

## COMPOSITIONS AND METHODS FOR STIMULATING HAIR GROWTH

### REFERENCE TO RELATED APPLICATION

[0001] The application claims benefit of US Provisional Serial No. 63/522,012 filed June 20, 2023, the contents of which are incorporated by reference.

### FIELD OF THE INVENTION

[0002] The present invention relates to compositions comprising a peptide containing a CD44 binding site and/or a calcium binding site and methods for stimulating hair growth by using the compositions.

### BACKGROUND

[0003] Hair loss often has a negative social and psychological impact on the individual suffering therefrom. Many factors are believed to contribute to hair loss, including genetics, hormones, environmental exposure, medications, psychological stress, and nutrition. One known treatment is hair transplantation, which requires anesthesia, is costly, time-consuming, and sometimes painful. Other approaches include massage and acupuncture, but these have not been shown to be effective. Hormones and other drugs have been used to treat hair loss. However, these treatments frequently cause undesirable side effects such as hair growth in unwanted areas. Accordingly, there is a need for an effective therapy for stimulating hair growth.

### BRIEF SUMMARY

[0004] The disclosure provides, in a first aspect, a peptide for stimulating hair growth, comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. In some embodiments, the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. In some embodiments, the peptide comprises a CD44 binding site, e.g., an amino acid sequence of KSKEEDKHLKFRISHEL (SEQ ID NO: 97) or a variant thereof. In some embodiments, the peptide comprises a calcium binding site, e.g., an amino acid sequence of DWDSRGKDSYETS (SEQ ID NO: 98) or a variant thereof. In some embodiments, the peptide comprises a CD44 binding site and a calcium binding site. In some embodiments, the peptide has

a length of no more than 295 amino acids, e.g., no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.

**[0005]** In another aspect, the disclosure provides a composition for stimulating hair growth, comprising a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. In some embodiments, the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. In some embodiments, the peptide comprises a CD44 binding site, e.g., an amino acid sequence of KSKEEDKHLKFRISHEL (SEQ ID NO: 97) or a variant thereof. In some embodiments, the peptide comprises a calcium binding site, e.g., an amino acid sequence of DWDSRGKDSYETS (SEQ ID NO: 98) or a variant thereof. In some embodiments, the peptide comprises a CD44 binding site and a calcium binding site. In some embodiments, the peptide has a length of no more than 295 amino acids, e.g., no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.

**[0006]** In some embodiments, the composition comprises about 0.01 wt % or greater of the peptide. In some embodiments, the composition comprises, about 0.025 wt % or greater, e.g., about 0.05 wt % or greater, about 0.075 wt % or greater, about 0.1 wt % or greater, about 0.25 wt % or greater, about 0.5 wt % or greater, about 0.75 wt % or greater, about 1 wt % or greater, about 2.5

wt % or greater, about 5 wt % or greater, about 7.5 wt % or greater, or about 10 wt % or greater, of the peptide.

**[0007]** In some embodiments, the composition further comprises one or more additional ligands that binds to CD44. In some embodiments, the one or more additional ligands that binds to CD44 are selected from the group consisting of serglycin, chondroitin or a salt thereof (e.g., chondroitin sulfate), fibrin, collagen, fibronectin, insulin-like growth factor-binding protein (IGFBP) (e.g., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP4, IGFBP-5, and IGFBP-6), green fluorescent protein (GFP), and any combinations thereof.

**[0008]** In some embodiments, the composition further comprises hyaluronic acid. The hyaluronic acid may have an average molecular weight in a range of about 20 kDa to 1350 kDa, about 4 kDa to about 10 kDa, about 10 kDa to about 100 kDa, about 15 kDa to about 50 kDa, or about 75 kDa to about 350 kDa. The hyaluronic acid may be cross linked. In some embodiments, the hyaluronic acid has a cross-link density of about 20% or greater. In some embodiments, the hyaluronic acid is present in a concentration of 25 mcg/mL or greater, about 25 mcg/mL to about 250 mcg/mL, about 25 mcg/mL to about 100 mcg/mL, about 100 mcg/mL to about 250 mcg/mL, about 1 mcg/mL to about 250 mcg/mL, or about 100 ug/mL or less. In some embodiments, the hyaluronic acid is present in a concentration of about 100 mcg/mL to about 950 mcg/mL, about 200 mcg/mL to about 400 mcg/mL, about 400 mcg/mL to about 600 mcg/mL, about 600 mcg/mL to about 800 mcg/mL, or about 800 mcg/mL to about 950 mcg/mL.

**[0001]** In some embodiments, the composition further comprises a hyaluronidase inhibitor. In some embodiment, the hyaluronidase inhibitor is selected from high molecular mass poly (styrene-4-sulfonate) (PSS), gossypol, sodium aurothiomalate, fenoprofen, glycyrrhizin acid, fatty acids, plant-derived compounds, heparin, and O-sulfated hyaluronic acid (sHA), or any combinations thereof.

**[0009]** In another aspect, the disclosure further provides a method of stimulating hair growth in a skin of a patient in need thereof, includes administering an effective amount of the composition as disclosed herein to the skin of the patient. In some embodiments, administering includes applying the composition to a surface of the skin, while in other embodiments, administering includes injecting the composition into a dermal layer of the skin. The composition may be injected about 400 microns to about 2 mm deep into the skin. In some embodiments, the composition is administered in a plurality of injections in an amount of about 400 injections/cm<sup>2</sup> skin to about 650

injections/cm<sup>2</sup> skin. In some embodiments, the needle is a microneedle. In some embodiments, the composition may be encased in a liposome, for example a liposome comprising hydrogenated phospholipids.

[0010] In some embodiments, the method of stimulating hair growth further comprises applying iontophoresis to the skin. In some embodiments, the method of stimulating hair growth further comprises applying electroporation to the skin. In some embodiments, the method of stimulating hair growth further comprises applying laser ablation to the skin. In some embodiments, the method of stimulating hair growth further comprises applying radiofrequency thermal ablation to the skin. In some embodiments, the method of stimulating hair growth further comprises applying a microneedle device to the skin.

[0011] Further areas of applicability of the present disclosure will become apparent from the detailed description provided hereinafter. It should be understood that the detailed description and specific examples, while indicating the preferred embodiment of the disclosure, are intended for purposes of illustration only and are not intended to limit the scope of the disclosure.

#### DETAILED DESCRIPTION

[0012] The following description of the preferred embodiment(s) is merely exemplary in nature and is in no way intended to limit the disclosure, its application, or uses.

[0013] As used throughout, ranges are used as shorthand for describing each and every value that is within the range. Any value within the range can be selected as the terminus of the range. In addition, all references cited herein are hereby incorporated by referenced in their entireties. In the event of a conflict in a definition in the present disclosure and that of a cited reference, the present disclosure controls.

[0014] Unless otherwise specified, all percentages and amounts expressed herein and elsewhere in the specification should be understood to refer to percentages by weight. The amounts given are based on the active weight of the material.

[0015] The present invention provides, in an aspect, a peptide (Peptide 1.0) for stimulating hair growth, comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. It is understood and conventional that the term polypeptide can be used to describe the sequences detailed by SEQ ID NOs 1 to 98 and such terms may be used interchangeably.

[0016] For example, the invention includes:

- 1.1. Peptide 1.0, wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 96.
- 1.2. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 20, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 20.
- 1.3. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 21 to 39, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 21 to 39.
- 1.4. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 40 to 60, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 40 to 60.
- 1.5. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 61 to 63, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 61 to 63.
- 1.6. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 64 to 71, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 64 to 71.
- 1.7. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 72 to 79, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 72 to 79.
- 1.8. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected

from the group consisting of SEQ ID NOs: 80 to 87, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 80 to 87.

1.9. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 88 to 95, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 88 to 95.

1.10. Peptide 1.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 96, optionally wherein the peptide comprises SEQ ID NO: 96.

1.11. Any of the preceding peptides, wherein the peptide comprises a CD44 binding site.

1.12. Peptide 1.11, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof.

1.13. Peptide 1.12, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97.

1.14. Any of the preceding peptides, wherein the peptide comprises a calcium binding site.

1.15. Peptide 1.14, wherein the peptide comprises SEQ ID NO: 98 or a variant thereof.

1.16. Peptide 1.15, wherein the variant of SEQ ID NO: 98 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.

1.17. Any of the preceding peptides, wherein the peptide comprises a CD4 binding site and a calcium binding site.

1.18. Peptide 1.17, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof and SEQ ID NO: 98 or a variant thereof.

1.19. Peptide 1.18, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97 and the variant of SEQ ID NO: 98 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.

1.20. Any of the preceding peptides, wherein the peptide has a length of no more than 295 amino acids.

1.21. Any of the preceding peptides, wherein the peptide has a length of no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.

[0017] The present invention provides, in another aspect, a composition (Composition 2.0) for stimulating hair growth, comprising a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. For example, the invention includes:

2.1. Composition 2.0, wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 96.

2.2. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 20, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 20.

2.3. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 21 to 39, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 21 to 39.

2.4. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 40 to 60, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 40 to 60.

2.5. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 61 to 63, optionally wherein the peptide comprises

a sequence selected from the group consisting of SEQ ID NOs: 61 to 63.

2.6. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 64 to 71, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 64 to 71.

2.7. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 72 to 79, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 72 to 79.

2.8. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 80 to 87, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 80 to 87.

2.9. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 88 to 95, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 88 to 95.

2.10. Composition 2.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 96, optionally wherein the peptide comprises SEQ ID NO: 96.

2.11. Any of the preceding compositions, wherein the peptide comprises a CD44 binding site.

2.12. Composition 2.11, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof.

2.13. Composition 2.12, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97.

2.14. Any of the preceding compositions, wherein the peptide comprises a calcium binding site.

2.15. Composition 2.14, wherein the peptide comprises SEQ ID NO: 98 or a variant thereof.

2.16. Composition 2.15, wherein the variant of SEQ ID NO: 98 has at least 80%, at least

85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.

2.17. Any of the preceding compositions, wherein the peptide comprises a CD4 binding site and a calcium binding site.

2.18. Composition 2.17, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof and SEQ ID NO: 98 or a variant thereof.

2.19. Composition 2.18, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97 and the variant of SEQ ID NO: 98 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.

2.20. Any of the preceding compositions, wherein the peptide has a length of no more than 295 amino acids.

2.21. Composition 2.20, wherein the peptide has a length of no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.

2.22. Any of the preceding compositions, wherein the composition comprises about 0.01 wt % or greater of the peptide, optionally wherein the composition comprises, about 0.025 wt % or greater, e.g., about 0.05 wt % or greater, about 0.075 wt % or greater, about 0.1 wt % or greater, about 0.25 wt % or greater, about 0.5 wt % or greater, about 0.75 wt % or greater, about 1 wt % or greater, about 2.5 wt % or greater, about 5 wt % or greater, about 7.5 wt % or greater, or about 10 wt % or greater, of the peptide.

2.23. Any of the preceding compositions, wherein the composition comprises 0.01-20 wt% of the peptide, optionally wherein the composition comprises 0.025-20 wt%, 0.05-20 wt%, 0.75-20 wt%, 0.1-20 wt%, 0.25-20 wt%, 0.5-20 wt%, 0.75-20 wt%, 1-20 wt%, 2.5-20 wt%,

5-20 wt%, 7.5-20 wt%, 10-20 wt%, 0.01-15 wt%, 0.025-15 wt%, 0.05-15 wt%, 0.75-15 wt%, 0.1-15 wt%, 0.25-15 wt%, 0.5-15 wt%, 0.75-15 wt%, 1-15 wt%, 2.5-15 wt%, 5-15 wt%, 7.5-15 wt%, or 10-15 wt% of the peptide.

2.24. Any of the preceding compositions, wherein the composition comprises between about 0.01 wt % and about 0.025 wt %, between about 0.025 wt % and about 0.05 wt %, between about 0.025 wt % and about 0.075 wt %, between about 0.025 wt % and about 0.1 wt %, between about 0.01 wt % and about 0.1 wt %, between about 0.05 wt % and about 0.075 wt %, between about 0.05 wt % and about 0.1 wt %, between about 0.075 wt % and about 0.1 wt %, between about 0.1 wt % and about 0.2 wt %, between about 0.1 wt % and about 0.5 wt %, between about 0.2 wt % and about 0.4 wt %, between about 0.5 wt % and about 1 wt %, between about 0.4 wt % and about 0.6 wt %, between about 0.6 and about 0.8 wt %, between about 0.8 wt % and about 1 wt %, between about 1 wt % and about 2 wt %, between about 1 wt % and about 5 wt %, between about 2 wt % and about 4 wt %, between about 5 wt % and about 10 wt %, between about 4 wt % and about 6 wt %, between about 6 and about 8 wt %, or between about 8 wt % and about 10 wt % of the peptide.

