## SUMMARY

**[0004]** In accordance with the foregoing objectives and others, the present disclosure features compositions, such as nasal sprays, oral sprays, oral rinses, lozenges, and the like, and associated methods of using such compositions for enhancing the ability of the epithelial membranes to filter certain airborne pathogens. In particular, the disclosure provides antimicrobial compositions that prevent and treat respiratory infections and allergies caused by irritants, allergens, bacteria, fungi, and viruses. In preferred implementations, the compositions protect a subject from viral infections, particularly from human rhinovirus and/or human influenza virus.

**[0005]** Disclosed herein is for prophylaxis or treatment of a human subject suffering from, or at risk of suffering from, a respiratory infection. The composition may comprise one or more antimicrobial or antiviral compounds dispersed in a carrier, typically, but not necessarily, a liquid carrier. The liquid carrier is ideally, but not necessarily, of suitable rheology to be sprayed as an aerosol or fine mist. The composition may comprise one or more ingredients selected from the group consisting of an emollient, an occlusive, a humectant, a carrier, an excipient, an emulsifier, and an essential oil. In some embodiments, the composition for prophylaxis or treatment of respiratory infection may comprise active ingredient that combat infection against viruses that bind intercellular adhesion molecule 1 (ICAM-1) and/or viruses that bind sialic acid (or extracellular portions thereof). In one implementation, a composition is provided for prophylaxis or treatment of a human subject suffering from, or at risk of suffering from, infection of the respiratory tract with human rhinovirus (HRV) comprising, in a suitable liquid carrier: (i) soluble ICAM-1 ("sICAM-1") and/or an ICAM-1 inhibitor; (ii) lysozyme; and (iii) lactoferrin (*e.g.*, apolactoferrin). In another implementation, a composition is provided for prophylaxis or treatment of a human subject suffering from, or at risk of suffering from, infection of the respiratory tract with human influenza virus comprising, in a suitable liquid carrier: (i) silalic acid (*e.g.*, sialyllactose); (ii) lysozyme; (iii) lactoferrin; and (iv) optionally, a neuraminidase inhibitor such as, for example, quercetin. In yet another implementation, a composition is provided for prophylaxis or treatment of a human subject suffering from, or at risk of suffering from, infection of the respiratory tract with human rhinovirus (HRV) and human influenza virus comprising, in a suitable liquid carrier: (i) soluble ICAM-1 (sICAM-1) and/or an ICAM-1 inhibitor; (ii) lysozyme; (iii) lactoferrin, (iv) silalic acid and/or a derivate therefore (*e.g.*, sialyllactose); and (v) optionally, a neuraminidase inhibitor. Any of the compositions according to these embodiments, may further comprise one or more of zinc peroxide, copper, and silver. Any of the compositions according to these

least 1 minute, more preferably, at least 5, 10, 15, 20, 25, or 30 minutes following application. The composition should be semi-permeable in order to permit virions and other pathogens to penetrate the film and come into contact with the active ingredients, while possessing a sufficient barrier function to inhibit evaporation of water and volatile solvents in order to maintain the actives in solution.

**[0005a]** According to an aspect there is provided a pharmaceutical composition for preventing or treating respiratory infection comprising:

(i) soluble ICAM-1 or an ICAM-1 inhibitor;

(ii) silalic acid (*e.g.*, sialyllactose);

(iii) lysozyme; and

(iv) lactoferrin; and

a pharmaceutically acceptable carrier.

**[0006]** In some embodiments, the composition may comprise:

(i) about 0.00000001%-10% by weight ICAM-1 (*e.g.*, soluble ICAM-1);

(ii) 0% (or from about 0.00000001%) to about 10% by weight of a neuraminidase inhibitor;

(iii) about 0.00000001% to about 10% by weight of sialic acid (*e.g.*, sialyllactose, 2,3'-sialyllactose, and/or 2,6' sialyllactose);

(iv) about 0.00000001% to about 10% by weight of lysozyme; and

(v) about 0.00000001% to about 10% by weight of lactoferrin (*e.g.*, apolactoferrin);

a pharmaceutically acceptable carrier and, optionally, one or more excipients.

