neurotransmitters. The beneficial effects of cyclosporine A treatment in DED are well established; however, it is clear that many patients with DED do not show a consistent therapeutic response to topical cyclosporine A.

[00012] Thus, there are currently few effective therapeutic options for the majority of patients with dry eye and ocular diseases associated with inflammation. Surprisingly, the disclosed modified peptides can be shown to inhibit T cell migration in response to inflammation in ocular diseases. As such, there is a high unmet need for effective and safe therapies. The present invention satisfies this need and provides other advantages as well.

SUMMARY

[00013] In one example, provided herein are compositions and methods for treating dry eye and ocular diseases associated with inflammation in a subject in need thereof. The method comprises administering to the subject a therapeutically effective amount of a composition comprising a peptide compound referred to as peptide inhibitors of trans-endothelial migration of T cells or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient to treat ocular diseases associated with inflammation in the subject. In some examples, the composition includes two or more different, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 or more different peptides or analogues thereof or pharmaceutically acceptable salts thereof.

[00014] In some examples, the peptide is represented by the peptide sequences as illustrated below in Table 1. In one example included are analogues, variants, derivatives, and pharmaceutically acceptable salts thereof of the peptides of Table 1. In one example, the ophthalmic composition comprises a peptide selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:35, including an analogue thereof, a variant thereof and a derivative thereof. In one example a polynucleotide sequence encodes the peptide of any one of SEQ ID NO:1 to SEQ ID NO:35. The polynucleotide encoding the peptide can be the DNA form or DNA/RNA hybrid forms thereof; and any complementary sequence thereof. In one example, the ophthalmic composition has a peptide or analogue thereof of the peptides in Table 1 or a polynucleotide sequence encoding the peptide of any one of SEQ ID NO:1 to SEQ ID NO:35. The polynucleotide encoding the peptide can be the DNA form or DNA/RNA hybrid forms thereof; and any complementary sequence thereof. In one example the peptide is a synthetic peptide.

[00015] In one aspect, the present disclosure is a composition comprising one or more peptides comprising a peptide selected from the group consisting of H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:1), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH2 (SEQ ID NO:2), H-Hyp-Val-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-Glu-Aha-NH2 (SEQ ID NO:3), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:4), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:5), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:6), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH2 (SEQ ID NO:7), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:8), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:9), H-Chex-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-DGln-NH2 (SEQ ID NO:10), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:11), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:12), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:13), H-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:14), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:15), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:16), H-DSer-Glu-Gln-Gly-Ala-Glu-Leu-DSer-DAsn-DGln-NH2 (SEQ ID NO:17), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-NH2 (SEQ ID NO:18), H-DSer-Val-Thr-Glu-Gln-Nva-Ala-Glu-Nle-NH2 (SEQ ID NO:19), H-Hyp-Val-Thr-Glu-Gln-Gly-βAla-Glu-Aha-NH2 (SEQ ID NO:20), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-NH2 (SEQ ID NO:21), H-Nva-Thr-Glu-Gln-Nva-Ala-Glu-Leu-DSer-NH2 (SEQ ID NO:22), H-Chex-Thr-Glu-Gln-Gly-βAla-Glu-Leu-Hyp-NH2 (SEQ ID NO:23), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-NH2 (SEQ ID NO:24), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Leu-Ser-DAsn-NH2 (SEQ ID NO:25), H-DSer-Glu-Gln-Gly-βAla-Glu-Leu-Ser-DGln-NH2 (SEQ ID NO:26), H-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:27), H-NMeGlu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:28), H-IsoGln-Gln-Gly-βAla-Glu-Leu-Ser-Asn-GluOMe-NH2 (SEQ ID NO:29), H-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:30), H-DAsn-Gly-Ala-Glu-Nle-Ser-Asn-Glu-NMeGlu-NH2 (SEQ ID NO:31), H-IsoGln-Gly-βAla-Glu-Leu-Ser-Asn-Glu-GluOMe-NH2 (SEQ ID NO:32), H-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:33), H-Nva-Ala-Glu-Nle-Ser-Asn-Glu-Glu-Orn-NH2 (SEQ ID NO:34), and H-βAla-Ala-Glu-Leu-DSer-Asn-Glu-Glu-NMeArg-NH2 (SEQ ID NO:35), an analogue thereof, a variant thereof, and a derivative thereof.