2.25. Any of the preceding compositions, wherein the composition comprises one or more additional ligands that bind to CD44.

2.26. Composition 2.25, wherein the one or more additional ligands that bind to CD44 are selected from the group consisting of serglycin, chondroitin or a salt thereof (e.g., chondroitin sulfate), fibrin, collagen, fibronectin, insulin-like growth factor-binding protein (IGFBP) (e.g., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP4, IGFBP-5, and IGFBP-6), green fluorescent protein (GFP), and any combinations thereof.

2.27. Any of the preceding compositions, wherein the composition comprises serglycin, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, serglycin.

2.28. Any of the preceding compositions, wherein the composition comprises chondroitin or a salt thereof, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, chondroitin or a salt thereof.

2.29. Composition 2.28, wherein the composition comprises chondroitin sulfate.

2.30. Any of the preceding compositions, wherein the composition comprises fibrin, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, fibrin.

2.31. Any of the preceding compositions, wherein the composition comprises collagen, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, collagen.

2.32. Any of the preceding compositions, wherein the composition comprises fibronectin, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, fibronectin.

2.33. Any of the preceding compositions, wherein the composition comprises insulin-like growth factor-binding protein (IGFBP), optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, insulin-like growth factor-binding protein.

2.34. Any of the preceding compositions, wherein the composition comprises green fluorescent protein (GFP), optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, GFP.

2.35. Any of the preceding compositions, wherein the composition comprises hyaluronic acid.

2.36. Composition 2.35, wherein the hyaluronic acid has a molecular weight in a range of about 20 kDa to 1350 kDa, about 4 kDa to about 10 kDa, about 10 kDa to about 100 kDa, about 15 kDa to about 50 kDa, or about 75 kDa to about 350 kDa.

2.37. Any of Compositions 2.35 to 2.36, wherein the hyaluronic acid is cross-linked, optionally wherein the hyaluronic acid has a cross-link density of about 20% or greater.

2.38. Any of Compositions 2.35 to 2.37, wherein the hyaluronic acid is present in a concentration of 25 mcg/mL or greater, about 25 mcg/mL to about 250 mcg/mL, about 25 mcg/mL to about 100 mcg/mL, about 100 mcg/mL to about 250 mcg/mL, about 1 mcg/mL to about 250 mcg/mL, about 100 ug/mL or less, about 100 mcg/mL to about 950 mcg/mL, about 200 mcg/mL to about 400 mcg/mL, about 400 mcg/mL to about 600 mcg/mL, about 600 mcg/mL to about 800 mcg/mL, or about 800 mcg/mL to about 950 mcg/mL.

2.39. Any of the preceding compositions, wherein the composition comprises a

hyaluronidase inhibitor.

2.40. Composition 2.39, wherein the hyaluronidase inhibitor is selected from high molecular mass poly (styrene-4-sulfonate) (PSS), gossypol, sodium aurothiomalate, fenoprofen, glycyrrhizin acid, fatty acids, plant-derived compounds, heparin, and O-sulfated hyaluronic acid (sHA), or any combinations thereof.

2.41. Any of Compositions 2.39 to 2.40, wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, hyaluronidase inhibitor.

2.42. Any of the preceding compositions, wherein the composition comprises a carrier medium.

2.43. Composition 2.42, wherein the carrier medium comprises a saline solution.

2.44. Any of the preceding compositions, wherein the composition comprises a preservative or a biocide.

2.45. Any of the preceding compositions, wherein the composition comprises a microemulsifier, a nanoemulsifier, a solid lipid nanoparticle, a nanostructured lipid carrier, a liposome or a vesicle.

2.46. Any of the preceding compositions, wherein the composition comprises a surfactant.

2.47. Any of the preceding compositions, wherein the composition comprises one or more of soybean oil, jojoba oil, aloe vera oil, soybean phosphatidylcholine, water, polysorbate 80, ethanol, benzyl alcohol, isopropyl alcohol, glycerin, glyceryl monostearate, propylene glycol.

**[0018]** The composition of the present invention comprises a peptide comprising a CD44 binding and/or calcium binding fragment of osteopontin or a variant thereof. Osteopontin is an extracellular signaling protein that is a natural ligand for CD44. Without being bound by theory, it is believed that osteopontin may induce CD44 activation by proteolytically cleaving CD44 resulting in the intra-cellular release of the CD44 intracellular domain (ICD). The CD44-ICD is then free to go into the nucleus and modulate gene expression. Osteopontin are discussed in International Patent Publication No. WO 2018175630 and International Patent Publication No. WO 2023028542, which are hereby incorporated by reference in its entirety. Osteopontin is composed of about 300 amino acids (314 amino acids in human). Osteopontin contains a putative CD44-binding site (KSKEEDKHLKFRISHEL, SEQ ID NO: 97) and a putative calcium binding site

(DWDSRGKDSYETS, SEQ ID NO: 98) in the C-terminal region. In some embodiments, the peptide of the present invention comprises a CD44-binding site, e.g., SEQ ID NO: 97 or a variant thereof. The variants of SEQ ID NO: 97 may have at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97. In some embodiments, the peptide comprises a calcium binding site, e.g., SEQ ID NO:98 or a variant thereof. The variants of SEQ ID NO: 98 may have at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98. In some embodiments, the peptide comprises a CD44-binding site, e.g., SEQ ID NO: 97 or a variant thereof and a calcium binding site, e.g., SEQ ID NO: 98 or a variant thereof.

**[0019]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. The sequences of SEQ ID NOs: 1 to 96 are shown in Table 1.

Table 1

| SEQ ID NO: | Sequence                                                                                                                                                 | # residues |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| 1          | SKSKKFRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQ LDDQSAETHSIKQSRL YKRKANDESNEIISDVIDSQELSKVSREFIISHI EFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN | 146        |
| 2          | SKKFRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN       | 144        |
| 3          | FRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN          | 141        |
| 4          | RPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN           | 139        |
| 5          | QYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN               | 135        |

|    |                                                                                                                                           |     |
|----|-------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 6  | PDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN | 133 |
| 7  | TDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPKSK EEDKHLKFRISHELDSASSEVN    | 130 |
| 8  | EDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN      | 128 |
| 9  | TSHMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN         | 125 |
| 10 | HMESEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN           | 123 |
| 11 | SEELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN              | 120 |
| 12 | ELNGAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                | 118 |
| 13 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                   | 115 |
| 14 | YKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                     | 113 |
| 15 | IPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                        | 110 |
| 16 | VAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                          | 108 |
| 17 | DLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                             | 105 |
| 18 | NAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK VSREFHSHEFHSHEDML VVDPK SKEEDKHLKFRISHELDSASSEVN                               | 103 |

|    |                                                                                                             |     |
|----|-------------------------------------------------------------------------------------------------------------|-----|
| 19 | SDWDSRGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSK<br>VSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN | 100 |
| 20 | WDSRGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVS<br>REFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN   | 98  |
| 21 | RGKDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREF<br>HSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN      | 95  |
| 22 | KDSYETSQ LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHS<br>HEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN        | 93  |
| 23 | SQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSH<br>EDML VVDPKSKEEDKHLKFRISHELDSASSEVN               | 87  |
| 24 | LDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHED<br>ML VVDPKSKEEDKHLKFRISHELDSASSEVN                 | 85  |
| 25 | QSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML V<br>VDPKSKEEDKHLKFRISHELDSASSEVN                    | 82  |
| 26 | AETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVD<br>PKSKEEDKHLKFRISHELDSASSEVN                      | 80  |
| 27 | HSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKS<br>KEEDKHLKFRISHELDSASSEVN                         | 77  |
| 28 | HKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKE<br>EDKHLKFRISHELDSASSEVN                           | 75  |
| 29 | SRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDK<br>HLKFRISHELDSASSEVN                              | 72  |
| 30 | LYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHL<br>KFRISHELDSASSEVN                                 | 70  |
| 31 | RKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFR<br>ISHELDSASSEVN                                    | 67  |
| 32 | ANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISH<br>ELDSASSEVN                                      | 65  |
| 33 | ESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELD<br>SASSEVN                                         | 62  |
| 34 | NEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSA<br>SSEVN                                           | 60  |
| 35 | SDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSE<br>VN                                              | 57  |
| 36 | VIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN                                                    | 55  |
| 37 | SQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEVN                                                       | 52  |

|    |                                                                                                                                                          |     |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 38 | ELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASSEVN                                                                                                       | 50  |
| 39 | KVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASSEVN                                                                                                          | 47  |
| 40 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASSE | 144 |
| 41 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISHELDSAS   | 142 |
| 42 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISHELDS     | 140 |
| 43 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISHEL       | 138 |
| 44 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISHE        | 137 |
| 45 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRISH         | 136 |
| 46 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRIS          | 135 |
| 47 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFRI           | 134 |
| 48 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKFR            | 133 |
| 49 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLKF             | 132 |
| 50 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDMLVVDPKSKEEDKHLK              | 131 |

|    |                                                                                                                                                 |     |
|----|-------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 51 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKEEDKHL   | 130 |
| 52 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKEEDKH    | 129 |
| 53 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKEEDK     | 128 |
| 54 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKEED      | 127 |
| 55 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKEE       | 126 |
| 56 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SKE        | 125 |
| 57 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK SK         | 124 |
| 58 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK S          | 123 |
| 59 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPK            | 122 |
| 60 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDP             | 121 |
| 61 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSQLDDQSAE<br>THSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPK<br>SKEEDKHLKFRISHELDSASSEVN | 133 |
| 62 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSDWDSRGK<br>DSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSH<br>EFHSHEDML VVDPDSASSEVN     | 129 |

|    |                                                                                                                          |     |
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| 63 | SKSKKFRRPDIQYPDATDEDITSHMESEELNGAYKAIPVAQDLNAPSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPD<br>SASSEVN | 116 |
| 64 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>SASSEV   | 114 |
| 65 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>SASSE    | 113 |
| 66 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>SASS     | 112 |
| 67 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>SAS      | 111 |
| 68 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>SA       | 110 |
| 69 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD<br>S        | 109 |
| 70 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD             | 108 |
| 71 | GAYKAIPVAQDLNAPSDWDSRGKDSYETSQLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELD             | 107 |
| 72 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASSEV                                    | 85  |
| 73 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASSE                                     | 84  |
| 74 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSASS                                      | 83  |
| 75 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSAS                                       | 82  |
| 76 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDSA                                        | 81  |
| 77 | QLDDQSAETHSHKQSRLYKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDMLVVDPKSKEEDKHLKFRISHELDS                                         | 80  |

|    |                                                                                              |    |
|----|----------------------------------------------------------------------------------------------|----|
| 78 | QLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELD            | 79 |
| 79 | QLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHEL             | 78 |
| 80 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEV                           | 65 |
| 81 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSE                            | 64 |
| 82 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASS                             | 63 |
| 83 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSAS                              | 62 |
| 84 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSA                               | 61 |
| 85 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDS                                | 60 |
| 86 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELD                                 | 59 |
| 87 | KANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHEL                                  | 58 |
| 88 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSEV                                   | 57 |
| 89 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASSE                                    | 56 |
| 90 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSASS                                     | 55 |
| 91 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSAS                                      | 54 |
| 92 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDSA                                       | 53 |
| 93 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELDS                                        | 52 |
| 94 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHELD                                         | 51 |
| 95 | HSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHEL                                          | 50 |
| 96 | WDSRGKDSYETSQLDDQSAETHSHKQSRL YKRKANDESNEHSDVIDSQELSKVSREFHSHEFHSHEDML VVDPKSKEEDKHLKFRISHEL | 90 |

**[0020]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 20. In some embodiments, the

composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 1 to 20.

**[0021]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 21 to 39. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 21 to 39.

**[0022]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 40 to 60. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 40 to 60.

**[0023]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 61 to 63. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 61 to 63.

**[0024]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 64 to 71. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 64 to 71.

**[0025]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 72 to 79. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 72 to 79.

**[0026]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 80 to 87. In some embodiments, the

composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 80 to 87.

**[0027]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 88 to 95. In some embodiments, the composition comprises a peptide comprising a sequence selected from the group consisting of SEQ ID NOs: 88 to 95.

**[0028]** In some embodiments, the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 96. In some embodiments, the composition comprises a peptide comprising SEQ ID NO 96.