**[0007]** In some embodiments, the composition may comprise:

(i) about 0.000001%-1% (or to about 0.1%) by weight ICAM-1 (*e.g.*, soluble ICAM-1); and/or

(ii) 0% (or from about 0.000001%) to about 1% (or to about 0.1%) by weight of a neuraminidase inhibitor; and/or

(iii) about 0.000001% to about 0.001% (or to about 0.01%) by weight of sialic acid (*e.g.*, sialyllactose, 2,3'-sialyllactose, and/or 2,6' sialyllactose); and/or

(iv) about 0.0001% to about 5% (or to about 1%) by weight of lysozyme; and/or

(v) about 0.00005% to about 5% (or to about 0.5%) by weight of lactoferrin (*e.g.*, apolactoferrin);

a pharmaceutically acceptable carrier and, optionally, one or more excipients.

**[0008]** In some embodiments, the composition may comprise:

(i) about 0.0005%-0.05% by weight ICAM-1 (*e.g.*, soluble ICAM-1); and/or

(ii) 0% (or from about 0.005%) to about 0.05% by weight of a neuraminidase inhibitor; and/or(iii) about 0.000005% to about 0.05% by weight of sialic acid (*e.g.*, sialyllactose, 2,3'-sialyllactose, and/or 2,6' sialyllactose); and/or

(iv) about 0.0025% to about 0.25% by weight of lysozyme; and/or

**[00013]** In some embodiments, a composition for preventing or treating respiratory infection from human influenza virus may comprise:

(i) about 0.000005% to about 0.05% by weight of said sialic acid (*e.g.*, sialyllactose);

(ii) about 0.0001% to about 5% (or to about 1%) by weight of said lysozyme;

(iii) about 0.00005% to about 5% (or to about 0.5%) by weight of said lactoferrin; and

(v) 0% (or from about 0.01%) to about 10% by weight of a neuraminidase inhibitor;

and a pharmaceutically acceptable carrier and, optionally, one or more excipients.

**[00014]** In some embodiments, a composition for preventing or treating respiratory infection from human influenza virus may comprise:

(i) about 0.000005% to about 0.05% by weight of said sialic acid (*e.g.*, sialyllactose); and/or

(ii) about 0.0025% to about 0.25% by weight of said lysozyme; and/or

(iii) about 0.00005% to about 0.1% by weight of said lactoferrin; and/or

(vi) 0% (or from about 0.000001%) to about 1% (or to about 0.1%) by weight of a neuraminidase inhibitor;

and a pharmaceutically acceptable carrier and, optionally, one or more excipients.

**[00015]** In some embodiments, the compositions will be aqueous solutions or suspensions comprising from about 0.5–5000 μg/mL (or from about 1–1000 μg/mL or from about 5–500 μg/mL) of lactoferrin (*e.g.*, apolactoferrin). In some embodiments, the compositions will be aqueous solutions or suspensions comprising from about 0.25–10000 μg/mL (or from about 1–5000 μg/mL or from about 25–2500 μg/mL) of lysozyme. In some embodiments, the compositions will be aqueous solutions or suspensions comprising from about 0.01–500 μg/mL (or from about 0.1–100 μg/mL or from about 0.5–50 μg/mL) of ICAM-1 (*e.g*, soluble ICAM-1). In some embodiments, the compositions will be aqueous solutions or suspensions comprising from about 0.01–2000 μg/mL (or from about 0.1–1000 μg/mL or from about 0.5–750 μg/mL) of sialic acid (*e.g.*, sialyllactose). In some embodiments, the compositions will be aqueous solutions or suspensions comprising from about 0.005–1000 μg/mL (or from about 0.5–500 μg/mL or from about 0.25–375 μg/mL) of 3' sialyllactose and/or from about 0.005–1000 μg/mL (or from about 0.5–500 μg/mL or from about 0.25–375 μg/mL) of 6' sialyllactose.

**[00016]** The pharmaceutical compositions according to the disclosure may be in the form of a nasal spray, nasal drops, oral spray, oral rinse, or lozenge. The carrier of the pharmaceutical composition may be selected to provide residence time of the composition on the nasal and/or oral mucosa of at least 1 minute, or at least 5 minutes, or at least 10 minutes, or at least 15 minutes, or at least 20 minutes, or at least 25 minutes, or at least 30 minutes following application. In some embodiments, the composition for application to the nasal or oral mucosa comprises one or more antiviral and/or antimicrobial agents dispersed in a liquid carrier comprising from about 1-99% (v/v) water or from about 60-90% (v/v) water and from about 10-40% (or from 20-30%) (v/v) of a polyol. In some embodiments, the pharmaceutically acceptable carrier is an aqueous solution comprising from about 5-50% (v/v), or from about 10-40% (v/v), or from about 15-35% (v/v), or from about 20-30% (v/v) 1,3-propanediol. The composition may be capable of being sprayed or ingested onto the mucosa, and is adapted to remain on the mucosa for at least 5 minutes (or at least 10 minutes, or at least 15 minutes, or at least 20 minutes, or at least 25 minutes, or at least 30 minutes) following application without substantially irritating or drying the mucosa.

