriaceae	Staphylococcaceae	Staphylococcaceae
Genus	Propionibacterium	Propionibacterium	Staphylococcus	Staphylococcus
Species	<i>P. acnes</i>	<i>P. avidum</i>	<i>S. epidermidis</i>	<i>S. aureus</i>

[00358] A portion of a 23S sequence from bacteria commonly found on the human face was aligned with known sequences, see **FIG. 4**, and SEQ ID NOs: 33 to 43. Despite two Single

Nucleotide Polymorphisms at this loci (denoted by bold and underlined letters), careful placement of primers (gray and black) and TaqMan reporter (white) enable quantification of widely diverse bacteria from both Actinobacteria and Firmicutes.

[00359] A standard curve for all assays was generated with *P. acnes*. Percentages of health-associated *P. acnes* were computed using a dilution series with *S. epidermidis* or pathogenic *P. acnes* which were used to quantitate a percentage of health-associated *P. acnes* in a collected sample. These percentages were determined by measuring deoR⁺ or Cas5⁺ bacteria in the overall sample of bacteria (PANBAC), see, *e.g.*, **FIG. 5**.

Example 6. Determination of Percentage of pIMPLE plasmid

[00360] The percentage of pIMPLE plasmid was determined from biological samples.

[00361] Biological samples were collected and grown in 200 µL of liquid culture. DNA was isolated using QIAGEN's DNeasy Blood & Tissue kit, following the manufacturer's instructions. Paired-end DNA sequencing (2 x 300bp) was done on an Illumina MiSeq using reagent kit v3, following the manufacturer's instructions, yielding 200,000 to 600,000 reads for each sample. Initial analysis was performed in Illumina's BaseSpace Sequence Hub, all reads from each sample are aligned with a Burrows-Wheeler Aligner (BWA) Aligner to pIMPLE. Alignments were interrogated with the Broad Institute's Integrative Genomics Viewer and confirmed using Biomatter's Geneious version 9.1.

[00362] The percentage of pIMPLE was determined by the percentage of total sequencing reads that aligned to pIMPLE plasmid from HL096PA1. pIMPLE is 55kb long and thus 2.2% of total genome. (*P. acnes* genome = 2.5Mbp, pIMPLE/*P. acnes* genome=2.234%). As an example and reference, RT4s and RT5s often have 2-3 copies of pIMPLE. % pIMPLE = % of total sequencing reads that align to pIMPLE. The percentage of pIMPLE was also calculated as the coverage * copy number.

[00363] Using these methods, the percentage of pIMPLE in the different ribotypes was determined as seen in **Table 8**.

Table 8. Presence of pIMPLE plasmid in different *P. acnes* strains.

Ribotype	Strain	%pIMPLE
1	HP3A11	0.23%
1	HP3A11	0.24%
2	HP5G4	0.26%
2	HP5G4	0.24%

Ribotype	Strain	%pIMPLE
2	HP4G1	0.26%
2	HP4G1	0.25%
4	HL045PA1	3.62%
4	HL045PA1	3.22%
5	HL043PA1	4.32%
5	HL043PA1	3.75%
6	HL110PA3	12.94%
6	HL110PA3	12.59%
6	HL110PA4	13.19%
6	HL110PA4	14.06%

[00364] These results show that strains of health-associated microbes disclosed herein have less than 0.5% pIMPLE plasmid, that *P. acnes* RT 6 strains can have more than 10% pIMPLE plasmid, and that *P. acnes* RT 6 strains can have more than 3% pIMPLE plasmid.

Example 7. Genetic Modification of *P. Acnes*

[00365] In order to improve healthy *P. acnes* clones, the expression of a gene in the porphyrin synthetic pathway was knocked out. This was accomplished by inserting stop codons in the middle of the open reading frame of the gene HemY (protoporphyrinogen oxidase, EC:1.3.3.4 1.3.3.15) in the *P. acnes* genome. Briefly, the RNA-guided DNA endonuclease **Cas9** (CRISPR associated protein 9) was targeted to HemY with specific CRISPR RNA (crRNA), and trans-activating RNA (tracrRNA) cleaving a double stranded break at the desired location in the HemY gene. A specific sequence was inserted at the site of the cleavage with a Homology Directed Repair cassette (HDR).

[00366] The Cas9, crRNA, tracrRNA, and HDR donor template were introduced into *P. acnes* using electroporation to transform the cells. Cells must be electrocompetent before undergoing electroporation. Electrocompetent *P. acnes* were prepared by growing them to stationary phase and washing them in a buffer of sucrose, magnesium chloride, and monosodium phosphate.

[00367] The tracrRNA and crRNA were duplexed using IDT's duplex-forming buffer. Then the tracrRNA:crRNA duplex was incubated in a solution of Cas9 and phosphate-buffered saline, forming the ribonucleoprotein (RNP) complex. The RNPs, HDR, and electrocompetent *P. acnes* were combined, incubated on ice (transformation culture) and

transferred to a pre-chilled BioRAD electroporation cuvette. The transformation culture was electroporated using a BioRAD Micropulser. BD Difco Reinforced clostridium medium was immediately added to the transformation culture and transferred to separate container for a 24 hour, room temperature incubation. The transformation culture was evaluated with qPCR (see **FIG. 6**) and spread out over multiple Brucella plates for a final 72 hour anaerobic incubation at 37°C.

[00368] **FIG. 6** compares a qPCR result from cells transformed with a 921bp (921) or a 123bp HDR. Each sample was evaluated with primers that recognized either the inserted sequence (Insert) or the untransformed or wild-type (wt) genomic sequence. Note, using the longer, 921 bp, HDR transformed a greater percentage of the cells. The '921' sample had more cells resulting the leftward shift of both Insert and wt lines.

Example 8. Packaging Compositions of Bacteria as Swabs for Topical Application

[00369] A packaging system was created to store and deliver therapeutically effective doses of pharmaceutical compositions disclosed herein to the human face. These devices need to safely store and deliver approximately 2 milliliters of *P. acnes* in a pharmaceutically acceptable excipient, anaerobically. Furthermore, these systems were amenable to storage at temperatures as low as -80°C. The packaging system prevented contamination of both the *P.acnes* microbes (by the environment) and the environment (by the health-associated microbe), minimize exposure to any air, and enable easy application.

[00370] An example of an aforementioned package is shown in **FIG. 8**. Briefly an approximately 2 inch diameter circular cotton pad (Buddha Bath Premium All Natural Cotton Round) was placed in a laminated polypropylene bag (Elkay Laminated Poly-Nylon Vacuum Pouch # 30NV0408). Approximately two milliliters of *P. acnes* solution, at $\sim 10^9$ microbes per milliliter, was aseptically applied to the cotton pad. Almost all of the air was evacuated, and the bag was thermally sealed in a chamber vacuum sealer (Vacmaster VP215). These packages were easily opened and the pad removed for application of the health-associated microbe or measurement of recovery and viability. Near quantitative aseptic recovery was achieved by centrifugation of the pad in a 15 milliliter conical tube. To confirm that the cotton pad, polypropylene bags and high vacuum do not compromise viability of *P. acnes*, or retain *P. acnes*, samples were collected from four different conditions and determined CFUs/milliliter by plating and counting colonies. **FIG. 9** compares recovery from *P. acnes* samples stored for one week at -20 °C in either a micro centrifuge tube (control), or in our packaging in a residential frost free freezer, a laboratory freezer or in the lab freezer with

only a light vacuum before sealing. Large numbers of viable *P. acnes* were recovered from all conditions.

[00371] Alternative types of pads and bags could be employed for such packaging. For example, if a polyester pad is used, heat sealing could affix the pad to one side of the bag providing a shield and handle to enable application of the liquid therapeutic without mess and exposure to the hand. Similarly if a peel-open pouch is used, scissors would not be necessary for clean easy application.

Example 9. Fluorescence used to measure porphyrin levels on skin

[00372] UV lighting was used to visualize porphyrin levels on facial skin of a subject after application with a composition comprising a health associate microbe disclosed herein. **FIG. 10** shows porphyrin levels immediately after last face wash (left panel), and 24 hours after application of the composition (right panel). UV-induced fluorescence of porphyrins can be quantified as shown in **FIG. 11**. In **FIG. 11** the -1 h timepoint is 12H from last face wash, 4 is 4H from last face wash and 21/22/25 is essentially 24H from last face wash and you can see high levels at 24H irrespective of treatment. Porphyrin levels have only increased with time after last face wash, but applied strains did not increase porphyrin levels.