**[0029]** In some embodiments, the peptide has a length of no more than 295 amino acids, e.g., no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.

**[0030]** In some embodiments, the composition comprises about 0.01 wt % or greater of the peptide. In some embodiments, the composition comprises, about 0.025 wt % or greater, e.g., about 0.05 wt % or greater, about 0.075 wt % or greater, about 0.1 wt % or greater, about 0.25 wt % or greater, about 0.5 wt % or greater, about 0.75 wt % or greater, about 1 wt % or greater, about 2.5 wt % or greater, about 5 wt % or greater, about 7.5 wt % or greater, or about 10 wt % or greater, of the peptide.

**[0031]** In some embodiments, the composition comprises 0.01-20 wt%, 0.025-20 wt%, 0.05-20 wt%, 0.75-20 wt%, 0.1-20 wt%, 0.25-20 wt%, 0.5-20 wt%, 0.75-20 wt%, 1-20 wt%, 2.5-20 wt%, 5-20 wt%, 7.5-20 wt%, or 10-20 wt% of the peptide. In some embodiments, the composition comprises 0.01-15 wt%, 0.025-15 wt%, 0.05-15 wt%, 0.75-15 wt%, 0.1-15 wt%, 0.25-15 wt%,

0.5-15 wt%, 0.75-15 wt%, 1-15 wt%, 2.5-15 wt%, 5-15 wt%, 7.5-15 wt%, or 10-15 wt% of the peptide.

**[0032]** In some embodiments the composition comprises between about 0.01 wt % and about 0.025 wt %, between about 0.025 wt % and about 0.05 wt %, between about 0.025 wt % and about 0.075 wt %, between about 0.025 wt % and about 0.1 wt %, between about 0.01 wt % and about 0.1 wt %, between about 0.05 wt % and about 0.075 wt %, between about 0.05 wt % and about 0.1 wt %, between about 0.075 wt % and about 0.1 wt %, between about 0.1 wt % and about 0.2 wt %, between about 0.1 wt % and about 0.5 wt %, between about 0.2 wt % and about 0.4 wt %, between about 0.5 wt % and about 1 wt %, between about 0.4 wt % and about 0.6 wt %, between about 0.6 and about 0.8 wt %, between about 0.8 wt % and about 1 wt %, between about 1 wt % and about 2 wt %, between about 1 wt % and about 5 wt %, between about 2 wt % and about 4 wt %, between about 5 wt % and about 10 wt %, between about 4 wt % and about 6 wt %, between about 6 and about 8 wt %, or between about 8 wt % and about 10 wt % of the peptide.

**[0033]** In some embodiments, the composition of the present invention may further comprise one or more additional ligands that bind to CD44. In some embodiments, the one or more additional ligands that binds to CD44 are selected from the group consisting of serglycin, chondroitin or a salt thereof (e.g., chondroitin sulfate), fibrin, collagen, fibronectin, insulin-like growth factor-binding protein (IGFBP) (e.g., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP4, IGFBP-5, and IGFBP-6), green fluorescent protein, and any combinations thereof.

**[0034]** In some embodiments, the composition comprises about 0.01 wt % or greater serglycin, about 0.025 wt % or greater serglycin, about 0.050 wt % or greater serglycin, about 0.075 wt % or greater serglycin, about 0.1 wt % or greater serglycin, about 0.25 wt % or greater serglycin, about 0.5 wt % or greater serglycin, about 0.75 wt % or greater serglycin, about 1 wt % or greater serglycin, about 2.5 wt % or greater serglycin, about 5 wt % or greater serglycin, about 7.5 wt % or greater serglycin, or about 10 wt % or greater serglycin. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% serglycin. In some embodiments, the composition comprises between about 0.01 wt % and about 0.025 wt % serglycin, between about 0.025 wt % and about 0.05 wt % serglycin, between about 0.025 wt % and about 0.075 wt % serglycin, between about 0.025 wt % and about 0.1 wt % serglycin, between about 0.01 wt % and about 0.1 wt % serglycin, between about 0.05 wt % and about 0.075 wt % serglycin, between about 0.05 wt % and about 0.1 wt % serglycin, between about 0.075 wt % and

about 0.1 wt % serglycin, between about 0.1 wt % and about 0.2 wt % serglycin, between about 0.1 wt % and about 0.5 wt % serglycin, between about 0.2 wt % and about 0.4 wt % serglycin, between about 0.5 wt % and about 1 wt % serglycin, between about 0.4 wt % and about 0.6 wt % serglycin, between about 0.6 and about 0.8 wt % serglycin, between about 0.8 wt % and about 1 wt % serglycin, between about 1 wt % and about 2 wt % serglycin, between about 1 wt % and about 5 wt % serglycin, between about 2 wt % and about 4 wt % serglycin, between about 5 wt % and about 10 wt % serglycin, between about 4 wt % and about 6 wt % serglycin, between about 6 and about 8 wt % serglycin, or between about 8 wt % and about 10 wt % serglycin.

[0035] In some embodiments, the composition comprises chondroitin or a salt thereof, e.g., chondroitin sulfate. In some embodiments, the composition comprises about 0.01 wt % or greater chondroitin or a salt thereof, about 0.025 wt % or greater chondroitin or a salt thereof, about 0.050 wt % or greater chondroitin or a salt thereof, about 0.075 wt % or greater chondroitin or a salt thereof, about 0.1 wt % or greater chondroitin or a salt thereof, about 0.25 wt % or greater chondroitin or a salt thereof, about 0.5 wt % or greater chondroitin or a salt thereof, about 0.75 wt % or greater chondroitin or a salt thereof, about 1 wt % or greater chondroitin or a salt thereof, about 2.5 wt % or greater chondroitin or a salt thereof, about 5 wt % or greater chondroitin or a salt thereof, about 7.5 wt % or greater chondroitin or a salt thereof, or about 10 wt % or greater chondroitin or a salt thereof. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% chondroitin or a salt thereof. In some embodiments, the composition comprises between about 0.01 wt % and about 0.025 wt % chondroitin or a salt thereof, between about 0.025 wt % and about 0.05 wt % chondroitin or a salt thereof, between about 0.025 wt % and about 0.075 wt % chondroitin or a salt thereof, between about 0.025 wt % and about 0.1 wt % chondroitin or a salt thereof, between about 0.01 wt % and about 0.1 wt % chondroitin or a salt thereof, between about 0.05 wt % and about 0.075 wt % chondroitin or a salt thereof, between about 0.05 wt % and about 0.1 wt % chondroitin or a salt thereof, between about 0.075 wt % and about 0.1 wt % chondroitin or a salt thereof, between about 0.1 wt % and about 0.2 wt % chondroitin or a salt thereof, between about 0.1 wt % and about 0.5 wt % chondroitin or a salt thereof, between about 0.2 wt % and about 0.4 wt % chondroitin or a salt thereof, between about 0.5 wt % and about 1 wt % chondroitin or a salt thereof, between about 0.4 wt % and about 0.6 wt % chondroitin or a salt thereof, between about 0.6 and about 0.8 wt % chondroitin or a salt thereof, between about 0.8 wt % and about 1 wt % chondroitin or a salt thereof, between about 1

wt % and about 2 wt % chondroitin or a salt thereof, between about 1 wt % and about 5 wt % chondroitin or a salt thereof, between about 2 wt % and about 4 wt % chondroitin or a salt thereof, between about 5 wt % and about 10 wt % chondroitin or a salt thereof, between about 4 wt % and about 6 wt % chondroitin or a salt thereof, between about 6 and about 8 wt % chondroitin or a salt thereof, or between about 8 wt % and about 10 wt % chondroitin or a salt thereof.

**[0036]** In some embodiments, the composition comprises about 0.01 wt % or greater fibrin, about 0.025 wt % or greater fibrin, about 0.050 wt % or greater fibrin, about 0.075 wt % or greater fibrin, about 0.1 wt % or greater fibrin, about 0.25 wt % or greater fibrin, about 0.5 wt % or greater fibrin, about 0.75 wt % or greater fibrin, about 1 wt % or greater fibrin, about 2.5 wt % or greater fibrin, about 5 wt % or greater fibrin, about 7.5 wt % or greater fibrin, or about 10 wt % or greater fibrin. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% fibrin. In some embodiments, the composition comprises between about 0.01 wt % and about 0.025 wt % fibrin, between about 0.025 wt % and about 0.05 wt % fibrin, between about 0.025 wt % and about 0.075 wt % fibrin, between about 0.025 wt % and about 0.1 wt % fibrin, between about 0.01 wt % and about 0.1 wt % fibrin, between about 0.05 wt % and about 0.075 wt % fibrin, between about 0.05 wt % and about 0.1 wt % fibrin, between about 0.075 wt % and about 0.1 wt % fibrin, between about 0.1 wt % and about 0.2 wt % fibrin, between about 0.1 wt % and about 0.5 wt % fibrin, between about 0.2 wt % and about 0.4 wt % fibrin, between about 0.5 wt % and about 1 wt % fibrin, between about 0.4 wt % and about 0.6 wt % fibrin, between about 0.6 and about 0.8 wt % fibrin, between about 0.8 wt % and about 1 wt % fibrin, between about 1 wt % and about 2 wt % fibrin, between about 1 wt % and about 5 wt % fibrin, between about 2 wt % and about 4 wt % fibrin, between about 5 wt % and about 10 wt % fibrin, between about 4 wt % and about 6 wt % fibrin, between about 6 and about 8 wt % fibrin, or between about 8 wt % and about 10 wt % fibrin.

**[0037]** In some embodiments, the composition comprises about 0.01 wt % or greater collagen, about 0.025 wt % or greater collagen, about 0.050 wt % or greater collagen, about 0.075 wt % or greater collagen, about 0.1 wt % or greater collagen, about 0.25 wt % or greater collagen, about 0.5 wt % or greater collagen, about 0.75 wt % or greater collagen, about 1 wt % or greater collagen, about 2.5 wt % or greater collagen, about 5 wt % or greater collagen, about 7.5 wt % or greater collagen, or about 10 wt % or greater collagen. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% collagen. In some embodiments, a

composition comprises between about 0.01 wt % and about 0.025 wt % collagen, between about 0.025 wt % and about 0.05 wt % collagen, between about 0.025 wt % and about 0.075 wt % collagen, between about 0.025 wt % and about 0.1 wt % collagen, between about 0.01 wt % and about 0.1 wt % collagen, between about 0.05 wt % and about 0.075 wt % collagen, between about 0.05 wt % and about 0.1 wt % collagen, between about 0.075 wt % and about 0.1 wt % collagen, between about 0.1 wt % and about 0.2 wt % collagen, between about 0.1 wt % and about 0.5 wt % collagen, between about 0.2 wt % and about 0.4 wt % collagen, between about 0.5 wt % and about 1 wt % collagen, between about 0.4 wt % and about 0.6 wt % collagen, between about 0.6 and about 0.8 wt % collagen, between about 0.8 wt % and about 1 wt % collagen, between about 1 wt % and about 2 wt % collagen, between about 1 wt % and about 5 wt % collagen, between about 2 wt % and about 4 wt % collagen, between about 5 wt % and about 10 wt % collagen, between about 4 wt % and about 6 wt % collagen, between about 6 and about 8 wt % collagen, or between about 8 wt % and about 10 wt % collagen.

**[0038]** In some embodiments, the composition comprises about 0.01 wt % or greater fibronectin, about 0.025 wt % or greater fibronectin, about 0.050 wt % or greater fibronectin, about 0.075 wt % or greater fibronectin, about 0.1 wt % or greater fibronectin, about 0.25 wt % or greater fibronectin, about 0.5 wt % or greater fibronectin, about 0.75 wt % or greater fibronectin, about 1 wt % or greater fibronectin, about 2.5 wt % or greater fibronectin, about 5 wt % or greater fibronectin, about 7.5 wt % or greater fibronectin, or about 10 wt % or greater fibronectin. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% fibronectin. In some embodiments, the composition comprises between about 0.01 wt % and about 0.025 wt % fibronectin, between about 0.025 wt % and about 0.05 wt % fibronectin, between about 0.025 wt % and about 0.075 wt % fibronectin, between about 0.025 wt % and about 0.1 wt % fibronectin, between about 0.01 wt % and about 0.1 wt % fibronectin, between about 0.05 wt % and about 0.075 wt % fibronectin, between about 0.05 wt % and about 0.1 wt % fibronectin, between about 0.075 wt % and about 0.1 wt % fibronectin, between about 0.1 wt % and about 0.2 wt % fibronectin, between about 0.1 wt % and about 0.5 wt % fibronectin, between about 0.2 wt % and about 0.4 wt % fibronectin, between about 0.5 wt % and about 1 wt % fibronectin, between about 0.4 wt % and about 0.6 wt % fibronectin, between about 0.6 and about 0.8 wt % fibronectin, between about 0.8 wt % and about 1 wt % fibronectin, between about 1 wt % and about 2 wt % fibronectin, between about 1 wt % and about 5 wt % fibronectin, between about 2 wt % and about

4 wt % fibronectin, between about 5 wt % and about 10 wt % fibronectin, between about 4 wt % and about 6 wt % fibronectin, between about 6 and about 8 wt % fibronectin, or between about 8 wt % and about 10 wt % fibronectin.