**[00017]** Methods for prophylaxis and/or treatment of various viral infections are provided. In some embodiments, the method for prophylaxis and/or treatment of human rhinovirus infection, comprises applying any of the composition described herein to the nasal and/or oral mucosa of an individual in need thereof. In some embodiments, the nasal and/or oral mucosa of individuals in need thereof has human rhinovirus in contact therewith.

**[00018]** The disclosure provides a pharmaceutical composition for preventing or treating subjects suffering from or at risk of suffering from a respiratory infection comprising: one or more antimicrobial or antiviral compounds; and a base mixture comprising one or more ingredients selected from the group consisting of a carrier, an emollient, an occlusive, a humectant, a polyol, an emulsifier, a preservative, a thickener or suspending agent, a surfactant, a pH adjuster, an isotonicity agent, and an essential oil. In an embodiment, the antimicrobial or antiviral compound is one or more selected from the group consisting of an antibody such as IgA, IgG, or IgM, a soluble ICAM-1, an ICAM-1 inhibitor, sialic acid, a neuraminidase inhibitor, lactoferrin, a lysozyme, zinc, zinc compounds, silver, silver compounds, copper, copper compounds, and combinations thereof. In an embodiment, the neuraminidase inhibitor is selected from the group consisting of quercetin, oseltamivir, zanamivir, laninamivir, and peramivir. In an embodiment, the ICAM-1 inhibitor is selected from the group consisting of an anti-ICAM-1 antibody, cytokine, CD11a, ezrin (EZR), CD18,

glycyrrhetinic acid, pyrrolidinedithiocarbamate, NFkB activation inhibitor, heterocyclic thiazole, lipoic acid, efalizumab, 4-[(4-Methylphenyl)thio]thieno[2,3-c]pyridine-2-carboxamide, silibinin, stilbenes, (+)-epigalloyl-catechin-gallate [(+)-EGCG], and combinations thereof. In an embodiment, the one or more antimicrobial or antiviral compounds include soluble ICAM-1 and sialic acid (*e.g.*, sialyllactose, 3' sialyllactose, and/or 6' sialyllactose). In an embodiment, the one or more antimicrobial or antiviral compounds include lactoferrin, lysozyme, neuraminidase inhibitor, IgA, IgG, IgM, zinc peroxide ($ZnO_2$), copper, and silver. In an embodiment, the respiratory infection is selected from the group consisting of a rhinovirus infection, an influenza virus infection, a fungal infection, and a bacterial infection. In an embodiment, one or more ingredients are selected from the group consisting of a marshmallow extract, a calendula extract, a citrus peel extract, a honey extracts, a rosemary extracts, a myrhh extract, a *Helichrysum* extract, a arrowroot extract, a neem oil, an argan oil, a vitamin C, a vitamin E, a grapefruit seed extract, and combinations thereof.

**[0018a]** According to another aspect there is provided a composition for preventing or treating respiratory infection comprising:

(i) soluble ICAM-1 or an ICAM-1 inhibitor;

(ii) sialic acid (*e.g.*, siallyllactose);

(iii) lysozyme;

(iv) lactoferrin; and

a pharmaceutically acceptable carrier.

**[0018b]** According to another aspect there is provided a pharmaceutical composition for preventing or treating respiratory infection from human rhinovirus (HRV) comprising:

(i) about 0.00000001% to about 10% by weight soluble ICAM-1;

(ii) about 0.00000001% to about 10% by weight lysozyme; and

(iii) about 0.00000001% to about 10% by weight lactoferrin; and

a pharmaceutically acceptable carrier.

**[0018c]** According to another aspect there is provided a pharmaceutical composition for preventing or treating respiratory infection from human influenza virus comprising:

(i) about 0.0000005% to about 10% by weight of said sialic acid (*e.g.*, sialyllactose);

(ii)about 0.000005% to about 10% by weight of said lysozyme;

(iii) about 0.00000025% to about 10% by weight of said lactoferrin; and

(iv) 0% (or from about 0.01%) to about 10% by weight of a neuraminidase inhibitor; and a pharmaceutically acceptable carrier.