Example 10. Determining health-associated gene signatures

[00373] In some instances, isolation and genotypic identification of candidate health-associated *P. acnes* clones for compositions disclosed herein were performed according to the following:

[00374] Either microcomedone or swab samples were collected from consented adult subjects. Clonal samples were isolated by limiting dilution on plates and grown in 200 µl liquid culture. Genomic DNA was collected from 96 individual cultures with QIAgen's DNeasy Blood & Tissue kit, following the manufacturer's instructions. Microbial whole-genome sequencing library preparation was performed with Illumina's Nextera XT kit, following the manufacturer's instructions. Paired-end DNA sequencing (2 x 300bp) was performed on an Illumina MiSeq using reagent kit v3, following the manufacturer's instructions, yielding 200,000 to 600,000 reads for each of the 96 samples. Initial analysis was performed in Illumina's BaseSpace Sequence Hub, all reads from each sample were aligned with BWA Aligner to: deoR, *Propionibacterium acnes* ATCC 11828 (accession CP003084), pIMPLE and other reference genomes. Alignments were interrogated with

Broad's Integrative Genomics Viewer. Further and confirmatory analysis was performed in Geneious version 9.1 created by Biomatters.

[00375] By way of example, deoR gene annotated on ATCC 11828 was located in ribotype 2 *P. acnes*. A sequence for the deoR gene is shown in Table 2. Location was confirmed with qPCR probes deoR-forward, 5' CTGGCACGAGAAGGAACAA 3' and deoR-reverse, 5' GAATCGAGCAGAACTAGGTAC 3.'

Example 11. Surface Engraftment of Applied Strains

[00376] A composition of a *P. acnes* strain of ribotype 2, as well as a composition of a combination of a *P. acnes* strain of ribotype 1 and a *P. acnes* strain of ribotype 2 were applied to facial skin. Samples of bacteria from the face, including applied strains and resident strains, were collected at various time points after application. Levels of deoR, Cas 5 and PanBac, representing applied strains, were measured in these samples and compared to that of a sample wherein the facial skin was treated with excipient alone.

[00377] 0h is 7 days post benzoyl peroxide therapy and pre application of 10^5 cfu/cm². L and R denote samples from the left and right side of the face respectively.

[00378] For the composition of a combination of a *P. acnes* strain of ribotype 1 and a *P. acnes* strain of ribotype 2, the formulation was 50% RT1 (has deoR only) and 50% RT2 (deoR and Cas5). Thus, the formulation represents 100% deoR-positive bacteria (RT1 and RT2) and 50% Cas5-positive bacteria (RT2).

[00379] **FIG. 12** shows data from this experiment, **FIG. 12A** showing data from application of a *P. acnes* strain of ribotype 1 and a *P. acnes* strain of ribotype 2, **FIG. 12B** showing data from application of *P. acnes* strain of ribotype 2 only, and **FIG. 12C** showing data from application of excipient only.

[00380] These data show that the compositions applied can shift the skin microbiome towards a that of the applied strains, possibly displacing pathogenic strains, and thereby promoting skin health. These data also show that the presence of the applied strains persists for at least 12 hours, which means compositions may only have to be applied once or twice daily to maintain presence of the applied strains.

Example 12. Lipid Pillar Engraftment of Applied Strains

[00381] A composition comprising a *P. acnes* strain of ribotype 2 (comprising 100% deoR and 100% Cas5) was applied to facial skin of an acne vulgaris subject with a history of less than 5% deoR and less than 5% Cas5. Two weeks after application, wherein repeat treatment

with benzoyl peroxide and multiple face washes occurred, lipid pillars (comprising the contents of pilosebaceous units) were retrieved from the facial skin as described in Example 13.

[00382] Genotyping the contents of six (6) of the subject's pilosebaceous units revealed 45% deoR and 58% Cas5 suggesting that the some of the applied ribotype 2 *P. acnes* potentially engrafted in a portion of pilosebaceous units. This is despite repeat treatment with BPO and multiple face washes.

Example 13: Genotyping the contents of the Pilosebaceous Unit

[00383] Significant amounts of *P. acnes* reside within the pilosebaceous unit, the site of most acne vulgaris pathology. To both quantify the face topical microbiome and demonstrate engraftment into the pilosebaceous unit a sample-preparation protocol was developed to genotype the bacteria residing in the lipid environment of the pilosebaceous unit with our standard TaqMan assays.

[00384] After careful washing of the face and nose, leaving the face wet a Bioré Deep Cleansing Pore Strips, or similar, is applied across the nose, allowed to dry completely, ~ 10 minutes, and carefully removed taking care not to disturb the attached lipid pillars and frozen for 30 minutes at -20 degrees Celsius. One to ten individual lipid pillars are collected with fine forceps and collected in a micro-centrifuge tube, and extracted with ThermoFisher's DNA Extract All Reagents Kit according to instructions, except for incubation at 95 deg C for 10 minutes. After the addition of stabilization buffer the resulting sample can be directly analyzed with our TaqMan Assays.

[00385] FIG. 13 shows the results of three samples of 6 lipid pillars each from a subject with acne vulgaris (Acne) and a subject without (Healthy). The Acne subject had fewer total bacteria (PanBac) and a wider diversity of genotypes while the Healthy subject had many more bacteria, many with deoR and none with Cas5.

Example 14: Synergistic effect of two strains of *P. acnes*

[00386] Competition experiments showed dose-related competition with *P. acnes* strains. A first *P. acnes* strain of ribotype 1 (RT1) and second strain *P. acnes* of ribotype 2 (RT2), were tested separately, and in combination, for their ability to compete against a lawn *P. acnes* of ribotype 4 (RT4).

[00387] In brief, increasing concentrations of the RT1 and/or RT2 *P. acnes* strains were added as large spots to a lawn of RT4 *P. acnes*, beginning with 10⁵ CFU/ml at the top to

10^9 CFU/ml at the bottom of the plate, as viewed in **FIG. 14**. The two leftmost circles on each plate were control RT4 inoculations against the lawn of RT4.

[00388] Results showed higher concentrations of RT1/RT2 strains provided a more marked zone of clearing in the RT4 lawn, likely related to resource competition. One can see there are fewer and sparser lawn colonies near the highest concentration of RT1 or RT2 inoculate added, implying perhaps some resource inhibition of pathogenic strains with high concentrations of added drug. Interestingly, this effect (i.e. fewer and sparser RT4 lawn colonies) is more dramatic when the combination of RT1 and RT2 *P. acnes* strains are applied (**FIG. 14C**) as compared to each strain alone (**FIGS. 14A** and **14B**), implying the two strains together having synergistic competing activity.

Example 15. Identification of viable HP4G1 from individual hair follicles

[00389] Since many *health-associated* strains of *P. acnes* contain both deoR and Cas5, the genomic DNA encoding the CRISPR locus was directly sequenced. Using primers (see Table 9) designed to span the entire region (see **FIG. 15**, black arrows labeled “F” and “R”), amplicons were generated containing all repetitive and spacer sequences. The entire sequence for each isolated clone was read using Sanger sequencing.

Table 9. Primers spanning CRISPR locus in health-associated strains of *P. acnes*

SEQ ID NO	Name	Sequence
435	Forward CRISPR primer	AATCTTGGTGTATACGGTA
436	Reverse CRISPR primer	AGTGATCGAGATGAGGAG

[00390] Shown in **FIG 15** are four easily distinguishable *P. acnes* strains that all contain both deoR and Cas5 and lack Transposase2. NB01 is HP4G1, ATCC 11828 a publicly available RT2 strain. *P. acnes* variant is a clone from a pilosebaceous unit. *P. acnes* variant #2 was collected from an IRB-approved trial. Note for these strains all repeat sequences (gray blocks) are identical. Some spacer sequences (numbered white blocks) are shared and thus labeled with the same number. NB01 has 7 unique spacer sequences, the most in this set.

[00391] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention.

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising:
 - a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
 - b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a biological stabilizer,wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.
2. The pharmaceutical composition of claim 1, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
3. A pharmaceutical composition comprising:
 - a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
 - b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a biological stabilizer,wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
4. The pharmaceutical composition of claim 3, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe is selected or engineered to have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.

5. The pharmaceutical composition of claim 2, wherein the virulence gene encodes a CAMP factor.
6. The pharmaceutical composition of claim 2, wherein the virulence gene encodes a CAMP2 protein.
7. The pharmaceutical composition of claim 2, wherein the virulence gene encodes a hemolysin or cytoxin.
8. The pharmaceutical composition of claim 2, wherein the virulence gene encodes a triglycerol lipase or precursor thereof.
9. The pharmaceutical composition of claim 2, wherein the virulence gene encodes an iron acquisition protein.
10. The pharmaceutical composition of claim 2, wherein the virulence gene encodes a heat shock protein.
11. The pharmaceutical composition of claim 2, wherein the virulence gene encodes an iron uptake protein.
12. The pharmaceutical composition of claim 2, wherein the virulence gene is selected from *pap60* and *pAmce*.
13. The pharmaceutical composition of claim 1, wherein the biological stabilizer comprises glycerol.
14. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is about 5% to about 55% glycerol by volume.
15. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is about 15% to about 40% glycerol by volume.
16. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is provided on a cotton pad, a fabric, a paper, or a combination thereof.
17. The pharmaceutical composition of claim 1, wherein the first therapeutically effective amount is less than an amount that would be effective if used to treat without the second health-associated microbe.
18. The pharmaceutical composition of claim 1, wherein the second therapeutically effective amount is less than an amount that would be effective if used to treat without the first health-associated microbe.
19. The pharmaceutical composition of claim 1, wherein the first health-associated microbe and the second health-associated microbe have synergistic activity as a therapy for a skin disorder.

20. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is lyophilized.
21. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition or a component thereof is freeze-dried or spray-dried.
22. The pharmaceutical composition of claim 1, wherein the wherein the biological stabilizer is an oil.
23. The pharmaceutical composition of claim 1, wherein the first health-associated *Propionibacterium* microbe has a phylotype of type I or type II.
24. The pharmaceutical composition of claim 1, wherein the first health-associated *Propionibacterium* microbe has a phylotype of type IB.
25. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe has a mutation in a Christie-Atkins-Much-Petersen (CAMP) gene.
26. The pharmaceutical composition of claim 25, wherein the CAMP gene is a CAMP2 gene.
27. The pharmaceutical composition of claim 25, wherein the mutation results in reduced expression of an exotoxin, reduced production of an exotoxin, reduced activity of a hemolysin, reduced activity of an exotoxin, or reduced secretion of an exotoxin.
28. The pharmaceutical composition of claim 25, wherein the mutation in the CAMP gene results in disruption of a STOP codon.
29. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe belongs to a CC72 clonal complex.
30. The pharmaceutical composition of claim 1, wherein the first health-associated *Propionibacterium* microbe or the second health-associated *Propionibacterium* microbe comprises at least one of an HP3A11 strain, an HP4G1 strain, or an HP5G4 strain.
31. The pharmaceutical composition of claim 1, wherein the first health-associated microbe produces less than about one micromolar porphyrin.
32. The pharmaceutical composition of claim 1, wherein the first health-associated *Propionibacterium* microbe and the second health-associated *Propionibacterium* microbe collectively produce less than about one micromolar porphyrin.
33. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT1.
34. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe comprises a *Propionibacterium acnes* of a ribotype RT2.

35. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding an ATP binding cassette transporter.
36. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a deoxyribose operon repressor.
37. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe comprises at least one gene encoding a type II lipase.
38. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe lacks a gene encoding a DNA binding response regulator.
39. The pharmaceutical composition of claim 1, wherein at least the first health-associated *Propionibacterium* microbe lacks a gene encoding a phosphoglycerate kinase.
40. The pharmaceutical composition of claim 1, comprising the first therapeutically effective amount of a first health-associated *Propionibacterium* microbe; and the biological stabilizer, wherein the first health-associated *Propionibacterium* microbe has a CRISPR locus in its genome, and wherein the CRISPR locus comprises at least four different spacer sequences.
41. The pharmaceutical composition of claim of claim 1, wherein the first health-associated *Propionibacterium* microbe has reduced activity of the virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe.
42. A method of treating a skin disorder or condition comprising applying a therapeutically effective amount of a pharmaceutical composition of claim 1 to at least a region of skin on a subject in need thereof.
43. The method of claim 42, wherein the skin disorder or condition comprises acne, eczema, seborrheic dermatitis, psoriasis, or rosacea, or a combination thereof.
44. The method of claim 42, wherein applying is topical.
45. The method of claim 42, wherein applying comprises applying the therapeutically effective amount of a pharmaceutical composition with a cotton pad.
46. The method of claim 45, comprising rubbing the cotton pad on the region of skin.
47. The method of claim 42, wherein the at least one of the health-associated microbes remains present on the region of skin after at least one wash.
48. The method of claim 47, wherein the wash comprises applying soap and water to the region of skin.
49. The method of claim 47, wherein the wash comprises applying an antibacterial agent.

50. The method of claim 49, wherein the antibacterial agent is benzoyl peroxide.
51. The method of claim 42, comprising applying the pharmaceutical composition at least once daily.
52. A pharmaceutical composition comprising:
- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;
 - b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a metabolic enhancing compound,
- wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have a CRISPR locus in its genome, wherein the CRISPR locus comprises at least four different spacer sequences.
53. The pharmaceutical composition of claim 52, wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
54. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound suppresses lipase activity and/or increases propionic acid production.
55. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound suppresses secreted lipase activity and/or increases secreted propionic acid production.
56. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound suppresses *S. aureus*.
57. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound comprises a humectant.
58. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound comprises glycerol.
59. The pharmaceutical composition of claim 52, wherein the metabolic enhancing compound consists essentially of glycerol.
60. A pharmaceutical composition comprising:
- a) a first therapeutically effective amount of a first health-associated *Propionibacterium* microbe;

- b) optionally, a second therapeutically effective amount of a second health-associated *Propionibacterium* microbe or *Lactobacillus* microbe; and
 - c) a metabolic enhancing compound,
- wherein at least one of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe have reduced activity of a virulence gene encoding protein relative to wildtype versions of the first health-associated *Propionibacterium* microbe and second health-associated *Propionibacterium* microbe, respectively.
- 61. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound suppresses lipase activity and/or increases propionic acid production.
 - 62. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound suppresses secreted lipase activity and/or increases secreted propionic acid production.
 - 63. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound suppresses *S. aureus*.
 - 64. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound comprises a humectant.
 - 65. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound comprises glycerol.
 - 66. The pharmaceutical composition of claim 60, wherein the metabolic enhancing compound consists essentially of glycerol.

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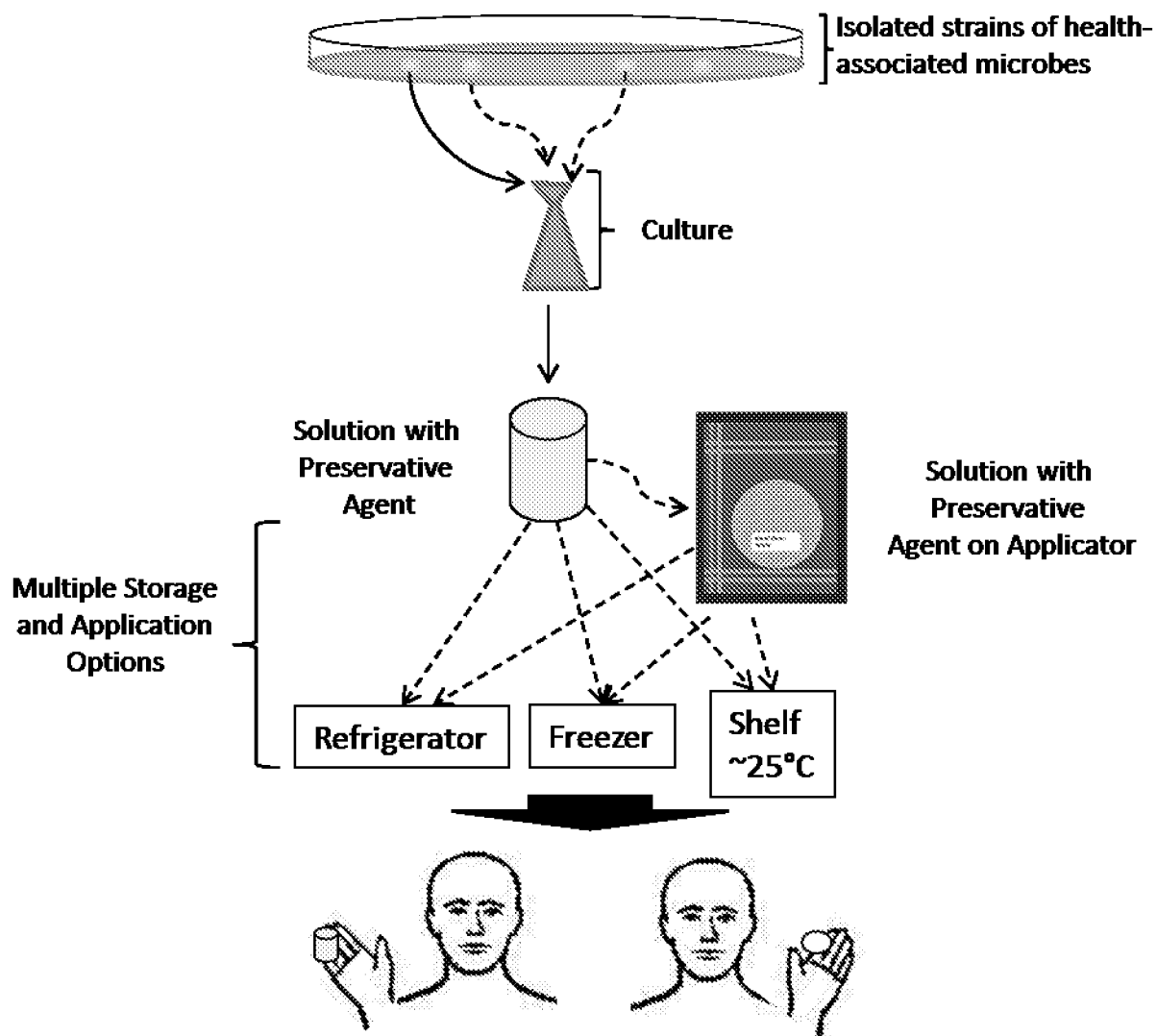