**[0039]** In some embodiments, the composition comprises about 0.01 wt % or greater insulin-like growth factor-binding protein, about 0.025 wt % or greater insulin-like growth factor-binding protein, about 0.050 wt % or greater insulin-like growth factor-binding protein, about 0.075 wt % or greater insulin-like growth factor-binding protein, about 0.1 wt % or greater insulin-like growth factor-binding protein, about 0.25 wt % or greater insulin-like growth factor-binding protein, about 0.5 wt % or greater insulin-like growth factor-binding protein, about 0.75 wt % or greater insulin-like growth factor-binding protein, about 1 wt % or greater insulin-like growth factor-binding protein, about 2.5 wt % or greater insulin-like growth factor-binding protein, about 5 wt % or greater insulin-like growth factor-binding protein, about 7.5 wt % or greater insulin-like growth factor-binding protein, or about 10 wt % or greater insulin-like growth factor-binding protein. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% insulin-like growth factor-binding protein. In some embodiments, the composition comprises between about 0.01 wt % and about 0.025 wt % insulin-like growth factor-binding protein, between about 0.025 wt % and about 0.05 wt % insulin-like growth factor-binding protein, between about 0.025 wt % and about 0.075 wt % insulin-like growth factor-binding protein, between about 0.025 wt % and about 0.1 wt % insulin-like growth factor-binding protein, between about 0.01 wt % and about 0.1 wt % insulin-like growth factor-binding protein, between about 0.05 wt % and about 0.075 wt % insulin-like growth factor-binding protein, between about 0.05 wt % and about 0.1 wt % insulin-like growth factor-binding protein, between about 0.075 wt % and about 0.1 wt % insulin-like growth factor-binding protein, between about 0.1 wt % and about 0.2 wt % insulin-like growth factor-binding protein, between about 0.1 wt % and about 0.5 wt % insulin-like growth factor-binding protein, between about 0.2 wt % and about 0.4 wt % insulin-like growth factor-binding protein, between about 0.5 wt % and about 1 wt % insulin-like growth factor-binding protein, between about 0.4 wt % and about 0.6 wt % insulin-like growth factor-binding protein, between about 0.6 and about 0.8 wt % insulin-like growth factor-binding protein, between about 0.8 wt % and about 1 wt % insulin-like growth factor-binding protein, between about 1 wt % and about 2 wt % insulin-like growth factor-binding protein, between about 1 wt % and about 5 wt % insulin-like growth factor-binding protein, between about 2 wt % and about 4

wt % insulin-like growth factor-binding protein, between about 5 wt % and about 10 wt % insulin-like growth factor-binding protein, between about 4 wt % and about 6 wt % insulin-like growth factor-binding protein, between about 6 and about 8 wt % insulin-like growth factor-binding protein, or between about 8 wt % and about 10 wt % insulin-like growth factor-binding protein.

**[0040]** In some embodiments, the composition comprises about 0.01 wt % or greater green fluorescent protein, about 0.025 wt % or greater green fluorescent protein, about 0.050 wt % or greater green fluorescent protein, about 0.075 wt % or greater green fluorescent protein, about 0.1 wt % or greater green fluorescent protein, about 0.25 wt % or greater green fluorescent protein, about 0.5 wt % or greater green fluorescent protein, about 0.75 wt % or greater green fluorescent protein, about 1 wt % or greater green fluorescent protein, about 2.5 wt % or greater green fluorescent protein, about 5 wt % or greater green fluorescent protein, about 7.5 wt % or greater green fluorescent protein, or about 10 wt % or greater green fluorescent protein. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt% green fluorescent protein. In some embodiments a composition comprises between about 0.01 wt % and about 0.025 wt % green fluorescent protein, between about 0.025 wt % and about 0.05 wt % green fluorescent protein, between about 0.025 wt % and about 0.075 wt % green fluorescent protein, between about 0.025 wt % and about 0.1 wt % green fluorescent protein, between about 0.01 wt % and about 0.1 wt % green fluorescent protein, between about 0.05 wt % and about 0.075 wt % green fluorescent protein, between about 0.05 wt % and about 0.1 wt % green fluorescent protein, between about 0.075 wt % and about 0.1 wt % green fluorescent protein, between about 0.1 wt % and about 0.2 wt % green fluorescent protein, between about 0.1 wt % and about 0.5 wt % green fluorescent protein, between about 0.2 wt % and about 0.4 wt % green fluorescent protein, between about 0.5 wt % and about 1 wt % green fluorescent protein, between about 0.4 wt % and about 0.6 wt % green fluorescent protein, between about 0.6 and about 0.8 wt % green fluorescent protein, between about 0.8 wt % and about 1 wt % green fluorescent protein, between about 1 wt % and about 2 wt % green fluorescent protein, between about 1 wt % and about 5 wt % green fluorescent protein, between about 2 wt % and about 4 wt % green fluorescent protein, between about 5 wt % and about 10 wt % green fluorescent protein, between about 4 wt % and about 6 wt % green fluorescent protein, between about 6 and about 8 wt % green fluorescent protein, or between about 8 wt % and about 10 wt % green fluorescent protein.

[0041] In some embodiments, the composition of the present invention may further comprise hyaluronic acid. Hyaluronic acid is a natural ligand for CD44 and is pro-inflammatory and stimulate hair growth. Hyaluronic acid is a natural linear polymer containing repeated units of a disaccharide of beta-1,4-D-glucuronic acid and beta-1,3-N-acetyl-D-glucosamine. In some embodiments, the hyaluronic acid has a low average molecular weight, which as used herein refers to ranges from about 15,000 Da to about 40,000 Da. In some embodiments, the hyaluronic acid has an intermediate average molecular weight, which as used herein refers to ranges from about 75,000 Da to about 350,000 Da. In some embodiments the hyaluronic acid has a high average molecular weight, which as used herein refers to about 950,000 Da and greater.

[0042] In some embodiments, the hyaluronic acid has an average molecular weight ranging from about 4,000 Da or less to about 10,000 Da. In some embodiments the hyaluronic acid has an average molecular weight ranging from about 10,000 Da to about 100,000 Da. In some embodiments the hyaluronic acid has an average molecular weight ranging from about 100,000 Da to about 1,500,000 Da or greater.

[0043] In some embodiments hyaluronic acid has an average molecular weight between about 1 kDa and about 10 kDa, between about 10 kDa and about 50 kDa, between about 50 kDa and about 100 kDa, between about 100 kDa and about 150 kDa, between about 200 kDa and about 250 kDa, between about 300 kDa and about 350 kDa, between about 400 kDa and about 450 kDa, between about 500 kDa and about 550 kDa, between about 600 kDa and about 650 kDa, between about 700 kDa and about 750 kDa, between about 800 kDa and about 850 kDa, between about 900 kDa and about 1000 kDa, between about 1000 kDa and about 1100 kDa, between about 1100 kDa and about 1200 kDa, between about 1200 kDa and about 1300 kDa, between about 1300 kDa and about 1400 kDa, between about 1400 kDa and about 1500 kDa, between about 1 kDa and about 100 kDa, between about 100 kDa and about 250 kDa, between about 250 kDa and about 500 kDa, between about 500 kDa and about 750 kDa, between about 750 kDa and about 1000 kDa, between about 1000 kDa and about 1250 kDa, between about 1250 kDa and about 1500 kDa, between about 1 kDa and about 250 kDa, between about 1 kDa and about 500 kDa, between about 100 kDa and about 500 kDa, between about 250 kDa and about 750 kDa, between about 500 kDa and about 1000 kDa, between about 750 kDa and about 1250 kDa, or between about 1000 kDa and about 1500 kDa.

[0044] In some embodiments, the hyaluronic acid is cross-linked. In some embodiments, the hyaluronic acid has a cross-link density of about 20% or greater. Cross-linking may improve the lifetime of the hyaluronic acid and in some embodiments, some degree of cross-linking can be desirable. In some embodiments the hyaluronic acid has sufficient cross-linking to last for about a week. However, without being bound by a mechanism of action, it is believed that hyaluronic acid is effective in stimulating hair growth by interacting with CD44 receptors. Accordingly, it is desirable that the hyaluronic acid is not cross-linked so extensively that the cross-linking interferes with the ability of the hyaluronic acid to interact with a CD44 receptor.

[0045] The hydroxyl ( $--OH$ ), carboxylic ( $--COOH$ ), and/or amide ( $--NHCOCH_3$ ) functional groups of hyaluronic acid can cross link via an ether bond ( $R--O--R$ ), ester linkage ( $R--COO--R$ ), or carbodiimide, respectively. In some embodiments hyaluronic acid is cross-linked with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), glutaraldehyde (GTA), poly (ethylene glycol) diglycidyl ether (PEGDE), ethylene glycol diglycidyl ether (EGDE), divinyl sulfonate (DVS), or pentaerythritol tetraacrylate (PT).

[0046] The hyaluronic acid may have a cross-link density of about  $1 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $2 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $3 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $4 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $5 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $6 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $7 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $8 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $9 \times 10^{-7}$  mol/cm<sup>3</sup> or greater, about  $1 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $2 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $3 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $4 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $5 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $6 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $7 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $8 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, about  $9 \times 10^{-6}$  mol/cm<sup>3</sup> or greater, or about  $1 \times 10^{-6}$  mol/cm<sup>3</sup> or greater. In some embodiments the hyaluronic acid may have a cross-link density between about  $1 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-5}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-6}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $5 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $5 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-6}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $2 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $2 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $4 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $4 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $6 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $6 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $8 \times 10^{-7}$  mol/cm<sup>3</sup>, or between about  $8 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-6}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-6}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-5}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-6}$  mol/cm<sup>3</sup> and about  $5 \times 10^{-6}$  mol/cm<sup>3</sup>, between about  $5 \times 10^{-6}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-5}$  mol/cm<sup>3</sup>, between about  $1 \times 10^{-6}$  mol/cm<sup>3</sup> and about  $2 \times 10^{-6}$  mol/cm<sup>3</sup>, between about  $2 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $4 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $4 \times 10^{-7}$

mol/cm<sup>3</sup> and about  $6 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $6 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $8 \times 10^{-7}$  mol/cm<sup>3</sup>, between about  $8 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $1 \times 10^{-5}$  mol/cm<sup>3</sup>, or between about  $5 \times 10^{-7}$  mol/cm<sup>3</sup> and about  $5 \times 10^{-6}$  mol/cm<sup>3</sup>.