[00016] In yet another aspect, the present disclosure is a composition of one or more peptides consisting of a peptide selected from the group consisting of H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:1), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH2 (SEQ ID NO:2), H-Hyp-Val-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-Glu-Aha-NH2 (SEQ ID NO:3), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:4), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:5), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:6), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH2 (SEQ ID NO:7), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:8), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:9), H-Chex-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-DGln-NH2 (SEQ ID NO:10), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:11), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:12), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:13), H-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH2 (SEQ ID NO:14), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:15), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:16), H-DSer-Glu-Gln-Gly-Ala-Glu-Leu-DSer-DAsn-DGln-NH2 (SEQ ID NO:17), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-NH2 (SEQ ID NO:18), H-DSer-Val-Thr-Glu-Gln-Nva-Ala-Glu-Nle-NH2 (SEQ ID NO:19), H-Hyp-Val-Thr-Glu-Gln-Gly-βAla-Glu-Aha-NH2 (SEQ ID NO:20), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-NH2 (SEQ ID NO:21), H-Nva-Thr-Glu-Gln-Nva-Ala-Glu-Leu-DSer-NH2 (SEQ ID NO:22), H-Chex-Thr-Glu-Gln-Gly-βAla-Glu-Leu-Hyp-NH2 (SEQ ID NO:23), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-NH2 (SEQ ID NO:24), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Leu-Ser-DAsn-NH2 (SEQ ID NO:25), H-DSer-Glu-Gln-Gly-βAla-Glu-Leu-Ser-DGln-NH2 (SEQ ID NO:26), H-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH2 (SEQ ID NO:27), H-NMeGlu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH2 (SEQ ID NO:28), H-IsoGln-Gln-Gly-βAla-Glu-Leu-Ser-Asn-GluOMe-NH2 (SEQ ID NO:29), H-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH2 (SEQ ID NO:30), H-DAsn-Gly-Ala-Glu-Nle-Ser-Asn-Glu-NMeGlu-NH2 (SEQ ID NO:31), H-IsoGln-Gly-βAla-Glu-Leu-Ser-Asn-Glu-GluOMe-NH2 (SEQ ID NO:32), H-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH2 (SEQ ID NO:33), H-Nva-Ala-Glu-Nle-Ser-Asn-Glu-Glu-Orn-NH2 (SEQ ID NO:34), and H-βAla-Ala-Glu-Leu-DSer-Asn-Glu-Glu-NMeArg-NH2 (SEQ ID NO:35), an analogue thereof, a variant thereof, and a derivative thereof.

[00016a] In another aspect, the present disclosure refers to a pharmaceutical composition as disclosed herein, and a pharmaceutically acceptable excipient.

[00016b] In another aspect, the present disclosure refers to a use of an ophthalmic composition as disclosed herein in the manufacture of a medicament for treating dry eye, wherein the medicament is to be administered via topical treatment, intravitreal injection, subconjunctival injection, conjunctival injection, intramuscular injection, subcutaneous injection, intravenous injection, intracameral injection, and implantation into a subject's eye.

[00016c] In another aspect, the present disclosure refers to a use of a composition comprising a peptide as disclosed herein and a pharmaceutically acceptable excipient in the manufacture of a medicament treating dry eye in a subject in need thereof.

[00017] In one example, provided is a pharmaceutical composition comprising at least one peptide compound of Table 1, or a pharmaceutically active salt thereof; and a pharmaceutically acceptable excipient. The pharmaceutical composition with the at least one peptide compound of Table 1, or a pharmaceutically active salt thereof can be present in the composition in an amount sufficient to improve tear film stability when the pharmaceutical composition is administered to the subject in need thereof. In one example the pharmaceutically acceptable excipient can comprise at least one of a solvent, a buffering agent, a preservative, a chelating agent, an antioxidant, a stabilizer, an emulsifying agent, a suspending agent, and a diluent. In one example the composition further has 1.0% to 10.0% Lifitegrast or a salt thereof.