FIG. 1

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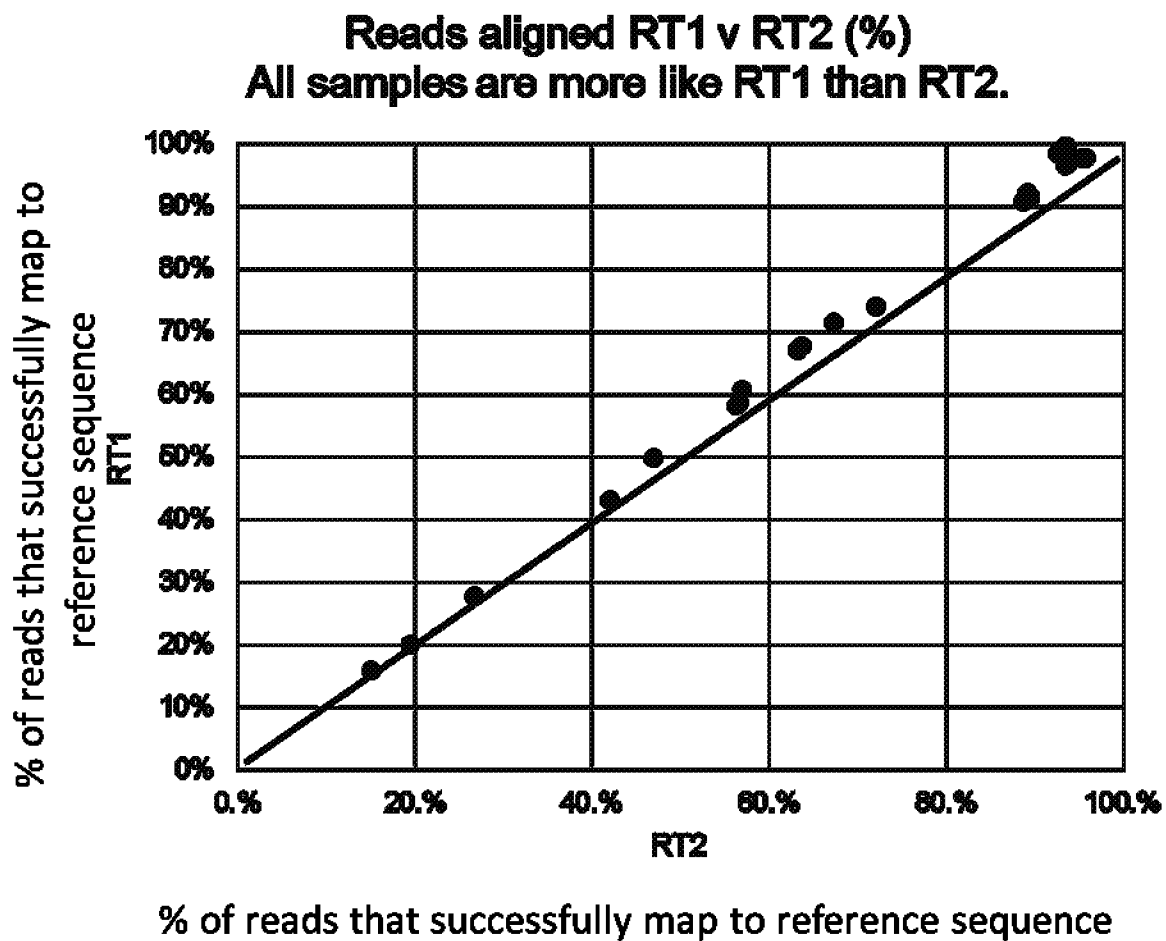


FIG. 2

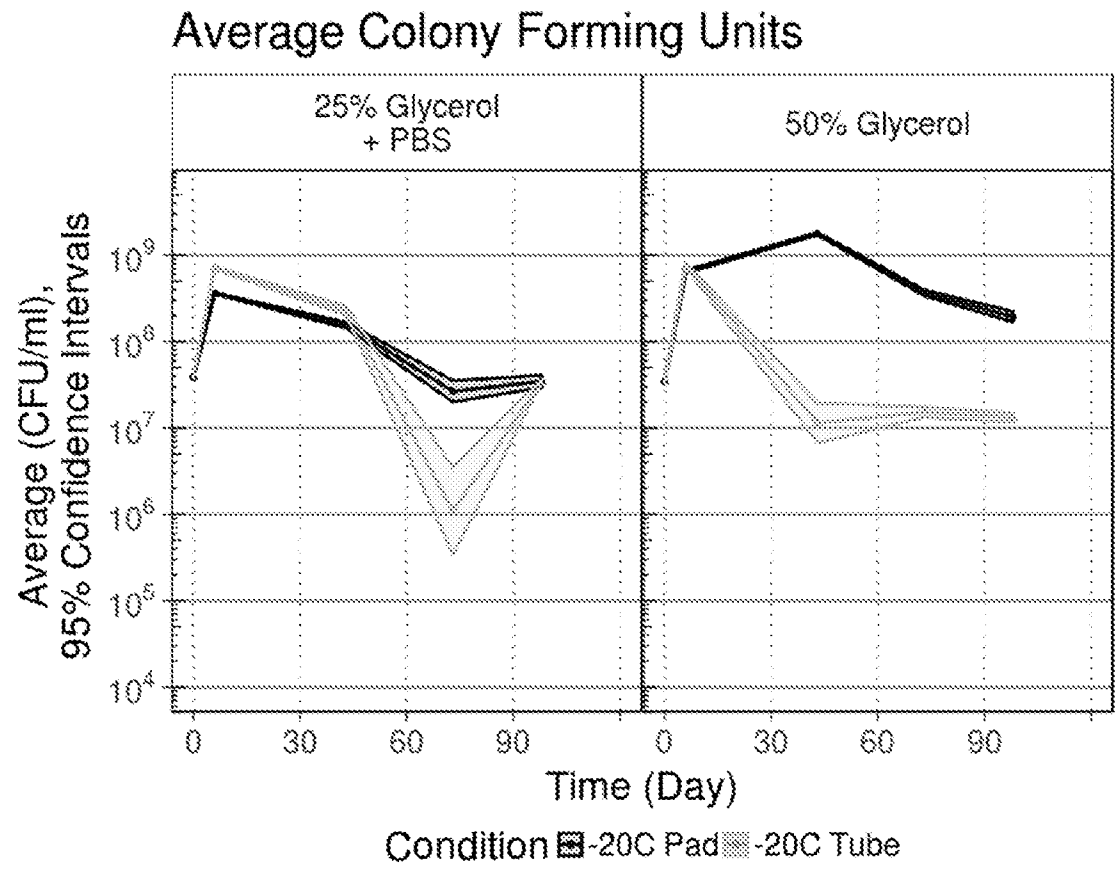


FIG. 3

1 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
2 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
3 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
4 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
5 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
6 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
7 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
8 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
9 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
10 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG
11 AGTCGGTCCCAAGGGTTGGGCTGTTGGCCCATTAAGCGGACGGCGAGCTGGGTTAGAACGTCGTGAGACAGTTCGGTCCCTATCCG