[0047] In some embodiments, the composition may include an amount of hyaluronic acid sufficient to provide a therapeutic effect, for example stimulating hair growth in a patient in need thereof. However, higher concentrations of hyaluronic acid may result in undesirable inflammation. In some embodiments compositions of the invention include an amount of hyaluronic acid sufficient to provide a therapeutic effect, for example stimulating hair growth in a patient in need thereof, and insufficient to provide an unacceptable inflammatory response. As used throughout this description, both mcg/mL and ug/mL refer to micrograms per milliliter. In some embodiments hyaluronic acid is present in an amount of about 10 mcg/mL of composition or greater, about 15 mcg/mL of composition or greater, about 20 mcg/mL of composition or greater, about 25 mcg/mL of composition or greater, about 30 mcg/mL of composition or greater, about 35 mcg/mL of composition or greater, about 40 mcg/mL of composition or greater, about 45 mcg/mL of composition or greater, about 50 mcg/mL of composition or greater, about 55 mcg/mL of composition or greater, about 60 mcg/mL of composition or greater, about 65 mcg/mL of composition or greater, about 70 mcg/mL of composition or greater, about 75 mcg/mL of composition or greater, about 80 mcg/mL of composition or greater, about 85 mcg/mL of composition or greater, about 90 mcg/mL of composition or greater, about 95 mcg/mL of composition or greater, about 100 mcg/mL of composition or greater, about 120 mcg/mL of composition or greater, about 140 mcg/mL of composition or greater, about 1600 mcg/mL of composition or greater, about 180 mcg/mL of composition or greater, about 200 mcg/mL of composition or greater, about 220 mcg/mL of composition or greater, about 240 mcg/mL of composition or greater, about 260 mcg/mL of composition or greater, about 280 mcg/mL of composition or greater, about 300 mcg/mL of composition or greater, about 320 mcg/mL of composition or greater, about 340 mcg/mL of composition or greater, about 360 mcg/mL of composition or greater, about 380 mcg/mL of composition or greater, about 400 mcg/mL of composition or greater, about 420 mcg/mL of composition or greater, about 440 mcg/mL of composition or greater, about 460 mcg/mL of composition or greater, about 480 mcg/mL of composition or greater, about 500 mcg/mL of composition or greater, about 520 mcg/mL of composition or greater, about 540 mcg/mL of composition or greater, about 560 mcg/mL of

composition or greater, about 580 mcg/mL of composition or greater, about 600 mcg/mL of composition or greater, about 620 mcg/mL of composition or greater, about 640 mcg/mL of composition or greater, about 660 mcg/mL of composition or greater, about 680 mcg/mL of composition or greater, about 700 mcg/mL of composition or greater, about 720 mcg/mL of composition or greater, about 740 mcg/mL of composition or greater, about 760 mcg/mL of composition or greater, about 780 mcg/mL of composition or greater, about 800 mcg/mL of composition or greater, about 820 mcg/mL of composition or greater, about 840 mcg/mL of composition or greater, about 860 mcg/mL of composition or greater, about 880 mcg/mL of composition or greater, about 900 mcg/mL of composition or greater, about 920 mcg/mL of composition or greater, about 940 mcg/mL of composition or greater, about 960 mcg/mL of composition or greater, or about 980 mcg/mL of composition or greater.

**[0048]** In some embodiments, hyaluronic acid is present in an amount in a range of about 1 mcg/mL of composition to about 250 mcg/mL of composition, about 10 mcg/mL of composition to about 250 mcg/mL of composition, about 10 mcg/mL of composition to about 200 mcg/mL of composition, 10 mcg/mL of composition to about 150 mcg/mL of composition, 10 mcg/mL of composition to about 100 mcg/mL of composition, about 25 mcg/mL of composition to about 250 mcg/mL of composition, about 25 mcg/mL of composition to about 200 mcg/mL of composition, about 25 mcg/mL of composition to about 150 mcg/mL of composition, about 25 mcg/mL of composition to about 100 mcg/mL of composition, about 50 mcg/mL of composition to about 250 mcg/mL of composition, about 50 mcg/mL of composition to about 200 mcg/mL of composition, about 50 mcg/mL of composition to about 150 mcg/mL of composition, about 50 mcg/mL of composition to about 100 mcg/mL of composition, about 75 mcg/mL of composition to about 250 mcg/mL of composition, about 75 mcg/mL of composition to about 200 mcg/mL of composition, about 75 mcg/mL of composition to about 150 mcg/mL of composition, about 75 mcg/mL of composition to about 100 mcg/mL of composition, about 100 mcg/mL of composition to about 250 mcg/mL of composition, about 100 mcg/mL of composition to about 200 mcg/mL of composition, about 100 mcg/mL of composition to about 150 mcg/mL of composition, about 150 mcg/mL of composition to about 250 mcg/mL of composition, about 200 mcg/mL of composition to about 250 mcg/mL of composition, about 60 mcg/mL of composition to about 80 mcg/mL of composition, about 50 mcg/mL of composition to about 75 mcg/mL of composition, about 25 mcg/mL of composition to about 75 mcg/mL of composition, about 10 mcg/mL of composition to

about 50 mcg/mL of composition, or about 10 mcg/mL of composition to about 25 mcg/mL of composition.

**[0049]** In some embodiments, hyaluronic acid is present in an amount in a range of about 1 mcg/mL of composition to about 500 mcg/mL of composition, about 10 mcg/mL of composition to about 500 mcg/mL of composition, about 10 mcg/mL of composition to about 450 mcg/mL of composition, 10 mcg/mL of composition to about 400 mcg/mL of composition, 10 mcg/mL of composition to about 350 mcg/mL of composition, about 25 mcg/mL of composition to about 500 mcg/mL of composition, about 25 mcg/mL of composition to about 450 mcg/mL of composition, about 25 mcg/mL of composition to about 400 mcg/mL of composition, about 25 mcg/mL of composition to about 350 mcg/mL of composition, about 50 mcg/mL of composition to about 500 mcg/mL of composition, about 50 mcg/mL of composition to about 450 mcg/mL of composition, about 50 mcg/mL of composition to about 400 mcg/mL of composition, about 50 mcg/mL of composition to about 350 mcg/mL of composition, about 75 mcg/mL of composition to about 500 mcg/mL of composition, about 75 mcg/mL of composition to about 450 mcg/mL of composition, about 75 mcg/mL of composition to about 400 mcg/mL of composition, about 75 mcg/mL of composition to about 350 mcg/mL of composition, about 100 mcg/mL of composition to about 500 mcg/mL of composition, about 100 mcg/mL of composition to about 450 mcg/mL of composition, about 100 mcg/mL of composition to about 400 mcg/mL of composition, about 100 mcg/mL of composition to about 350 mcg/mL of composition, about 200 mcg/mL of composition to about 500 mcg/mL of composition, about 200 mcg/mL of composition to about 450 mcg/mL of composition, about 200 mcg/mL of composition to about 400 mcg/mL of composition, about 200 mcg/mL of composition to about 350 mcg/mL of composition, about 300 mcg/mL of composition to about 500 mcg/mL of composition, about 300 mcg/mL of composition to about 450 mcg/mL of composition, about 300 mcg/mL of composition to about 400 mcg/mL of composition, about 300 mcg/mL of composition to about 350 mcg/mL of composition.

**[0050]** In some embodiments, hyaluronic acid is present in an amount in a range of about 1 mcg/mL of composition to about 750 mcg/mL of composition, about 10 mcg/mL of composition to about 750 mcg/mL of composition, about 10 mcg/mL of composition to about 700 mcg/mL of composition, 10 mcg/mL of composition to about 650 mcg/mL of composition, 10 mcg/mL of composition to about 600 mcg/mL of composition, about 25 mcg/mL of composition to about 750 mcg/mL of composition, about 25 mcg/mL of composition to about 700 mcg/mL of composition,

about 25 mcg/mL of composition to about 650 mcg/mL of composition, about 25 mcg/mL of composition to about 600 mcg/mL of composition, about 50 mcg/mL of composition to about 750 mcg/mL of composition, about 50 mcg/mL of composition to about 700 mcg/mL of composition, about 50 mcg/mL of composition to about 650 mcg/mL of composition, about 50 mcg/mL of composition to about 600 mcg/mL of composition, about 75 mcg/mL of composition to about 750 mcg/mL of composition, about 75 mcg/mL of composition to about 700 mcg/mL of composition, about 75 mcg/mL of composition to about 650 mcg/mL of composition, about 75 mcg/mL of composition to about 600 mcg/mL of composition, about 100 mcg/mL of composition to about 750 mcg/mL of composition, about 100 mcg/mL of composition to about 700 mcg/mL of composition, about 100 mcg/mL of composition to about 650 mcg/mL of composition, about 100 mcg/mL of composition to about 600 mcg/mL of composition, about 200 mcg/mL of composition to about 750 mcg/mL of composition, about 200 mcg/mL of composition to about 700 mcg/mL of composition, about 200 mcg/mL of composition to about 650 mcg/mL of composition, about 200 mcg/mL of composition to about 600 mcg/mL of composition, about 300 mcg/mL of composition to about 750 mcg/mL of composition, about 300 mcg/mL of composition to about 700 mcg/mL of composition, about 300 mcg/mL of composition to about 650 mcg/mL of composition, about 300 mcg/mL of composition to about 600 mcg/mL of composition.

[0051] In some embodiments, hyaluronic acid is present in an amount in a range of about 1 mcg/mL of composition to about 950 mcg/mL of composition, about 10 mcg/mL of composition to about 950 mcg/mL of composition, about 10 mcg/mL of composition to about 900 mcg/mL of composition, 10 mcg/mL of composition to about 850 mcg/mL of composition, 10 mcg/mL of composition to about 800 mcg/mL of composition, about 25 mcg/mL of composition to about 950 mcg/mL of composition, about 25 mcg/mL of composition to about 900 mcg/mL of composition, about 25 mcg/mL of composition to about 850 mcg/mL of composition, about 25 mcg/mL of composition to about 800 mcg/mL of composition, about 50 mcg/mL of composition to about 950 mcg/mL of composition, about 50 mcg/mL of composition to about 900 mcg/mL of composition, about 50 mcg/mL of composition to about 850 mcg/mL of composition, about 50 mcg/mL of composition to about 800 mcg/mL of composition, about 75 mcg/mL of composition to about 950 mcg/mL of composition, about 75 mcg/mL of composition to about 900 mcg/mL of composition, about 75 mcg/mL of composition to about 850 mcg/mL of composition, about 75 mcg/mL of composition to about 800 mcg/mL of composition, about 100 mcg/mL of composition to about

950 mcg/mL of composition, about 100 mcg/mL of composition to about 900 mcg/mL of composition, about 100 mcg/mL of composition to about 850 mcg/mL of composition, about 100 mcg/mL of composition to about 800 mcg/mL of composition, about 200 mcg/mL of composition to about 950 mcg/mL of composition, about 200 mcg/mL of composition to about 900 mcg/mL of composition, about 200 mcg/mL of composition to about 850 mcg/mL of composition, about 200 mcg/mL of composition to about 800 mcg/mL of composition, about 300 mcg/mL of composition to about 950 mcg/mL of composition, about 300 mcg/mL of composition to about 900 mcg/mL of composition, about 300 mcg/mL of composition to about 850 mcg/mL of composition, about 300 mcg/mL of composition to about 800 mcg/mL of composition, about 400 mcg/mL of composition to about 950 mcg/mL of composition, about 400 mcg/mL of composition to about 900 mcg/mL of composition, about 400 mcg/mL of composition to about 850 mcg/mL of composition, about 400 mcg/mL of composition to about 800 mcg/mL of composition, about 500 mcg/mL of composition to about 950 mcg/mL of composition, about 500 mcg/mL of composition to about 900 mcg/mL of composition, about 500 mcg/mL of composition to about 850 mcg/mL of composition, about 500 mcg/mL of composition to about 800 mcg/mL of composition, about 600 mcg/mL of composition to about 950 mcg/mL of composition, about 600 mcg/mL of composition to about 900 mcg/mL of composition, about 600 mcg/mL of composition to about 850 mcg/mL of composition, about 600 mcg/mL of composition to about 800 mcg/mL of composition, about 700 mcg/mL of composition to about 950 mcg/mL of composition, about 700 mcg/mL of composition to about 900 mcg/mL of composition, about 700 mcg/mL of composition to about 850 mcg/mL of composition, or about 700 mcg/mL of composition to about 800 mcg/mL of composition, about 800 mcg/mL of composition to about 950 mcg/mL of composition, about 800 mcg/mL of composition to about 900 mcg/mL of composition, or about 800 mcg/mL of composition to about 850 mcg/mL of composition.