[00018] In some examples, the composition can be used to treat dry eye having at least one symptom of dry eye is selected from the group consisting of redness, discharge, excessive tearing, inability to produce tears, dryness, irritation, itchiness, pain, discomfort, inflammation, fatigue, foreign body sensation, light sensitivity, blurred vision, and any combination thereof of the eye, stinging, burning or scratchy sensation in the eye; ocular dryness or grittiness; stringy mucus in or around the eye; increase eye irritation; eye fatigue; sensitivity to light (photophobia); eye redness; excessive tearing; episode of blurred vision; foreign body sensation in the eye; pain or soreness around or in the eye; inability to cry when emotionally stressed; decreased tolerance of an activity requiring sustained visual attention; and any combination thereof. In some examples, the dry eye presents at least one symptom or clinical sign of dry eye including but not limited to a change in tear secretion, a change in tear clearance, ocular surface damage, corneal epithelial defects, a change in ocular surface cells, a change in tear film stability, a change in tear volume, a change in tear film composition, a change in tear osmolarity, and any combination thereof. In some examples, the dry eye is selected from the group consisting of hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens-Johnson syndrome, ocular pemphigoid, blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact lens wearing-associated dry eye. In one example, the dry eye is an ocular disease associated with inflammation selected from the group consisting of uveitis, scleritis, post-eye surgery inflammation, corneal transplantation, corneal

wound healing, conjunctivitis, retinal disease, glaucoma, ocular hypertension, pterygium and a combination thereof.

[00019] In some examples the composition for treatment of dry eye can be administered topically, by intravitreal injection, by subconjunctival injection, by conjunctival injection, by intramuscular injection, by subcutaneous injection, by intravenous injection, by intracameral injection, or by implantation into the subject's eye. In some examples, the composition is in a formulation selected from the group consisting of a solution, suspension, syrup, liquid, gel, hydrogel, emulsion, liposome, aerosol, mist, film, suspension, plug, polymer, implant, contact lens, ocular insert, nanoparticle, microparticle, a sustained release formulation, and a formulation suitable for an ocular medical device. In some examples, the peptide compound is present in an amount between about 0.01% (wt) to about 5.0% (wt) of the final composition. In some examples, the composition is administered to the subject once a day, two times a day, three times a day or more often (more frequently). In other examples, the composition is administered every other day or less often (less frequently). In some examples, the subject in need thereof can further receive a composition comprising cyclosporine, artificial tears, lifitegrast, tavilermide, a corticosteroid, an anti-inflammatory agent, or any combination thereof.

[00020] In another example, provided herein is a method for treating dry eye in a subject in need thereof. The method comprises administering to the subject a therapeutically effective amount of a composition comprising at least one peptide of Table 1 or a pharmaceutically salt thereof and a pharmaceutically acceptable excipient to treat dry eye in the subject. In some examples, the peptide can be administered topically, by intravitreal injection, by subconjunctival injection, by conjunctival injection, by intramuscular injection, by subcutaneous injection, by intravenous injection, by intracameral injection, or by implantation into the subject's eye. In some examples, the dry eye presents at least one symptom or clinical sign of dry eye diseases selected from the group consisting hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens- Johnson syndrome, ocular pemphigoid, blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact lens wearing-associated dry eye.

[00021] In one example the composition further has 1.0% to 10.0% Lifitegrast or a salt thereof. In some examples, the composition is administered to the subject once a day, two times a day, three times a day or more often (more frequently). In other examples, the composition is administered every other day or less often (less frequently). In some examples, the peptide compound is present in an amount between about 0.01% (wt) to about 5.0% (wt) of the final composition. In some examples, the subject in need thereof can further receive a composition comprising cyclosporine, artificial tears, a corticosteroid, an anti-inflammatory agent, or any combination thereof. In one example, the method administers a peptide selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:35, an analogue thereof, a variant thereof, a derivative thereof, or a pharmaceutically acceptable salt thereof. In another example the method utilizes a polynucleotide sequence encoding the peptide of any one of SEQ ID NO:1 to SEQ ID NO:35. The polynucleotide encoding the peptide can be the DNA form or DNA/RNA hybrid forms thereof; and any complementary sequence thereof. In one example, the method administers a pharmaceutically acceptable composition comprising the peptide or analogue thereof of SEQ ID NO:1 to SEQ ID NO:35. In one example the peptide is a synthetic peptide.