FIG. 4

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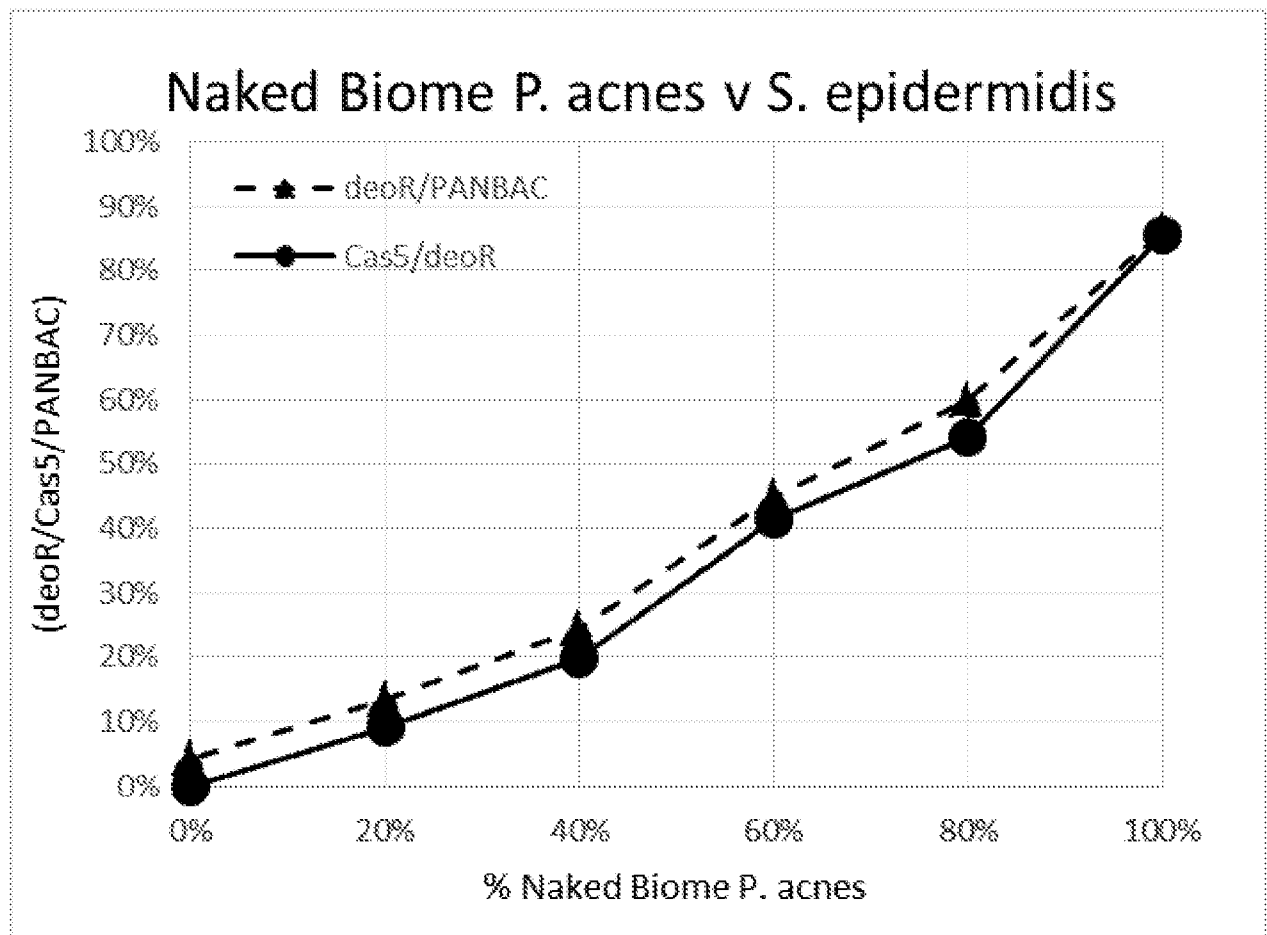