**[0019]** The disclosure provides a method of prophylaxis or treatment of respiratory infection in subjects suffering from or at risk of suffering from respiratory infection comprising: determining a subject is suffering from or at risk of suffering from a respiratory infection; and administering a composition according to the disclosure comprising one or more antimicrobial or antiviral compounds and a base mixture comprising one or more ingredients selected from the group consisting of a carrier, an emollient, an occlusive, a humectant, an emulsifier, and an essential oil. In an embodiment, the one or more antimicrobial or antiviral compounds comprise soluble ICAM-1. In an embodiment, the one or more antimicrobial or antiviral compounds comprise sialic acid or a derivative thereof (*e.g.*, sialyllactose). In one embodiment, the one or more antimicrobial or antiviral compounds comprise lactoferrin (*e.g.*, apolactoferrin). In one embodiment, the one or more antimicrobial or antiviral compounds comprise lysozyme. In one embodiment, the one or more antimicrobial or antiviral compounds comprise a neuraminidase inhibitor. In one embodiment, the one or more antimicrobial or antiviral compounds comprise IgA, IgG, and/or IgM. In one embodiment, the one or more antimicrobial or antiviral compounds comprise zinc peroxide ($ZnO_2$), copper, and/or silver. The compositions may be administered by any suitable route, including orally, topically, nasally, and combinations thereof. In an embodiment, the composition is administered to nasal membranes. In an embodiment, the composition is administered using a device selected from the group consisting of an atomizer, an inhaler, a nebulizer, a spray bottle, and a spray pump. The composition may include a propellant or may be free of propellants.

**[0019a]** According to another aspect there is provided use of the composition described herein in the preparation of a medicament for prophylaxis and/or treatment of human rhinovirus infection.

**[0019b]** According to another aspect there is provided use of the composition described herein in the preparation of a medicament for prophylaxis and/or treatment of human influenza virus infection.

**[0019c]** According to another aspect there is provided a composition for application to the nasal or oral mucosa, comprising one or more antiviral and/or antimicrobial agents dispersed in a liquid carrier comprising from about 60-90% (v/v) water and from about 10-40% (or from 20-30%) (v/v) of a polyol, wherein said composition is capable of being sprayed onto the mucosa, and is adapted to remain on the mucosa for at least 5 minutes (or at least 10 minutes, or at least 15 minutes, or at least 20 minutes, or at least 25 minutes, or at least 30 minutes) following application without substantially irritating or drying the mucosa.

9. The composition according to any one of claims 1-8, wherein the composition is formulated as a microsphere.

10. The composition according to any one of claims 1-9, wherein the composition contains soluble ICAM-1.

11. The composition according to any one of claims 1-10, comprising:

(i) about 0.00000001% to about 10% by weight soluble ICAM-1;

(ii) from 0% (or from about 0.00000001%) to about 10% by weight of a neuraminidase inhibitor;

(iii) about 0.00000001% to about 10% by weight of said sialic acid or sialyllactose;

(iv) about 0.0000001% to about 10% by weight of said lysozyme; and

(v) about 0.00000001% to about 10% by weight of said lactoferrin.

12. A composition for use in preventing or treating respiratory infection comprising:

(i) soluble ICAM-1 or an ICAM-1 inhibitor;
(ii) sialic acid (*e.g.*, siallyllactose);
(iii) lysozyme;
(iv) lactoferrin; and

a pharmaceutically acceptable carrier.

13. The composition for use according to claim 12, wherein said respiratory infection is due to human rhinovirus and/or human influenza virus.

14. The composition for use according to any one of claims 12-13, wherein said composition is in the form of a nasal spray, nasal drops, oral spray, oral rinse, or lozenge.

15. The composition for use according to any one of claims 12-14, wherein said composition further comprises one or more of zinc peroxide, copper, and silver.

16. The composition for use according to any one of claims 12-15, wherein said composition further comprises one or more of IgA, IgG, and IgM.

17. The composition for use according to any one of claims 12-16, wherein the neuraminidase inhibitor is selected from the group consisting of quercetin, oseltamivir, zanamivir, laninamivir, and peramivir.