**[0052]** In some embodiments, a composition comprises about 0.001 wt % or greater hyaluronic acid, about 0.0025 wt % or greater hyaluronic acid, about 0.0050 wt % or greater hyaluronic acid, about 0.0075 wt % or greater hyaluronic acid, about 0.01 wt % or greater hyaluronic acid, about 0.025 wt % or greater hyaluronic acid, about 0.05 wt % or greater hyaluronic acid, about 0.075 wt % or greater hyaluronic acid, about 0.1 wt % or greater hyaluronic acid, about 0.25 wt % or greater hyaluronic acid, about 0.5 wt % or greater hyaluronic acid, about 0.75 wt % or greater hyaluronic acid, about 1 wt % or greater hyaluronic acid, or about 5 wt % or greater hyaluronic acid.

acid. In some embodiments a composition comprises between about 0.001 wt % and about 0.0025 wt % hyaluronic acid, between about 0.0025 wt % and about 0.005 wt % hyaluronic acid, between about 0.0025 wt % and about 0.0075 wt % hyaluronic acid, between about 0.0025 wt % and about 0.01 wt % hyaluronic acid, between about 0.001 wt % and about 0.01 wt % hyaluronic acid, between about 0.005 wt % and about 0.0075 wt % hyaluronic acid, between about 0.005 wt % and about 0.01 wt % hyaluronic acid, between about 0.0075 wt % and about 0.01 wt % hyaluronic acid, between about 0.01 wt % and about 0.02 wt % hyaluronic acid, between about 0.01 wt % and about 0.05 wt % hyaluronic acid, between about 0.02 wt % and about 0.04 wt % hyaluronic acid, between about 0.05 wt % and about 0.1 wt % hyaluronic acid, between about 0.04 wt % and about 0.06 wt % hyaluronic acid, between about 0.06 and about 0.08 wt % hyaluronic acid, between about 0.08 wt % and about 0.1 wt % hyaluronic acid, between about 0.1 wt % and about 0.2 wt % hyaluronic acid, between about 0.1 wt % and about 0.5 wt % hyaluronic acid, between about 0.2 wt % and about 0.4 wt % hyaluronic acid, between about 0.5 wt % and about 1 wt % hyaluronic acid, between about 0.4 wt % and about 0.6 wt % hyaluronic acid, between about 0.6 and about 0.8 wt % hyaluronic acid, between about 0.8 wt % and about 1 wt % hyaluronic acid, between about 1 wt % and about 2 wt % hyaluronic acid, between about 2 wt % and about 4 wt % hyaluronic acid, between about 4 wt % and about 6 wt % hyaluronic acid, between about 6 wt % and about 8 wt % hyaluronic acid or between about 8 wt % and about 10 wt % hyaluronic acid. In some embodiments, a composition comprises between about 0.001 wt % and about 10 wt % hyaluronic acid, between about 0.01 wt % and about 10 wt % hyaluronic acid, between about 0.1 wt % and about 10 wt % hyaluronic acid, between about 1 wt % and about 10 wt % hyaluronic acid, between about 2 wt % and about 10 wt % hyaluronic acid, between about 3 wt % and about 10 wt % hyaluronic acid, between about 4 wt % and about 10 wt % hyaluronic acid, or between about 5 wt % and about 10 wt % hyaluronic acid.

**[0053]** In some embodiments, a composition according to an embodiment of the invention comprises a commercially available hyaluronic acid composition. For example, suitable commercially available hyaluronic acid compositions include, but are not limited to, hyaluronic acids sold under the trademarks JUVEDERM™, RESTYLANE-L™, CAPTIQUE™, BELOTERO BALANCE™, PREVELLE SILK™, ELEVESS™, HYLAFORM™, EUFLEXXA™, GEL-ONE™, HYALGAN™, ORTHOVISC™, MONOVISC™, SUPARTZ™, SYNVISIC™ and SYNVISIC-ONE™.

[0054] In some embodiments, the composition may include a hyaluronidase inhibitor. Examples of hyaluronidase inhibitors include, but are not limited to, high molecular mass poly (styrene-4-sulfonate) (PSS), gossypol, sodium aurothiomalate, fenoprofen, glycyrrhizin acid, heparin, and O-sulfated hyaluronic acid (sHA), and dextran sulfate, or combinations thereof.

[0055] In some embodiments, the composition comprises about 0.01 wt % or greater hyaluronidase inhibitor, about 0.025 wt % or greater hyaluronidase inhibitor, about 0.050 wt % or greater hyaluronidase inhibitor, about 0.075 wt % or greater hyaluronidase inhibitor, about 0.1 wt % or greater hyaluronidase inhibitor, about 0.25 wt % or greater hyaluronidase inhibitor, about 0.5 wt % or greater hyaluronidase inhibitor, about 0.75 wt % or greater hyaluronidase inhibitor, about 1 wt % or greater hyaluronidase inhibitor, about 2.5 wt % or greater hyaluronidase inhibitor, about 5 wt % or greater hyaluronidase inhibitor, about 7.5 wt % or greater hyaluronidase inhibitor, or about 10 wt % or greater hyaluronidase inhibitor. In some embodiments, the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, hyaluronidase inhibitor. In some embodiments a composition comprises between about 0.01 wt % and about 0.025 wt % hyaluronidase inhibitor, between about 0.025 wt % and about 0.05 wt % hyaluronidase inhibitor, between about 0.025 wt % and about 0.075 wt % hyaluronidase inhibitor, between about 0.025 wt % and about 0.1 wt % hyaluronidase inhibitor, between about 0.01 wt % and about 0.1 wt % hyaluronidase inhibitor, between about 0.05 wt % and about 0.075 wt % hyaluronidase inhibitor, between about 0.05 wt % and about 0.1 wt % hyaluronidase inhibitor, between about 0.075 wt % and about 0.1 wt % hyaluronidase inhibitor, between about 0.1 wt % and about 0.2 wt % hyaluronidase inhibitor, between about 0.1 wt % and about 0.5 wt % hyaluronidase inhibitor, between about 0.2 wt % and about 0.4 wt % hyaluronidase inhibitor, between about 0.5 wt % and about 1 wt % hyaluronidase inhibitor, between about 0.4 wt % and about 0.6 wt % hyaluronidase inhibitor, between about 0.6 and about 0.8 wt % hyaluronidase inhibitor, between about 0.8 wt % and about 1 wt % hyaluronidase inhibitor, between about 1 wt % and about 2 wt % hyaluronidase inhibitor, between about 1 wt % and about 5 wt % hyaluronidase inhibitor, between about 2 wt % and about 4 wt % hyaluronidase inhibitor, between about 5 wt % and about 10 wt % hyaluronidase inhibitor, between about 4 wt % and about 6 wt % hyaluronidase inhibitor, between about 6 and about 8 wt % hyaluronidase inhibitor, or between about 8 wt % and about 10 wt % hyaluronidase inhibitor.

[0056] In some embodiments, the composition includes a carrier medium. Such carrier medium may be a biocompatible fluid suitable for injection into a mammalian skin. In some embodiments, the carrier medium comprises a saline solution. In some embodiments, hyaluronic acid serves as the carrier medium as well as an active ingredient.

[0057] In some embodiments, the composition includes one or more additives. Such additives may include a preservative or a biocide.

[0058] In some embodiments, the composition includes a microemulsifier, a nanoemulsifier, a solid lipid nanoparticle, a nanostructured lipid carrier, a liposome or a vesicle.

[0059] In some embodiments a composition may comprise a fatty acid (e.g., oleic acid), ester of a fatty acid and alcohol (e.g., isopropyl myristate, isopropyl palmitate, ethyl oleate), medium chain triglycerides, triacetin, or a terpene (e.g., limonene, menthol, cineole). In some embodiments, a composition may comprise a surfactant. For example, suitable surfactants include, but are not limited to, TWEEN<sup>TM</sup> (polysorbates), CREMOPHOR<sup>TM</sup> (mixture of macrogol glycerol hydroxystearate, PEG-40 castor oil, polyoxyl 40 hydrogenated castor oil), TRANSCUTOL<sup>TM</sup> P (diethylene glycol monoethyl ether), PLUROL OLEIQUE<sup>TM</sup> (polyglyceryl-3-oleate), PLUROL ISOSTEARIQUE<sup>TM</sup> (isostearic acid ester of poly-glycerols and higher oligomers) and LABRASOL<sup>TM</sup> (mixture of mono-, di- and tri-glycerides of C8 and C10 fatty acids, and mono- and di-esters of PEG), and lecithin. In some embodiments, the composition may comprise a cosurfactant. For example, suitable cosurfactants include, but are not limited to short and medium chain alcohols and polyglyceryl derivatives, including ethanol, isopropanol, isopropyl myristate and propylene glycol.

[0060] In some embodiments, the composition comprises one or more of soybean oil, jojoba oil, aloe vera oil, soybean phosphatidylcholine, water, polysorbate 80, ethanol, benzyl alcohol, isopropyl alcohol, glycerin, glyceryl monostearate, propylene glycol.

[0061] A process for the production of a therapeutic composition according to an embodiment of the invention comprises mixing an effective amount of active agents if more than one active ingredients are included in the composition. For example, if the composition comprises a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96 and hyaluronic acid, an effective amount of hyaluronic acid is mixed with an effective amount of the peptide. Said processes may also include a step of preparing a physiologically acceptable carrier

medium, to which the active agents are added. Preferably, the physiologically acceptable carrier medium is injectable.

**[0062]** The method of production may include a step of forming a microemulsion or a nanoemulsion. A microemulsion or nanoemulsion may comprise oil, water, surfactant and cosurfactant to form a colloidal dispersion of droplet sizes in a range of about 10 nm to about 100 nm. In some embodiments, a microemulsion or nanoemulsion may comprise a fatty acid (e.g., oleic acid), ester of a fatty acid and alcohol (e.g., isopropyl myristate, isopropyl palmitate, ethyl oleate), medium chain triglycerides, triacetin, or a terpene (e.g., limonene, menthol, cineole). In some embodiments, the microemulsion or nanoemulsion may comprise a surfactant. For example, suitable surfactants include, but are not limited to, TWEEN<sup>TM</sup> (polysorbates), CREMOPHOR<sup>TM</sup> (mixture of macrogol glycerol hydroxystearate, PEG-40 castor oil, polyoxyl 40 hydrogenated castor oil), TRANSCUTOL<sup>TM</sup> P (diethylene glycol monoethyl ether), PLUROL OLEIQUE<sup>TM</sup> (polyglyceryl-3-oleate), PLUROL ISOSTEARIQUE<sup>TM</sup> (isostearic acid ester of poly-glycerols and higher oligomers) and LABRASOL<sup>TM</sup> (mixture of mono-, di- and tri-glycerides of C8 and C10 fatty acids, and mono- and di-esters of PEG), and lecithin. In some embodiments, the microemulsion or nanoemulsion may comprise a cosurfactant. For example, suitable cosurfactants include, but are not limited to short and medium chain alcohols and polyglyceryl derivatives, including ethanol, isopropanol, isopropyl myristate and propylene glycol. In some embodiments, formation of a microemulsion or nanoemulsion includes use of a high-pressure homogenizer, microfluidizer and/or ultrasonicator.

**[0063]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a solid nanoparticle. The solid nanoparticle may comprise an inorganic material such as a metal oxide (e.g., zinc oxide, titanium dioxide) or polymers that are solid at room temperature.

**[0064]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a solid lipid nanoparticle. The solid lipid nanoparticle may comprise a lipid that is solid at room temperature with a surface covering of surfactant to stabilize them as droplets having a size of less than about 100 nm when dispersed in water.

**[0065]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a nanostructured lipid carrier. The nanostructured lipid carrier

may comprise a fluid lipid phase embedded into a solid lipid matrix or localized at the surface of solid platelets and the surfactant layer.

**[0066]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a liposome. The liposome may comprise spherical vesicles composed of amphiphilic phospholipids and cholesterol, self-associated into multilamellar, large unilamellar and small unilamellar vesicles.

**[0067]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a flexible vesicle. The flexible vesicle may comprise a material that will associate into bilayer structures as well as components that confer flexibility. In some embodiments, the flexible vesicle comprises an ethosome (i.e., a phospholipid with a high proportion of ethanol), a niosome (i.e., non-ionic surfactant), an invasome (i.e., phospholipids, ethanol, and a mixture of terpene penetration enhancer), an SECosomes (i.e., surfactant, ethanol, and cholesterol), or a PEV (i.e., penetration enhancer vesicle). In some embodiments a PEV may comprise oleic acid, limonene, or propylene glycol.

**[0068]** The method of production may include a step of mixing a composition according to an embodiment of the invention with a polymeric micelle or polymeric dendrimer. The polymeric micelle may be a colloidal carrier with a hydrophilic exterior shell and a hydrophobic interior core. The polymeric micelle may be nanosized. The polymeric dendrimer may comprise a branched polymer structure.

**[0069]** In another aspect, the present invention provides a method (Method 3.0) of stimulating hair growth in a skin of a patient in need thereof, comprising administering to the skin of the patient a composition comprising a peptide comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96. For example, the invention includes:

3.1. Method 3.0, wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 96.

3.2. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 20, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 1 to 20.

3.3. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 21 to 39, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 21 to 39.

3.4. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 40 to 60, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 40 to 60.

3.5. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 61 to 63, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 61 to 63.

3.6. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 64 to 71, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 64 to 71.

3.7. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 72 to 79, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 72 to 79.

3.8. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 80 to 87, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 80 to 87.

3.9. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 88 to 95, optionally wherein the peptide comprises a sequence selected from the group consisting of SEQ ID NOs: 88 to 95.

3.10. Method 3.0, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 96, optionally wherein the peptide comprises SEQ ID NO: 96.