FIG. 5

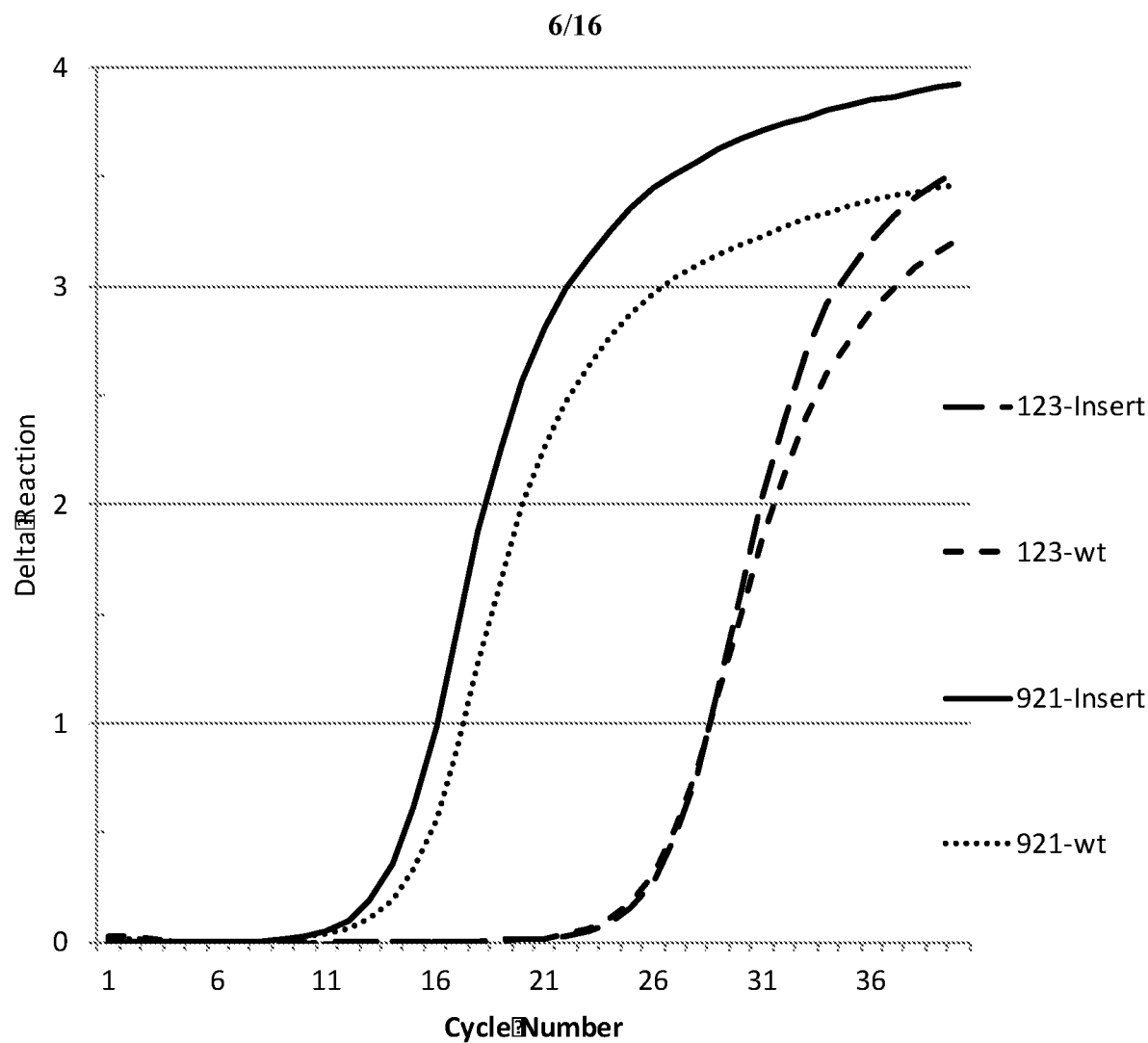


FIG. 6

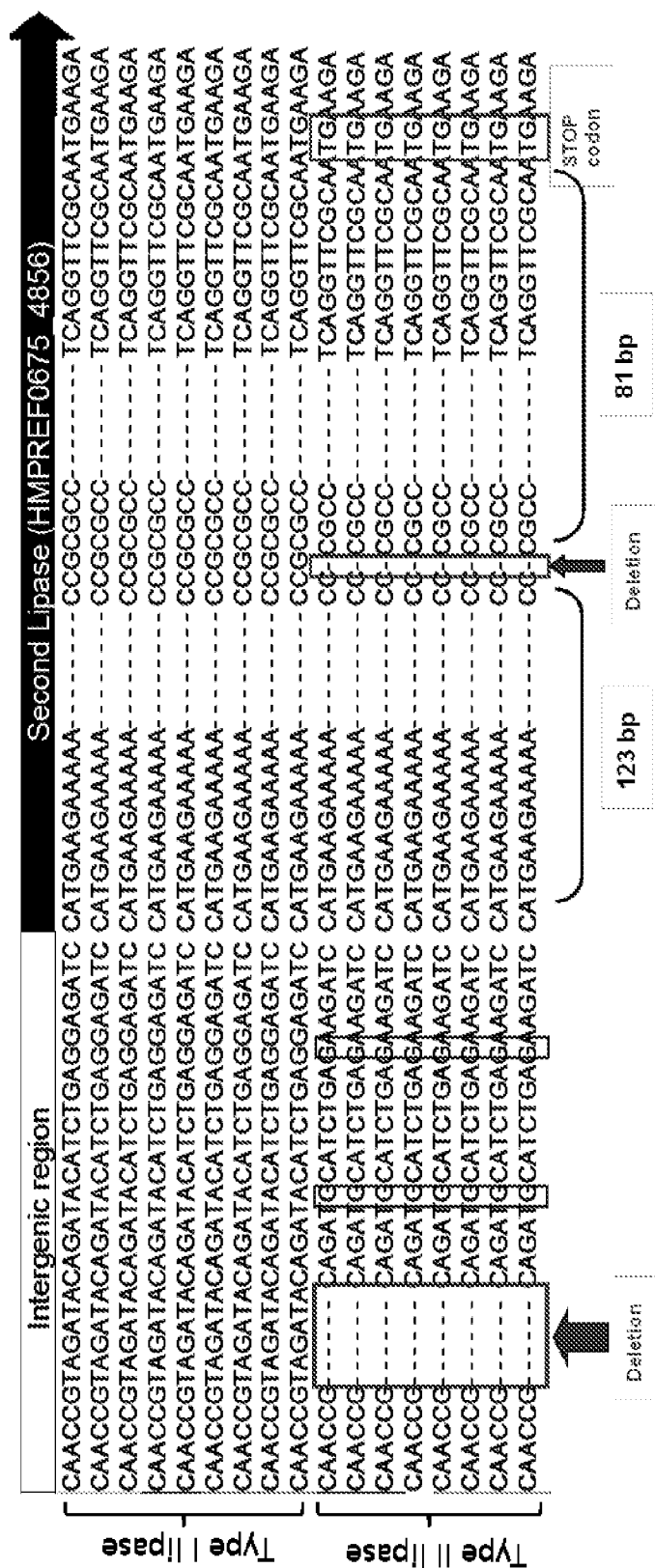


FIG. 7

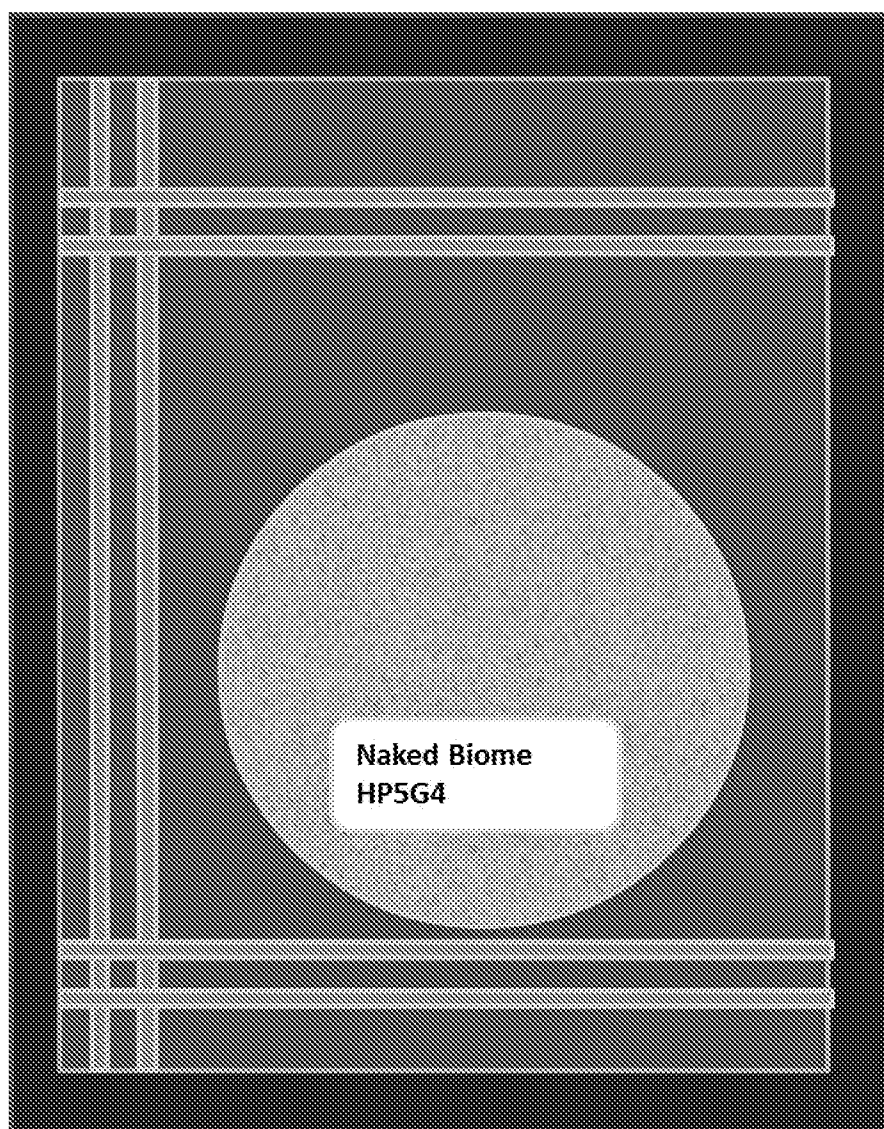


FIG. 8

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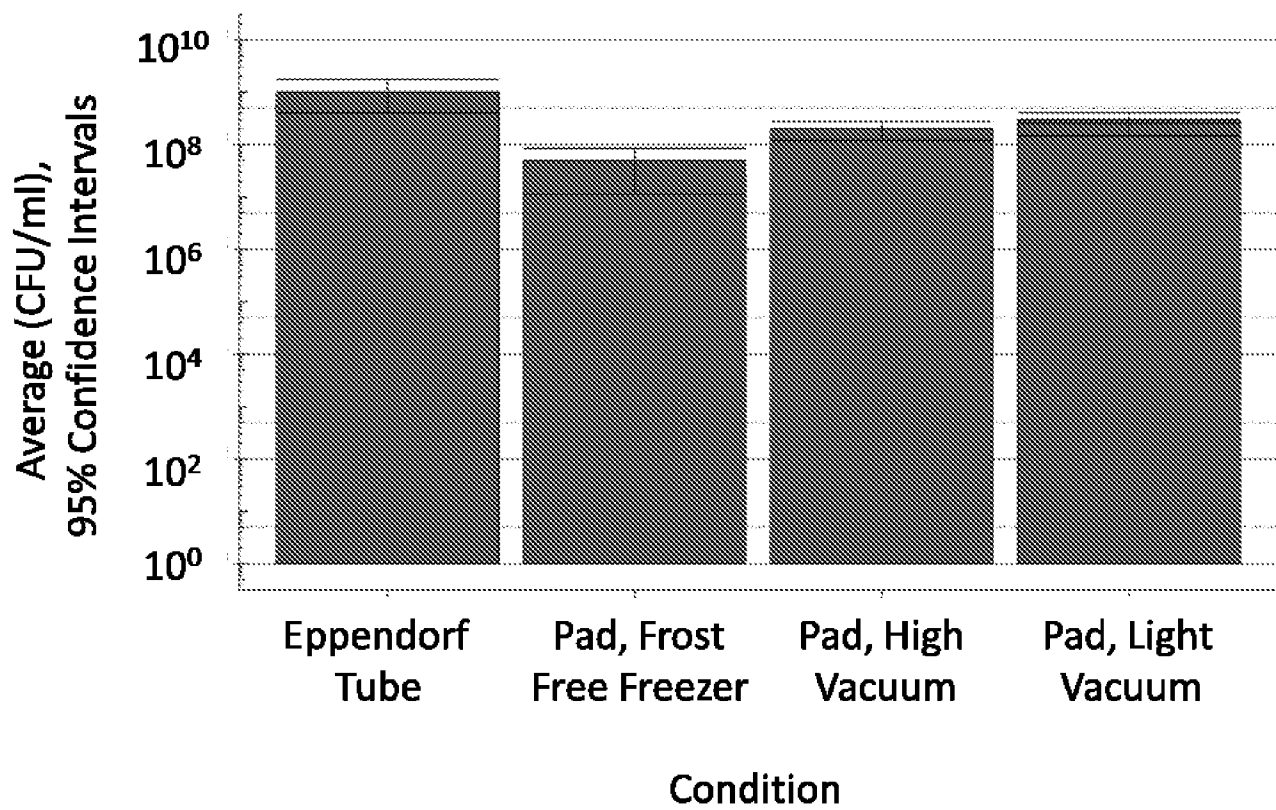
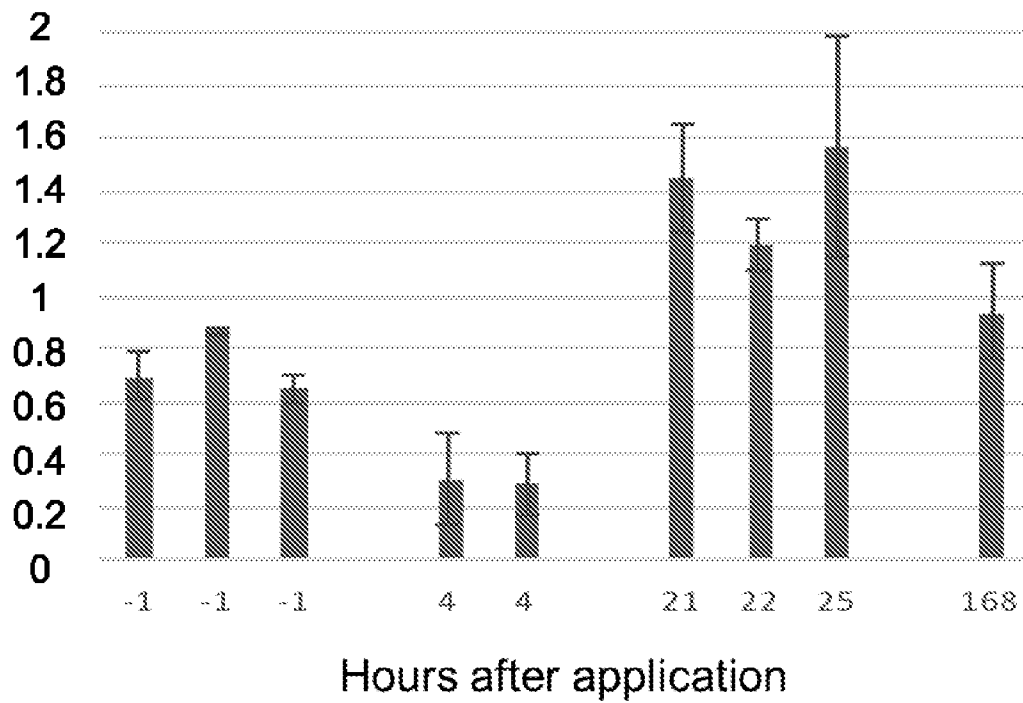