18. The composition for use according to any one of claims 12-17, wherein said composition comprises and ICAM-1 inhibitor, and wherein said ICAM-1 inhibitor is selected from the group consisting of an anti-ICAM-1 antibody, cytokine, CD11a, ezrin (EZR), CD18, glycyrrhetinic acid, pyrrolidiniedithiocarbamate, NFkB activation inhibitor, heteryclic thiazole, lipoic acid, efalizumab, 4-[4-methylphenyl)thio]thieno92,3-c]pyridine-2-carboxamide, silibinin, stilbenes, and (+)-epigalloyl-catechin-gallate [(+)-EGCG].

19. The composition for use according to any one of claims 12-18, further comprising one or more ingredients selected from the group consisting of marshmallow extract, calendula extract, citrus peel extract, honey extract, rosemary extract, myrrh extract, Helichrysum extract, arrowroot extract, neem oil, vitamin C, vitamin E, and grapefruit seed extract.

20. The composition for use according to any one of claims 12-19, wherein said composition comprises:

(i) about 0.00000001% to about 10% by weight of said ICAM-1;

(ii) 0% (or from about 0.01%) to about 10% by weight of a neuraminidase inhibitor;

(iii) about 0.00000001% to about 10% by weight of said sialic acid (*e.g.*, sialyllactose);

(iv) about 0.00000001% to about 10% by weight of said lysozyme; and

(v) about 0.00000001% to about 10% by weight of said lactoferrin.

21. A pharmaceutical composition for preventing or treating respiratory infection from human rhinovirus (HRV) comprising:

(i) about 0.00000001% to about 10% by weight soluble ICAM-1;

(ii) about 0.00000001% to about 10% by weight lysozyme; and

(iii) about 0.00000001% to about 10% by weight lactoferrin; and

a pharmaceutically acceptable carrier.

22. The pharmaceutical composition according to claim 21, wherein said carrier is adapted to provide residence time of said composition on the nasal and/or oral mucosa of at least 1 minute, or at least 5 minutes, or at least 10 minutes, or at least 15 minutes, or at least 20 minutes, or at least 25 minutes, or at least 30 minutes.

23. The pharmaceutical composition according to any one of claims 21-22, wherein said pharmaceutically acceptable carrier is an aqueous solution comprising from about 5-50% (v/v), or from about 10-40% (v/v), or from about 15-35% (v/v), or from about 20-30% (v/v) 1,3-propanediol.

24. Use of the composition according to any of claims 21-23 in the preparation of a medicament for prophylaxis and/or treatment of human rhinovirus infection in an individual in need thereof.

25. The use according to claim 24, wherein a nasal and/or oral mucosa of said individual in need thereof has human rhinovirus in contact therewith.

26. A pharmaceutical composition for preventing or treating respiratory infection from human influenza virus comprising:

(i) about 0.0000005% to about 10% by weight of said sialic acid (*e.g.*, sialyllactose);

(ii) about 0.000005% to about 10% by weight of said lysozyme;

(iii) about 0.00000025% to about 10% by weight of said lactoferrin; and

(iv) 0% (or from about 0.01%) to about 10% by weight of a neuraminidase inhibitor; and

a pharmaceutically acceptable carrier.

27. The pharmaceutical composition according to claim 26, wherein said carrier is adapted to provide residence time of said composition on the nasal and/or oral mucosa of at least 1 minute, or at least 5 minutes, or at least 10 minutes, or at least 15 minutes, or at least 20 minutes, or at least 25 minutes, or at least 30 minutes.

28. The pharmaceutical composition according to one of claims 26-27, wherein said pharmaceutically acceptable carrier is an aqueous solution comprising from about 5-50% (v/v), or from about 10-40% (v/v), or from about 15-35% (v/v), or from about 20-30% (v/v) 1,3-propanediol.

29. Use of the composition according to any of claims 25-27 in the preparation of a medicament for prophylaxis and/or treatment of human influenza virus infection in an individual in need thereof.

30. The use according to claim 29, wherein a nasal and/or oral mucosa of said individual in need thereof has human influenza virus in contact therewith.

31. A composition for application to the nasal or oral mucosa, comprising one or more antiviral and/or antimicrobial agents dispersed in a liquid carrier comprising from about 60-90% (v/v) water and from about 10-40% (or from 20-30%) (v/v) of a polyol, wherein said composition is capable of being sprayed onto the mucosa, and is adapted to remain on the mucosa for at least 5 minutes (or at least 10 minutes, or at least 15 minutes, or at least 20

minutes, or at least 25 minutes, or at least 30 minutes) following application without substantially irritating or drying the mucosa.

32. The composition according to claim 31, wherein said polyol comprises 1-3 propanediol.