[00022] In one example, the method alleviates or treats at least one symptom of dry eye is selected from the group consisting of redness, discharge, excessive tearing, inability to produce tears, dryness, irritation, itchiness, pain, discomfort, inflammation, fatigue, foreign body sensation, light sensitivity, blurred vision, and any combination thereof of the eye. In some examples, the dry eye presents at least one symptom or clinical sign of dry eye including but not limited to a change in tear secretion, a change in tear clearance, ocular surface damage, corneal epithelial defects, a change in ocular surface cells, a change in tear film stability, a change in tear volume, a change in tear film composition, a change in tear osmolarity, and any combination thereof. In some examples, the dry eye presents at least one symptom or clinical sign of dry eye diseases selected from the group consisting hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens- Johnson syndrome, ocular pemphigoid, blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact

lens wearing-associated dry eye. In one example, the dry eye is an ocular disease associated with inflammation selected from the group consisting of uveitis, scleritis, post-eye surgery inflammation, corneal transplantation, corneal wound healing, conjunctivitis, retinal disease, glaucoma, ocular hypertension, pterygium and a combination thereof.

[00023] In yet another example, provided herein is a method for treating an ocular disease associated with inflammation in a subject in need thereof. The method comprises administering to the subject a therapeutically effective amount of a composition comprising a peptide compound or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient to treat the ocular disease associated with inflammation in the subject. In some examples, the composition includes two or more, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 or more different peptides or analogues thereof or pharmaceutically acceptable salts thereof. In some examples, the ocular disease associated with inflammation is selected from the group consisting of uveitis, scleritis, post-eye surgery inflammation, corneal transplantation, corneal wound healing, conjunctivitis, retinal disease, glaucoma, ocular hypertension, pterygium and a combination thereof.

[00024] In another example, provided herein is a method for alleviating at least one symptom or clinical sign of dry eye in a subject in need thereof. The method comprises administering to the subject a therapeutically effective amount of a composition comprising a peptide compound or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient to alleviate at least one symptom or clinical sign of dry eye in the subject. In some examples, the composition includes two or more different, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 or more different peptide compounds or pharmaceutically acceptable salts thereof.

[00025] In another example, provided herein is a method for treating an ocular disease associated with inflammation in a subject in need thereof. The method comprises administering to the subject a therapeutically effective amount of a composition comprising a peptide compound or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient to treat the ocular disease associated with inflammation in the subject. In some examples, the composition includes two or more different, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 or more different peptide compounds or pharmaceutically acceptable salts thereof.

[00026] In one example, the method for alleviating at least one symptom or

clinical sign of dry eye or for treating an ocular disease can be administered topically, by intravitreal injection, by subconjunctival injection, by conjunctival injection, by intramuscular injection, by subcutaneous injection, by intravenous injection, by intracameral injection, or by implantation into the subject's eye. In one example, the method for alleviating at least one symptom or clinical sign of dry eye or for treating an ocular disease is selected from the group consisting of hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens-Johnson syndrome, ocular pemphigoid blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact lens wearing-associated dry eye. In one example, the method for alleviating at least one symptom or clinical sign of dry eye or for treating an ocular disease comprises at least one symptom of dry eye selected from the group consisting of redness, discharge, excessive tearing, inability to produce tears, dryness, irritation, itchiness, pain, discomfort, inflammation, fatigue, foreign body sensation, light sensitivity, blurred vision, and any combination thereof of the eye. In some examples, at least one clinical sign of dry eye is selected from the group consisting of a change in tear secretion, a change in tear clearance, a change in tear osmolarity, ocular surface damage, corneal epithelial defects, a change in ocular surface cells, a change in tear film stability, a change in tear volume, a change in tear film composition, a change in goblet cell or Meibomian or lacrimal gland physiology, appearance, number, or function and any combination thereof.