FIG. 9

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*FIG. 10**FIG. 11*

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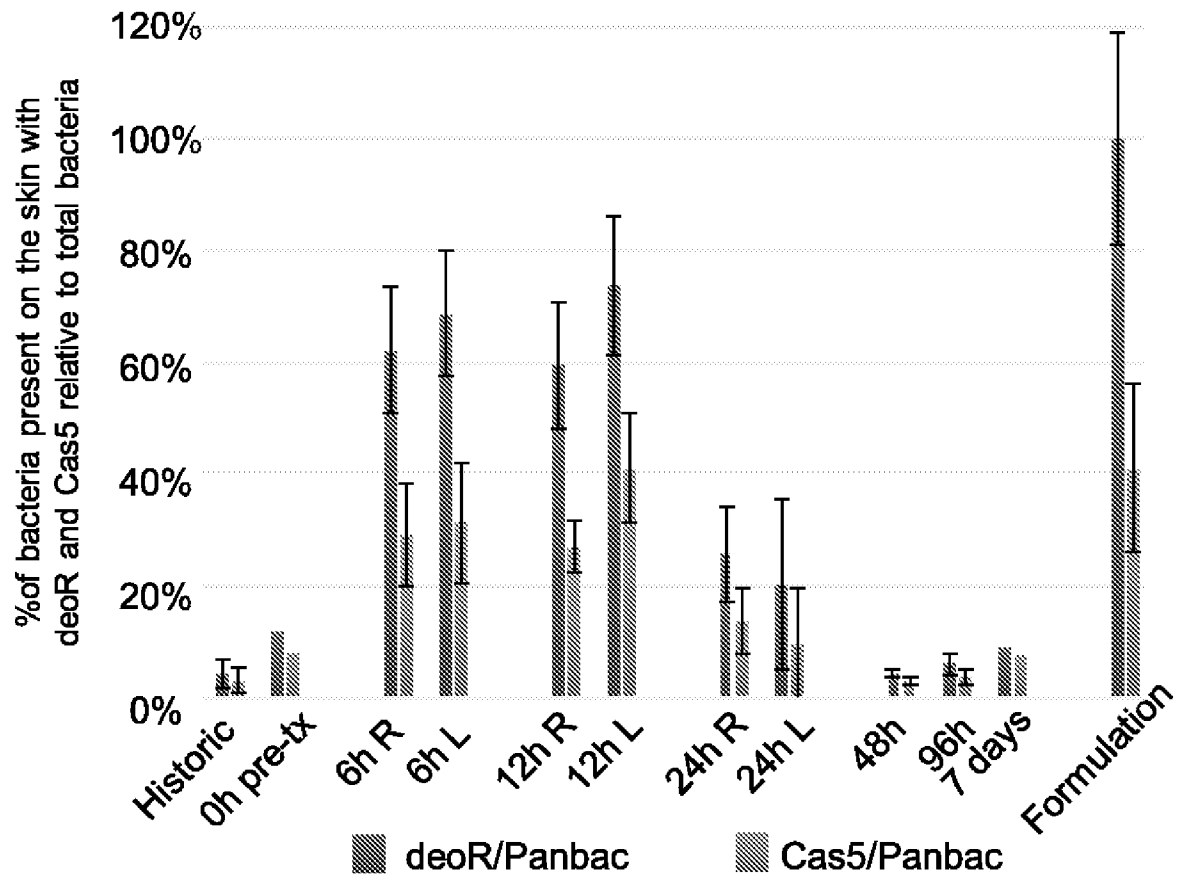


FIG. 12A

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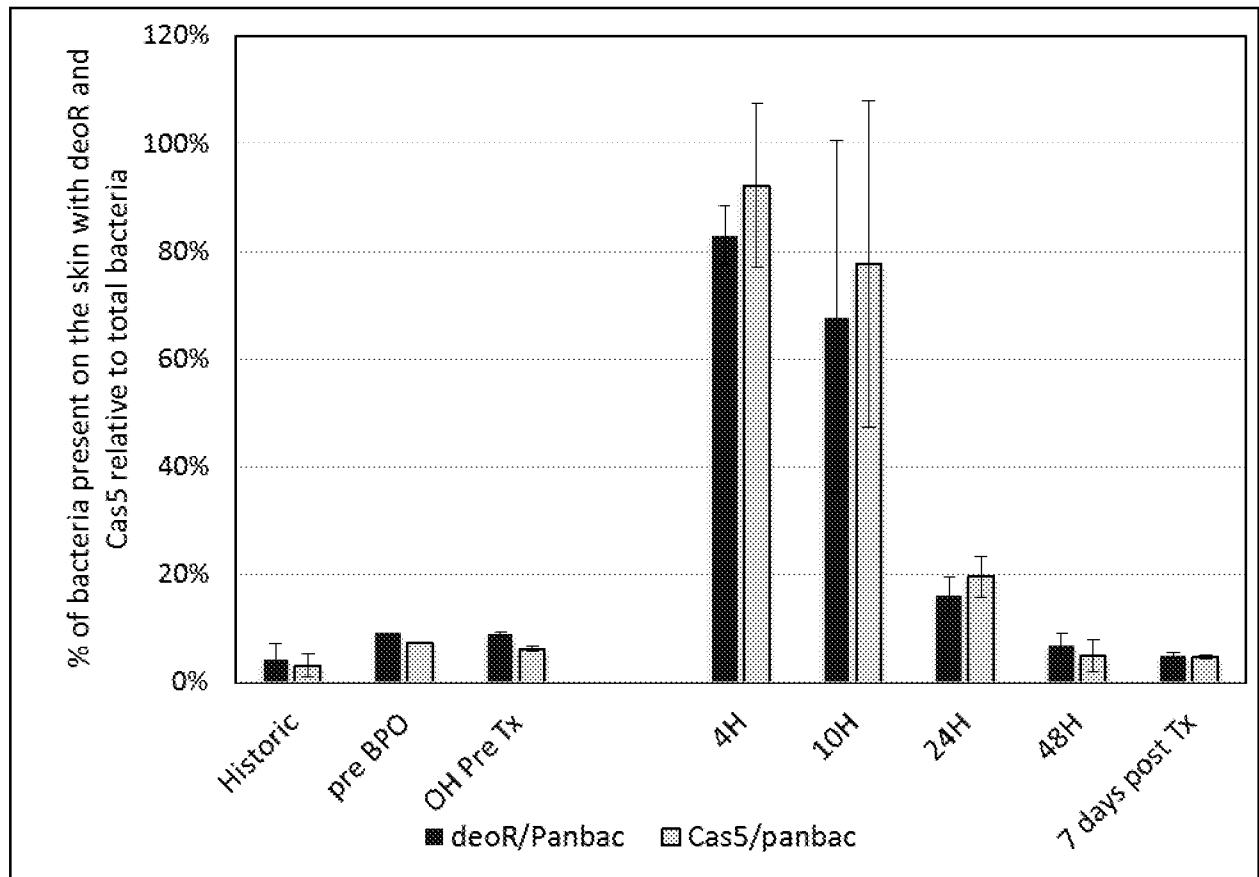