- 3.11. Any of the preceding methods, wherein the peptide comprises a CD44 binding site.
- 3.12. Method 3.11, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof.
- 3.13. Method 3.12, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97.
- 3.14. Any of the preceding methods, wherein the peptide comprises a calcium binding site.
- 3.15. Method 3.14, wherein the peptide comprises SEQ ID NO: 98 or a variant thereof.
- 3.16. Method 3.15, wherein the variant of SEQ ID NO: 98 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.
- 3.17. Any of the preceding methods, wherein the peptide comprises a CD4 binding site and a calcium binding site.
- 3.18. Method 3.17, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof and SEQ ID NO: 98 or a variant thereof.
- 3.19. Method 3.18, wherein the variant of SEQ ID NO: 97 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 97 and the variant of SEQ ID NO: 98 has at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 98.
- 3.20. Any of the preceding methods, wherein the peptide has a length of no more than 295 amino acids.
- 3.21. Method 3.20, wherein the peptide has a length of no more than 290 amino acids, no more than 280 amino acids, no more than 270 amino acids, no more than 260 amino acids, no more than 250 amino acids, no more than 240 amino acids, no more than 230 amino acids, no more than 220 amino acids, no more than 210 amino acids, no more than 200 amino acids, no more than 190 amino acids, no more than 180 amino acids, no more than 170 amino acids, no more than 160 amino acids, no more than 150 amino acids, no more than 140 amino acids, no more than 130 amino acids, no more than 120 amino acids, no more than 110 amino acids, no more than 100 amino acids, no more than 90 amino acids, no more than 80 amino acids, no more than 70 amino acids, or no more than 60 amino acids.
- 3.22. Any of the preceding methods, wherein the composition comprises about 0.01 wt % or greater of the peptide, optionally wherein the composition comprises, about 0.025 wt % or greater, e.g., about 0.05 wt % or greater, about 0.075 wt % or greater, about 0.1 wt % or greater, about 0.25 wt % or greater, about 0.5 wt % or greater, about 0.75 wt % or greater, about 1

wt % or greater, about 2.5 wt % or greater, about 5 wt % or greater, about 7.5 wt % or greater, or about 10 wt % or greater, of the peptide.

3.23. Any of the preceding methods, wherein the composition comprises 0.01-20 wt% of the peptide, optionally wherein the composition comprises 0.025-20 wt%, 0.05-20 wt%, 0.75-20 wt%, 0.1-20 wt%, 0.25-20 wt%, 0.5-20 wt%, 0.75-20 wt%, 1-20 wt%, 2.5-20 wt%, 5-20 wt%, 7.5-20 wt%, 10-20 wt%, 0.01-15 wt%, 0.025-15 wt%, 0.05-15 wt%, 0.75-15 wt%, 0.1-15 wt%, 0.25-15 wt%, 0.5-15 wt%, 0.75-15 wt%, 1-15 wt%, 2.5-15 wt%, 5-15 wt%, 7.5-15 wt%, or 10-15 wt% of the peptide.

3.24. Any of the preceding methods, wherein the composition comprises between about 0.01 wt % and about 0.025 wt %, between about 0.025 wt % and about 0.05 wt %, between about 0.025 wt % and about 0.075 wt %, between about 0.025 wt % and about 0.1 wt %, between about 0.01 wt % and about 0.1 wt %, between about 0.05 wt % and about 0.075 wt %, between about 0.05 wt % and about 0.1 wt %, between about 0.075 wt % and about 0.1 wt %, between about 0.1 wt % and about 0.2 wt %, between about 0.1 wt % and about 0.5 wt %, between about 0.2 wt % and about 0.4 wt %, between about 0.5 wt % and about 1 wt %, between about 0.4 wt % and about 0.6 wt %, between about 0.6 and about 0.8 wt %, between about 0.8 wt % and about 1 wt %, between about 1 wt % and about 2 wt %, between about 1 wt % and about 5 wt %, between about 2 wt % and about 4 wt %, between about 5 wt % and about 10 wt %, between about 4 wt % and about 6 wt %, between about 6 and about 8 wt %, or between about 8 wt % and about 10 wt % of the peptide.

3.25. Any of the preceding methods, wherein the composition comprises one or more additional ligands that bind to CD44.

3.26. Method 3.25, wherein the one or more additional ligands that bind to CD44 are selected from the group consisting of serglycin, chondroitin or a salt thereof (e.g., chondroitin sulfate), fibrin, collagen, fibronectin, insulin-like growth factor-binding protein (IGFBP) (e.g., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP4, IGFBP-5, and IGFBP-6), green fluorescent protein (GFP), and any combinations thereof.

3.27. Any of the preceding methods, wherein the composition comprises serglycin, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, serglycin.

3.28. Any of the preceding methods, wherein the composition comprises chondroitin or a salt thereof, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, chondroitin or a salt thereof.

3.29. Method 3.28, wherein the composition comprises chondroitin sulfate.

3.30. Any of the preceding methods, wherein the composition comprises fibrin optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, fibrin.

3.31. Any of the preceding methods, wherein the composition comprises collagen, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, collagen.

3.32. Any of the preceding methods, wherein the composition comprises fibronectin, optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, fibronectin.

3.33. Any of the preceding methods, wherein the composition comprises insulin-like growth factor-binding protein (IGFBP), optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, insulin-like growth factor-binding protein.

3.34. Any of the preceding methods, wherein the composition comprises green fluorescent protein (GFP), optionally wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, GFP.

3.35. Any of the preceding methods, wherein the composition comprises hyaluronic acid.

3.36. Method 3.35, wherein the hyaluronic acid has a molecular weight in a range of about 20 kDa to 1350 kDa, about 4 kDa to about 10 kDa, about 10 kDa to about 100 kDa, about 15 kDa to about 50 kDa, or about 75 kDa to about 350 kDa.

3.37. Any of Methods 3.35 to 3.36, wherein the hyaluronic acid is cross-linked, optionally wherein the hyaluronic acid has a cross-link density of about 20% or greater.

3.38. Any of Compositions 3.35 to 3.37, wherein the hyaluronic acid is present in a concentration of 25 mcg/mL or greater, about 25 mcg/mL to about 250 mcg/mL, about 25 mcg/mL to about 100 mcg/mL, about 100 mcg/mL to about 250 mcg/mL, about 1 mcg/mL to about 250 mcg/mL, about 100 ug/mL or less, about 100 mcg/mL to about 950 mcg/mL, about 200 mcg/mL to about 400 mcg/mL, about 400 mcg/mL to about 600 mcg/mL, about 600 mcg/mL to about 800 mcg/mL, or about 800 mcg/mL to about 950 mcg/mL.

3.39. Any of the preceding methods, wherein the composition comprises a hyaluronidase inhibitor.

3.40. Method 3.39, wherein the hyaluronidase inhibitor is selected from high molecular mass poly (styrene-4-sulfonate) (PSS), gossypol, sodium aurothiomalate, fenoprofen, glycyrrhizin acid, fatty acids, plant-derived compounds, heparin, and O-sulfated hyaluronic acid (sHA), or any combinations thereof.

3.41. Any of Methods 3.39 to 3.40, wherein the composition comprises 0.01 -15 wt%, e.g., 0.1-10 wt%, 1-10 wt%, or 5-10 wt%, hyaluronidase inhibitor.

3.42. Any of the preceding methods, wherein the composition comprises a carrier medium.

3.43. Method 3.42, wherein the carrier medium comprises a saline solution.

3.44. Any of the preceding methods, wherein the composition comprises a preservative or a biocide.

3.45. Any of the preceding methods, wherein the composition comprises a microemulsifier, a nanoemulsifier, a solid lipid nanoparticle, a nanostructured lipid carrier, a liposome or a vesicle.

3.46. Any of the preceding methods, wherein the composition comprises a surfactant.

3.47. Any of the preceding methods, wherein the composition comprises one or more of soybean oil, jojoba oil, aloe vera oil, soybean phosphatidylcholine, water, polysorbate 80, ethanol, benzyl alcohol, isopropyl alcohol, glycerin, glyceryl monostearate, propylene glycol.

3.48. Any of the preceding methods, wherein the administering comprises applying the composition to a surface of the skin, optionally wherein the method further comprises a step to enhance permeation prior to topical administration of the composition.

3.49. Any of Methods 3.0 to 3.47, wherein the administering comprises injecting the composition into a dermal layer or a hypodermal layer of the skin, optionally wherein the administering comprises injecting the composition into a dermal layer of the skin.

3.50. Method 3.49, wherein the composition is injected about 400 microns to about 2 mm deep into the skin.

3.51. Any of Methods 3.49 to 3.50, wherein the composition is administered in a plurality of injections, optionally wherein the composition is administered in a plurality of injections in an amount of about 400 injections/cm<sup>2</sup> skin to about 650 injections/cm<sup>2</sup> skin.

3.52. Any of Methods 3.49 to 3.51, wherein the composition is injected by a microneedle.

- 3.53. Any of the preceding methods, wherein the composition is encased in a liposome, optionally wherein the liposome comprises hydrogenated phospholipids.
- 3.54. Any of the preceding methods, wherein the method further comprises applying electroporation to the skin.
- 3.55. Any of the preceding methods, wherein the method further comprises applying sonophoresis to the skin.
- 3.56. Any of the preceding methods, wherein the method further comprises applying laser ablation to the skin.
- 3.57. Any of the preceding methods, wherein the method further comprises applying magnetophoresis to the skin.
- 3.58. Any of the preceding methods, wherein the method further comprises applying radiofrequency thermal ablation to the skin.
- 3.59. Any of the preceding methods, wherein the method further comprises applying a microneedle device to the skin.
- 3.60. Any of the preceding methods, wherein the composition is administered as a bolus or as an infusion.
- 3.61. Any of the preceding methods, wherein the composition is administered to the skin once a day for one day, once a day for one week, once a day for one month, once a day for one year, twice a day for one day, twice a day for one week, twice a day for one month, twice a day for one year, once a week for one week, once a week for one month, once a week for one year, twice a week for one week, twice a week for one month, twice a week for one year, once a month for one month, once a month for two months, once a month for six months, once a month for one year, twice a month for one month, twice a month for two months, twice a month for six months, twice a month for one year, once every two months for two months, once every two months for four months, once every two months for six months, once every two months for one year, once every three months for three months, once every three months for six months, once every three months for nine months, once every three months for one year, once every four months for four months, once every four months for eight months, once every four months for one year, once every six months for six months, or once every six months for one year.

[0070] The method of stimulating hair growth in a patient in need thereof includes administering a composition according to any embodiment of the present invention to the surface of or into the patient's skin. In some embodiments, the composition is administered topically by applying the composition to the surface of the patient's skin. In some embodiments, the composition is administered into the dermis or hypodermis of the patient's skin, for example, by injection as described herein.

[0071] A method of administering a composition according to an embodiment of the invention comprises delivery of a composition according to an embodiment of the invention to a hair follicle. In some embodiments, the delivery is effected by topical administration, that is, application of the composition to the surface of the skin and allowing the composition to permeate the skin. In some embodiments, the method of administration includes a step to enhance permeation prior to topical administration of a composition. In some embodiments, the delivery is effected by injection into the skin.

[0072] In some embodiments, topical delivery is performed following, or in conjunction with, application of iontophoresis. For example, iontophoresis may comprise application of a mild electric current (e.g., 0.1 to 1.0 mA/cm<sup>2</sup>) to increase skin permeation of the composition. Without being bound by theory, it is believed iontophoresis may improve permeation of the skin by electromigration, electroosmosis, and/or enhanced passive diffusion.

[0073] In some embodiments, topical delivery is performed following, or in conjunction with, application of electroporation. For example, electroporation may comprise application of high intensity, high voltage (e.g., 50-1500 V) electric pulses of short duration (10 microseconds to 10 milliseconds) to form aqueous pores in the lipid bilayers of the stratum corneum of the skin.

[0074] In some embodiments, topical delivery is performed following, or in conjunction with, application of sonophoresis. For example, sonophoresis may comprise application of acoustic waves at high frequency (e.g., about 500 kHz to 1250 kHz) or low frequency (e.g., about 20 to about 100 kHz) or (beginning with one of high or low frequency and progressing to the other of high or low frequency).

[0075] In some embodiments, topical delivery is performed following, or in conjunction with, application of laser ablation. Laser ablation may comprise generation of a photomechanical wave by laser ablation of a target material (e.g., polymer) placed on the surface of the skin.

[0076] In some embodiments, topical delivery is performed following, or in conjunction with, magnetophoresis. Magnetophoresis may comprise application of a magnetic field, for example pulsed electromagnetic fields, to the skin.

