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

In one aspect there is provided the use of an mRNA encoding a polypeptide involved in suppressing cell proliferation in the manufacture of a medicament for decreasing the likelihood of an epithelial cell proliferating in an anchorage-independent environment, wherein the medicament is to be introduced into the epithelial cell, wherein the cell is permitted to express the polypeptide in an amount effective to decrease the likelihood that the cell proliferates in the anchorage-independent environment.

In one aspect, there is provided an *in vitro* method comprising: introducing into an epithelial cell in a sample 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.

This disclosure describes, in one ~~aspect~~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.

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 cell being infected by a pathogen; wherein the medicament is to be introduced into the cell, 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.

In one aspect, there is provided an *in vitro* method comprising: introducing into a cell in a sample 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 another ~~aspect~~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 of either aspect 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.

In another ~~aspect~~embodiment, this disclosure describes a composition that generally includes an mRNA that encodes a polypeptide and an *in vivo* delivery vehicle.

In one aspect, there is provided a composition comprising: an mRNA that encodes a polypeptide that suppresses cell proliferation in an epithelial cell; and an in vivo delivery vehicle.

In one aspect, there is provided a composition comprising: an mRNA that encodes a polypeptide involved in innate immunity; and an in vivo delivery vehicle.

What is claimed is:

1. An *in vitro* method comprising:

introducing into an epithelial cell in a sample 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.

2. The method of claim 1 wherein the polypeptide comprises calprotectin, S100A8, or S100A9.

3. An *in vitro* method comprising:

introducing into a cell in a sample 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.

4. The method of claim 3 wherein the polypeptide comprises cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme.

5. The method of any preceding claim wherein the mRNA comprises a stabilizing moiety.

6. The method of claim 5 wherein the stabilizing moiety comprises a 5' cap.

7. The method of claim 5 wherein the stabilizing moiety comprises a 3' extension.

8. The method of any preceding claim wherein the cell is a mucosal epithelial cell.

9. The method of any one of claims 3-8 further comprising permitting the cell to be exposed to the pathogen.

10. The method of any one of claims 3-9 wherein the pathogen comprises a bacterium.

26. Use of an mRNA encoding a polypeptide involved in suppressing cell proliferation in the manufacture of a medicament for decreasing the likelihood of an epithelial cell proliferating in an anchorage-independent environment, wherein the medicament is to be introduced into the epithelial cell, wherein the cell is permitted to express the polypeptide in an amount effective to decrease the likelihood that the cell proliferates in the anchorage-independent environment.

27. The use of claim 26 wherein the polypeptide comprises calprotectin, S100A8, or S100A9.

28. Use of an mRNA encoding a polypeptide involved in innate immunity in the manufacture of a medicament for decreasing the likelihood of a cell being infected by a pathogen; wherein the medicament is to be introduced into the cell, 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.

29. The use of claim 28 wherein the polypeptide comprises cathelicin antimicrobial protein (CAMP), calprotectin, S100A8, S100A9, a β-defensin, S100A7, secretory leukocyte inhibitor, lipocalin 2, or lysozyme.

30. The use of any preceding claim wherein the mRNA comprises a stabilizing moiety.

31. The use of claim 30 wherein the stabilizing moiety comprises a 5' cap.

32. The use of claim 30 wherein the stabilizing moiety comprises a 3' extension.

33. The use of any preceding claim wherein the cell is a mucosal epithelial cell.

34. The use of any one of claims 28-33 wherein the cell is further permitted to be exposed to the pathogen.

35. The use of any one of claims 28-34 wherein the pathogen comprises a bacterium.

36. The use of claim 35 wherein the bacterium comprises *Capnocytophaga sputigena*, *Escherichia coli*, a *Staphylococcus* spp., a *Streptococcus* spp., *Listeria monocytogenes*, *Salmonella typhimurium*, *Borrelia burgdorferi*, *Porphyromonas gingivalis*, *Tannerella forsythia*,

Treponema denticola, *Pseudomonas aeruginosa*, a *Chlamydia* spp., a *Neisseria* spp., a *Gardnerella* spp., or a *Trichomonas* spp.

37. The use of any one of claims 28-34 wherein the pathogen comprises a fungus.

38. The use of claim 37 wherein the fungus comprises fungi *Candida albicans*, *Acinetobacter baumannii*, or an *Aspergillus* spp.

39. The use of any one of claims 28-38 wherein the cell is a cell of a subject having or at risk of having a condition caused by infection by the pathogen.

40. The use of claim 39 wherein the condition comprises a carcinoma.

41. 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.

42. The use of claim 41 wherein the mucosal fluid comprises saliva.