FIG. 12B

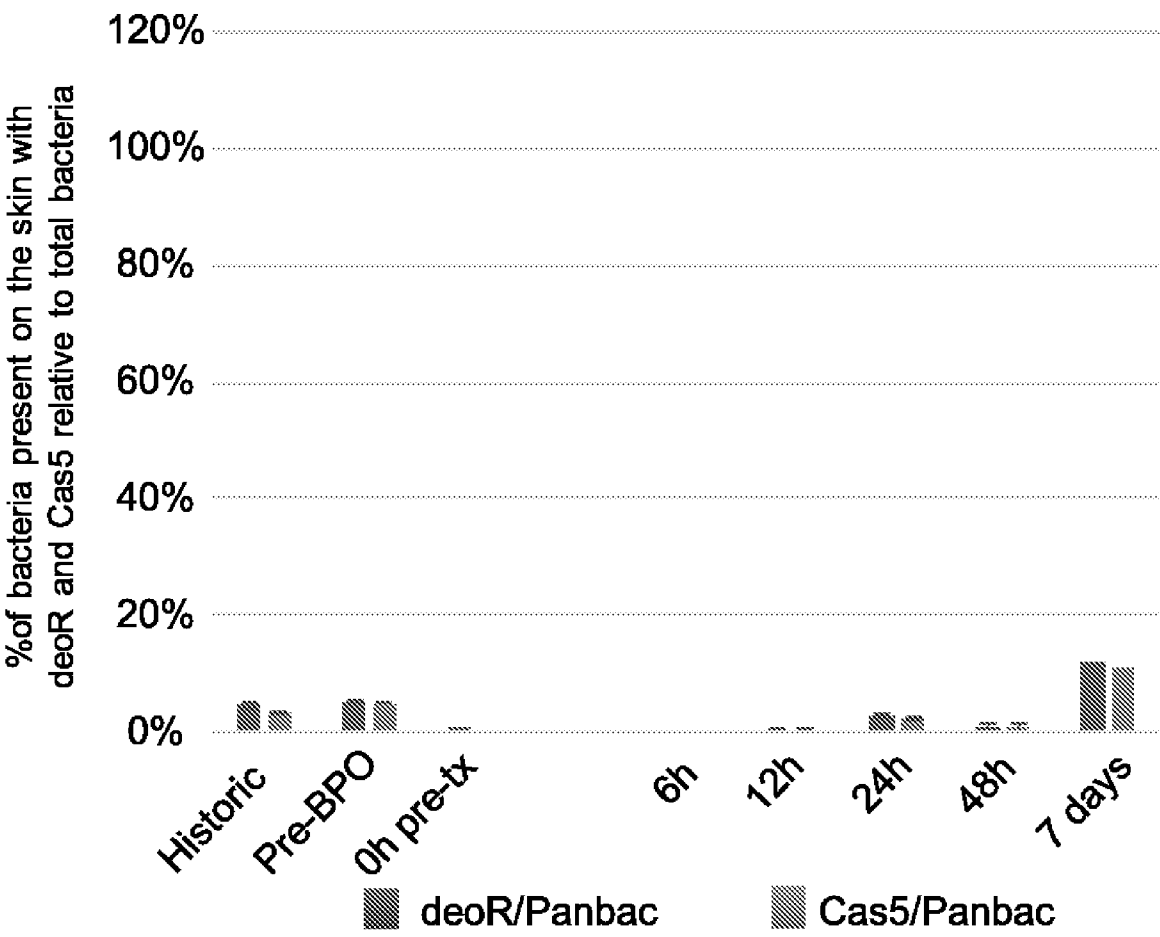


FIG. 12C

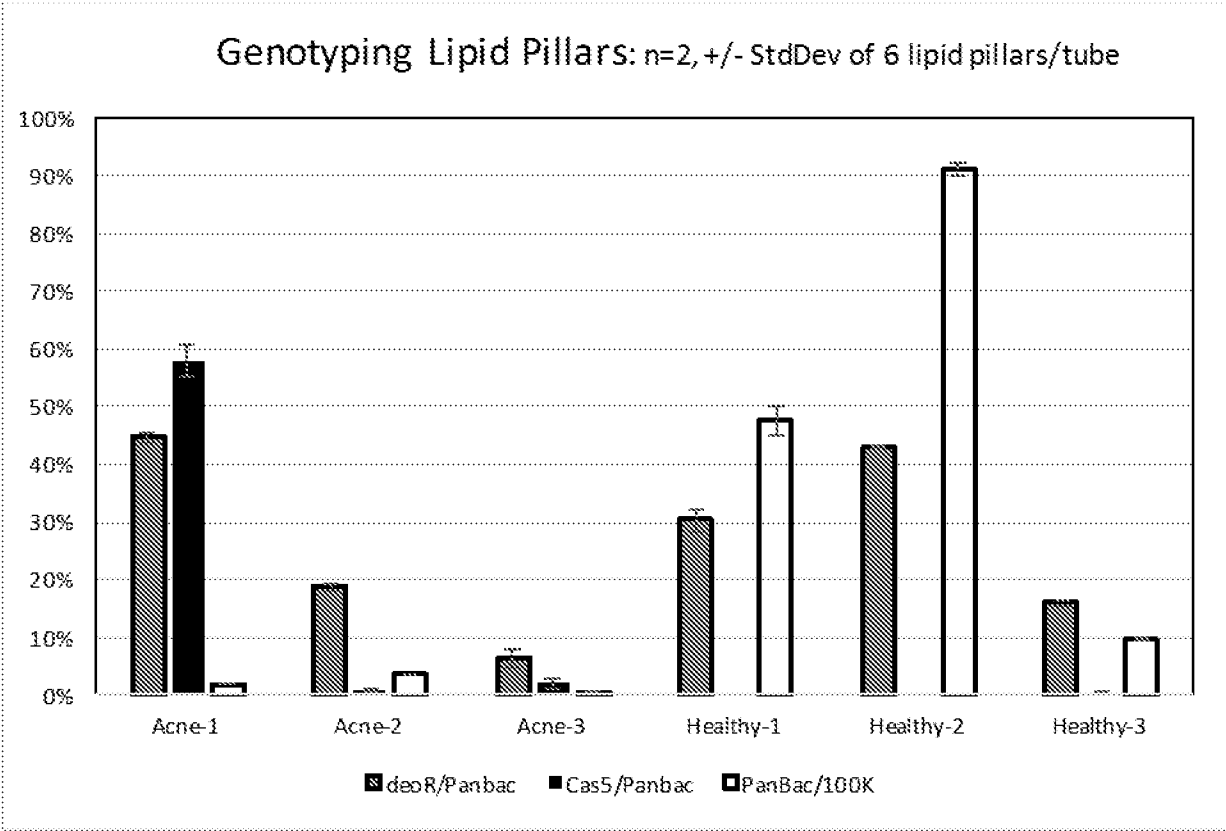


FIG. 13

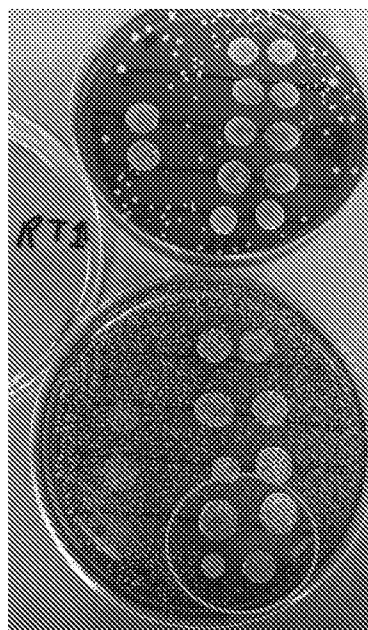


FIG. 14A

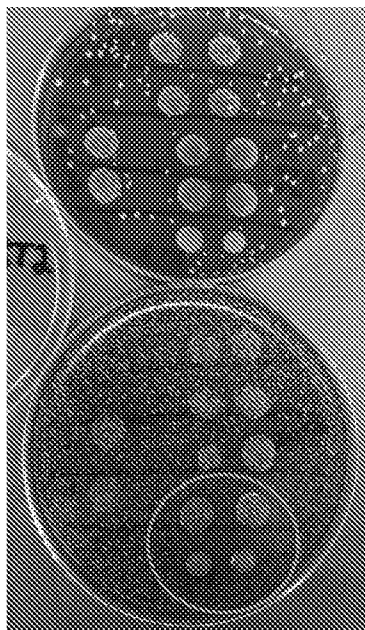


FIG. 14B

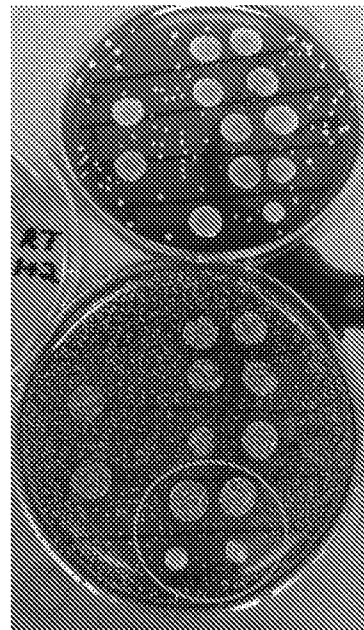


FIG. 14C

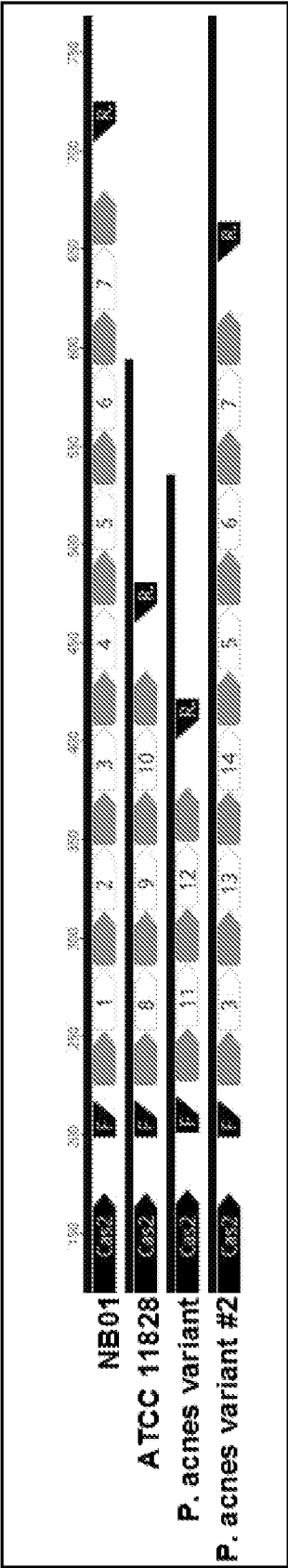


FIG. 15