[0077] In some embodiments, topical delivery is performed following application of radiofrequency thermal ablation. Thermal ablation may comprise application of extreme heat (e.g., about 300.degree. C. for microseconds) at the skin surface. Without being bound by theory, it is believed that thermal ablation may vaporize portions of the stratum corneum to create micron-scale channels. Thermal ablation may be accomplished with commercially available devices including VIADOR<sup>TM</sup> (Syneron Medical Ltd, Israel) and PASSPORT<sup>®</sup> (Nitto-Denko, Japan). In some embodiments thermal ablation may be accomplished with an erbium:yttrium-gallium-garnet (Er:YAG) emitting at 2,790 nm or yttrium scandium gallium garnet (YSGG) laser emitting at 2,940 nm. In some embodiments fractional laser ablation may be applied to sub-mm regions to generate spots mimicking a microneedle array-type pattern (e.g., 40-300  $\mu$ m with densities between 50-600 cm.

[0078] In some embodiments, topical delivery is performed following application of microneedle device.

[0079] In some embodiments, the method for administering a composition according to an embodiment of the invention comprises injecting a therapeutic amount of composition in the skin of a patient in need of treatment. In some embodiments, a composition according to an embodiment of the invention is administered as a bolus, which as used herein refers to the dosage being delivered in a time of less than ten minutes. In some embodiments, a composition according to an embodiment of the invention is administered as an infusion, which as used herein refers to the dosage being delivered in a time of about ten minutes or greater.

[0080] Such injection may be made via a single needle, microneedle, or similar device, or an array of needles, microneedles, or similar devices. In some embodiments, a composition according to an embodiment of the invention is delivered via a conventional syringe. In some embodiments, subdermal delivery is performed via a hollow microneedle injector. In some embodiments, subdermal delivery is performed a microneedle patch that has been coated with a composition according to an embodiment of the invention, for example that has been coated with a composition according to an embodiment of the invention by 3D printing. In some embodiments, the

composition is delivered via jet injector. The term "needle" as used herein refers to any such device for piercing the skin and injecting a composition according to an embodiment of the invention.

**[0081]** Preferably the composition is administered near the hair follicle of the patient. Accordingly, in some embodiments, the composition is administered by injecting a therapeutic amount of composition in the dermis of the patient. In some embodiments, the composition is administered by injecting a therapeutic amount of composition in the hypodermis of the patient. In some embodiments, the composition is administered about 0.4 mm to about 2 mm into the patient's skin (i.e., about 0.4 mm to about 3 mm from the surface of the skin). In some embodiments, the composition is administered about 0.4 mm, about 0.5 mm, about 0.6 mm, about 0.7 mm, about 0.8 mm, about 0.9 mm, about 1 mm, about 1.1 mm, about 1.2 mm, about 1.3 mm, about 1.4 mm, about 1.5 mm, about 1.6 mm, about 1.7 mm, about 1.8 mm, about 1.9 mm, about 2 mm, about 2.1 mm, about 2.2 mm, about 2.3 mm, about 2.4 mm, about 2.5 mm, about 2.6 mm, about 2.7 mm, about 2.8 mm, about 2.9 mm, or about 3 mm into the patient's skin. In some embodiments, the composition is administered between about 0.5 mm to about 1 mm, between about 1 mm to about 1.5 mm, between about 1.5 mm to about 2 mm, between about 2 mm to about 2.5 mm, between about 2.5 mm to about 3 mm, between about 1 mm to about 3 mm, between about 1.5 mm to about 3 mm, between about 0.4 mm to about 0.6 mm, between about 0.4 mm to about 0.8 mm, between about 0.4 mm to about 1 mm, between about 0.4 mm to about 1.2 mm, between about 0.4 mm to about 1.4 mm, between about 0.4 mm to about 1.6 mm, between about 0.4 mm to about 1.8 mm, between about 0.4 mm to about 2 mm, between about 0.4 mm to about 2.2 mm, between about 0.4 mm to about 2.4 mm, between about 0.4 mm to about 2.6 mm, between about 0.4 mm to about 2.8 mm, between about 0.4 mm to about 3 mm, between about 0.6 mm to about 0.8 mm, between about 0.6 mm to about 1 mm, about 0.6 mm to about 1.2 mm, between about 0.6 mm to about 1.4 mm, between about 0.6 mm to about 1.6 mm, between about 0.6 mm to about 1.8 mm, between about 0.6 mm to about 2 mm, between about 0.6 mm to about 2.2 mm, between about 0.6 mm to about 2.4 mm, between about 0.6 mm to about 2.6 mm, between about 0.6 mm to about 2.8 mm, between about 0.6 mm to about 3 mm, between about 0.8 mm to about 1 mm, between about 0.8 mm to about 1.2 mm, between about 0.8 mm to about 1.4 mm, between about 0.8 mm to about 1.6 mm, between about 0.8 mm to about 1.8 mm, between about 0.8 mm to about 2 mm, between about 0.8 mm to about 2.2 mm, between about 0.8 mm to about 2.4 mm, between about 0.8 mm to about 2.6 mm, between about 0.8 mm to about 2.8 mm, between about 0.8 mm to about 3 mm,

between about 1 mm to about 1.2 mm, between about 1 mm to about 1.4 mm, between about 1 mm to about 1.6 mm, between about 1 mm to about 1.8 mm, between about 1 mm to about 2 mm, between about 1 mm to about 2.2 mm, between about 1 mm to about 2.4 mm, between about 1 mm to about 2.6 mm, between about 1 mm to about 2.8 mm, between about 1 mm to about 3 mm, between about 1.2 mm to about 1.4 mm, between about 1.2 mm to about 1.6 mm, between about 1.2 mm to about 1.8 mm, between about 1.2 mm to about 2 mm, between about 1.2 mm to about 2.2 mm, between about 1.2 mm to about 2.4 mm, between about 1.2 mm to about 2.6 mm, between about 1.2 mm to about 2.8 mm, between about 1.2 mm to about 3 mm, between about 1.4 mm to about 1.6 mm, between about 1.4 mm to about 1.8 mm, between about 1.4 mm to about 2 mm, between about 1.4 mm to about 2.2 mm, between about 1.4 mm to about 2.4 mm, between about 1.4 mm to about 2.6 mm, between about 1.4 mm to about 2.8 mm, between about 1.4 mm to about 3 mm, between about 1.6 mm to about 1.8 mm, between about 1.6 mm to about 2 mm, between about 1.6 mm to about 2.2 mm, between about 1.6 mm to about 2.4 mm, between about 1.6 mm to about 2.6 mm, between about 1.6 mm to about 2.8 mm, between about 1.6 mm to about 3 mm, between about 1.8 mm to about 2 mm between about 1.8 mm to about 2.2 mm, between about 1.8 mm to about 2.4 mm, between about 1.8 mm to about 2.6 mm, between about 1.8 mm to about 2.8 mm, between about 1.8 mm to about 3 mm, between about 2.0 mm to about 2.2 mm, between about 2.0 mm to about 2.4 mm, between about 2.0 mm to about 2.6 mm, between about 2.0 mm to about 2.8 mm, between about 2.0 mm to about 3 mm, between about 2.2 mm to about 2.4 mm, between about 2.2 mm to about 2.6 mm, between about 2.2 mm to about 2.8 mm, between about 2.2 mm to about 3 mm, between about 2.4 mm to about 2.6 mm, between about 2.4 mm to about 2.8 mm, between about 2.4 mm to about 3 mm, between about 2.6 mm to about 2.8 mm, between about 2.6 mm to about 3 mm, or between about 2.8 mm to about 3 mm into the patient's skin.

**[0082]** In some embodiments, a composition according to an embodiment of the invention may be administered in a plurality of injections. In some embodiments, a composition according to an embodiment of the invention is administered in via about 1 injection/cm<sup>2</sup> skin to about 1000 injections/cm<sup>2</sup> skin, about 200 injections/cm<sup>2</sup> skin to about 800 injections/cm<sup>2</sup> skin, or about 400 injections/cm<sup>2</sup> skin to about 650 injections/cm<sup>2</sup> skin. In some embodiments a composition is administered via about 200 injections/cm<sup>2</sup> skin, about 250 injections/cm<sup>2</sup> skin, about 300 injections/cm<sup>2</sup> skin, about 350 injections/cm<sup>2</sup> skin, about 400 injections/cm<sup>2</sup> skin, about 450

injections/cm<sup>2</sup> skin, about 500 injections/cm<sup>2</sup> skin, about 550 injections/cm<sup>2</sup> skin, about 600 injections/cm<sup>2</sup> skin, or about 650 injections/cm<sup>2</sup> skin,

**[0083]** In some embodiments, the composition may be administered to a patient's skin once a day for one day, once a day for one week, once a day for one month, once a day for one year, twice a day for one day, twice a day for one week, twice a day for one month, twice a day for one year, once a week for one week, once a week for one month, once a week for one year, twice a week for one week, twice a week for one month, twice a week for one year, once a month for one month, once a month for two months, once a month for six months, once a month for one year, twice a month for one month, twice a month for two months, twice a month for six months, twice a month for one year, once every two months for two months, once every two months for four months, once every two months for six months, once every two months for one year, once every three months for three months, once every three months for six months, once every three months for nine months, once every three months for one year, once every four months for four months, once every four months for eight months, once every four months for one year, once every six months for six months, once every six months for one year, or as needed.

## CLAIMS

1. A peptide for stimulating hair growth, comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 96.
2. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 1 to 20.
3. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 21 to 39.
4. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 40 to 60.
5. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 61 to 63.
6. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 64 to 71.
7. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 72 to 79.
8. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 80 to 87.
9. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 88 to 95.
10. The peptide of claim 1, wherein the peptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with SEQ ID NO: 96.

11. The peptide of any of claims 1 to 10, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof.
12. The peptide of any of claims 1 to 10, wherein the peptide comprises SEQ ID NO: 98 or a variant thereof.
13. The peptide of any of claims 1 to 10, wherein the peptide comprises SEQ ID NO: 97 or a variant thereof and SEQ ID NO: 98 or a variant thereof.
14. The peptide of any preceding claims, wherein the peptide has a length of no more than 295 amino acids, no more than 250 amino acids, no more than 200 amino acids, no more than 150 amino acids, no more than 100 amino acids, or no more than 60 amino acids.
15. A composition for stimulating hair growth, comprising the peptide of any of claims 1 to 14.
16. The composition of claim 15, wherein the composition comprises about 0.01 wt % or greater of the peptide.
17. The composition of claim 15 or 16, wherein the composition further comprises one or more additional ligands that bind to CD44 that are selected from the group consisting of serglycin, chondroitin or a salt thereof, fibrin, collagen, fibronectin, insulin-like growth factor-binding protein (IGFBP), green fluorescent protein (GFP), and any combinations thereof.
18. The composition of any of claims 15 to 17, wherein the composition further comprises hyaluronic acid.
19. The composition of claim 18, wherein the hyaluronic acid has a molecular weight in a range of about 20 kDa to 1350 kDa, about 4 kDa to about 10 kDa, about 10 kDa to about 100 kDa, about 15 kDa to about 50 kDa, or about 75 kDa to about 350 kDa.
20. The composition of claim 18 or 19, wherein the hyaluronic acid is cross-linked.
21. The composition of any of claims 15 to 20, wherein the composition comprises a hyaluronidase inhibitor.
22. The composition of any of claims 15 to 21, wherein the composition comprises a carrier medium, optionally wherein the carrier medium comprises a saline solution.
23. A method of stimulating hair growth in a skin of a patient in need thereof, comprising administering to the skin of the patient the composition of any of claims 15 to 22.
24. The method of claim 23, wherein the administering comprises applying the composition to a surface of the skin.

25. The method of claim 23, wherein the administering comprises injecting the composition into a dermal layer or a hypodermal layer of the skin.
26. The method of any of claims 23 to 25, wherein the composition is encased in a liposome.
27. The method of any of claims 23 to 26, wherein the method further comprises applying electroporation to the skin.
28. The method of any of claims 23 to 27, wherein the method further comprises applying sonophoresis to the skin.
29. The method of any of claims 23 to 28, wherein the method further comprises applying laser ablation to the skin.
30. The method of any of claims 23 to 29, wherein the method further comprises applying magnetophoresis to the skin.
31. The method of any of claims 23 to 30, wherein the method further comprises applying radiofrequency thermal ablation to the skin.
32. The method of any of claims 23 to 31, wherein the method further comprises applying a microneedle device to the skin.
33. A peptide for stimulating hair growth, comprising a sequence having at least 80%, at least 85%, at least 90%, at least 95, or at least 99%, sequence identity with a sequence selected from the group consisting of SEQ ID NOs: 97 or 98.
34. A nucleotide encoding any of the peptides of claims 1 to 33.