THERAPEUTIC COMPOSITIONS AND METHODS INVOLVING mRNA TRANSFECTION

GOVERNMENT FUNDING

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CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Provisional Patent Application Serial No. 61/751,504, filed January 11, 2013, which is incorporated herein by reference.

SUMMARY

This disclosure describes, in one embodiment, a method of suppressing cell proliferation. Generally the method includes introducing into an epithelial cell an mRNA encoding a polypeptide involved in suppressing cell proliferation and permitting the cell to express the polypeptide in an amount effective to decrease the likelihood that the cell proliferates in an anchorage-independent environment. In some embodiments, the polypeptide can include calprotectin (S100A8 complexed with S100A9; S100A8/A9), S100A8, or S100A9.

Provided is a method comprising: introducing into a mucosal squamous epithelial cell a composition comprising (i) an mRNA that comprises a synthetic 5' cap and that encodes a polypeptide involved in innate immunity selected from cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme and (ii) a pharmaceutically acceptable *in vivo* delivery vehicle formulated for topical application; and permitting the cell to express the polypeptide in an amount effective to decrease the likelihood that the cell is infected by one or more pathogens.

In one aspect, there is provided the use of an mRNA encoding a polypeptide involved in innate immunity in the manufacture of a medicament for decreasing the likelihood of a squamous mucosal epithelial cell being infected by a pathogen; wherein the medicament is to be introduced into the cell in a pharmaceutically acceptable *in vivo* delivery vehicle formulated for topical application, wherein the cell is permitted to express the polypeptide in an amount effective to decrease the likelihood that the cell is infected by the pathogen, wherein the polypeptide comprises cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme, and wherein the mRNA comprises a synthetic 5' cap.

In another embodiment, this disclosure describes a method of inhibiting infection of a cell. Generally, the method includes introducing into a cell an mRNA encoding a polypeptide involved in innate immunity and permitting the cell to express the polypeptide in an amount effective to decrease the likelihood that the cell is infected by a pathogen. In some embodiments, the polypeptide can include cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme.

In some embodiments summarized above, the mRNA can include a stabilizing moiety such as, for example, a 5' cap or a 3' extension. In some embodiments, the cell can be a mucosal epithelial cell.

What is claimed is:

1. A composition comprising:
   an mRNA that comprises a synthetic 5' cap and that encodes a polypeptide involved in innate immunity selected from cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme; and
   a pharmaceutically acceptable *in vivo* delivery vehicle formulated for topical application.

2. The composition of claim 1 wherein the 5' cap is anti-reverse cap analogue (ARCA).

3. The composition of claim 1 wherein the mRNA further comprises a 3' extension stabilizing moiety.

4. Use of an mRNA encoding a polypeptide involved in innate immunity in the manufacture of a medicament for decreasing the likelihood of a squamous mucosal epithelial cell being infected by a pathogen; wherein the medicament is to be introduced into the cell in a pharmaceutically acceptable *in vivo* delivery vehicle formulated for topical application, wherein the cell is permitted to express the polypeptide in an amount effective to decrease the likelihood that the cell is infected by the pathogen, wherein the polypeptide comprises cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme, and wherein the mRNA comprises a synthetic 5' cap.

5. The use of claim 4 wherein the 5' cap is anti-reverse cap analogue (ARCA).

6. The use of claim 4 wherein the mRNA further comprises a 3' extension stabilizing moiety.

7. The use of any one of claims 4-6 wherein the cell is further permitted to be exposed to the pathogen.

8. The use of any one of claims 4-7 wherein the pathogen comprises a bacterium.

9. The use of claim 8 wherein the bacterium comprises *Capnocytophaga sputigena*, *Escherichia coli*, a *Staphylococcus* spp., a *Streptococcus* spp., *Listeria monocytogenes*, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponeam denticola*, *Pseudomonas aeruginosa*, a *Chlamydia* spp., a *Neisseria* spp., a *Gardnerella* spp., or a *Trichomonas* spp.

10. The use of any one of claims 4-7 wherein the pathogen comprises a fungus.

11. The use of claim 10 wherein the fungus comprises fungi *Candida albicans*, *Acinetobacter baumanni*, or an *Aspergillus* spp.

12. The use of any one of claims 4-11 wherein the cell is a cell of a subject having or at risk of having a condition caused by infection by the pathogen.

13. The use of any preceding claim wherein the cell is further washed to remove mucosal fluid from the cell prior to introducing the mRNA into the cell.

14. The use of claim 13, wherein the mucosal fluid comprises saliva.