[00027] In some examples, the method for alleviating at least one symptom or clinical sign of dry eye or for treating an ocular disease in which the composition can be administered in a formulation selected from the group consisting of a solution, suspension, syrup, liquid, gel, hydrogel, emulsion, liposome, aerosol, mist, film, suspension, plug, polymer, implant, contact lens, ocular insert, nanoparticle, microparticle, a sustained release formulation, and a formulation suitable for an ocular medical device. In some examples, the peptide compound is present in an amount between about 0.01% (wt) to about 5.0% (wt) of the final composition. In some examples, the composition is administered to the subject once a day, two times a day, three times a day or more often (more frequently). In other examples, the composition is administered every other day or less often (less

frequently). In some embodiments, the subject in need thereof can further receive a composition comprising cyclosporine, artificial tears, a corticosteroid, an anti-inflammatory agent, or any combination thereof. In one example the methods for treating dry eye further comprises administering to the subject a therapeutically effective amount of a peptide composition further having about 1.0% to about 10.0% Lifitegrast.

[00028] In one example, the method for alleviating at least one symptom or clinical sign of dry eye or for treating an ocular disease comprises administering a peptide selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:35, an analogue thereof, a variant thereof, a derivative thereof, or a pharmaceutically acceptable salt thereof. In one example, the peptide or an analogue thereof can be administered as a pharmaceutically acceptable composition. In one example, the peptide or an analogue thereof can be used for alleviating at least one symptom or clinical sign of dry eye or for treating an ocular disease.

BRIEF DESCRIPTION OF THE DRAWINGS

[00029] FIG. 1 is a bar chart illustrating the change in tear film break-up time when a dry eye is treated with either 5% Lifitegrast or 0.1% SEQ ID NO:1, a peptide inhibitor of trans-endothelial migration(PEPITEM) at five and ten days post treatment.

[00030] FIG. 2 is a bar chart illustrating changes in corneal staining when dry eye is treated with either 5% Lifitegrast or 0.1% SEQ ID NO:1, a peptide inhibitor of trans-endothelial migration(PEPITEM) at five and ten days post treatment.

[00031] FIG. 3 depicts four photos of corneal surface staining.

[00032] FIG. 4A-4E provides scatter plots illustrating the change in activated T cell presence when dry eye presents within the conjunctiva and 10 days after treatment. FIG. 4A represents the scatter plot of activated T cell level of normal (UT) eye; FIG. 4B represents the scatter plots of activated T cell level of dry eye (Vehicle); FIG. 4C represents scatter plots of activated T cell level after administration of 5% Lifitegrast; FIG. 4D represents scatter plots of activated T cell level after administration of 0.1% SEQ ID NO:1, a peptide inhibitor of trans-endothelial migration.

WHAT IS CLAIMED IS:

1. A composition comprising one or more peptides comprising the peptides selected from the group consisting of H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:1), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH_2 (SEQ ID NO:2), H-Hyp-Val-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-Glu-Aha-NH_2 (SEQ ID NO:3), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:4), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:5), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:6), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH_2 (SEQ ID NO:7), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:8), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:9), H-Chex-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-DGln-NH_2 (SEQ ID NO:10), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:11), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:12), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:13), H-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:14), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:15), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:16), H-DSer-Glu-Gln-Gly-Ala-Glu-Leu-DSer-DAsn-DGln-NH_2 (SEQ ID NO:17), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-NH_2 (SEQ ID NO:18), H-DSer-Val-Thr-Glu-Gln-Nva-Ala-Glu-Nle-NH_2 (SEQ ID NO:19), H-Hyp-Val-Thr-Glu-Gln-Gly-βAla-Glu-Aha-NH_2 (SEQ ID NO:20), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-NH_2 (SEQ ID NO:21), H-Nva-Thr-Glu-Gln-Nva-Ala-Glu-Leu-DSer-NH_2 (SEQ ID NO:22), H-Chex-Thr-Glu-Gln-Gly-βAla-Glu-Leu-Hyp-NH_2 (SEQ ID NO:23), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-NH_2 (SEQ ID NO:24), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Leu-Ser-DAsn-NH_2 (SEQ ID NO:25), H-DSer-Glu-Gln-Gly-βAla-Glu-Leu-Ser-DGln-NH_2 (SEQ ID NO:26), H-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:27), H-NMeGlu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:28), H-IsoGln-Gln-Gly-βAla-Glu-Leu-Ser-Asn-GluOMe-NH_2 (SEQ ID NO:29), H-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:30), H-DAsn-Gly-Ala-Glu-Nle-Ser-Asn-Glu-NMeGlu-NH_2 (SEQ ID NO:31), H-IsoGln-Gly-βAla-Glu-Leu-Ser-Asn-Glu-GluOMe-NH_2 (SEQ ID NO:32), H-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:33), H-Nva-Ala-Glu-Nle-Ser-Asn-Glu-Glu-Orn-NH_2 (SEQ ID NO:34), and H-βAla-Ala-Glu-Leu-DSer-Asn-Glu-Glu-NMeArg-NH_2 (SEQ ID NO:35), an analogue thereof, a variant thereof, and a derivative thereof.

2. A composition of one or more peptides consisting of a peptide selected from the group consisting of H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:1), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH_2 (SEQ ID NO:2), H-Hyp-Val-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-Glu-Aha-NH_2 (SEQ ID NO:3), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:4), H-DSer-Val-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-

Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:5), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:6), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-Glu-Orn-NH_2 (SEQ ID NO:7), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:8), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:9), H-Chex-Thr-NMeGlu-Gln-Gly-Ala-Glu-Leu-Hyp-DAsn-Glu-DGln-NH_2 (SEQ ID NO:10), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:11), H-Nva-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:12), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:13), H-AlloThr-Glu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-GluOMe-NH_2 (SEQ ID NO:14), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:15), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:16), H-DSer-Glu-Gln-Gly-Ala-Glu-Leu-DSer-DAsn-DGln-NH_2 (SEQ ID NO:17), H-Ser-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-NH_2 (SEQ ID NO:18), H-DSer-Val-Thr-Glu-Gln-Nva-Ala-Glu-Nle-NH_2 (SEQ ID NO:19), H-Hyp-Val-Thr-Glu-Gln-Gly-βAla-Glu-Aha-NH_2 (SEQ ID NO:20), H-Val-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-NH_2 (SEQ ID NO:21), H-Nva-Thr-Glu-Gln-Nva-Ala-Glu-Leu-DSer-NH_2 (SEQ ID NO:22), H-Chex-Thr-Glu-Gln-Gly-βAla-Glu-Leu-Hyp-NH_2 (SEQ ID NO:23), H-Thr-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-NH_2 (SEQ ID NO:24), H-AlloThr-Glu-Gln-Nva-Ala-Glu-Leu-Ser-DAsn-NH_2 (SEQ ID NO:25), H-DSer-Glu-Gln-Gly-βAla-Glu-Leu-Ser-DGln-NH_2 (SEQ ID NO:26), H-Glu-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-NH_2 (SEQ ID NO:27), H-NMeGlu-Gln-Gly-Ala-Glu-Nle-Ser-Asn-NMeGlu-NH_2 (SEQ ID NO:28), H-IsoGln-Gln-Gly-βAla-Glu-Leu-Ser-Asn-GluOMe-NH_2 (SEQ ID NO:29), H-Gln-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-NH_2 (SEQ ID NO:30), H-DAsn-Gly-Ala-Glu-Nle-Ser-Asn-Glu-NMeGlu-NH_2 (SEQ ID NO:31), H-IsoGln-Gly-βAla-Glu-Leu-Ser-Asn-Glu-GluOMe-NH_2 (SEQ ID NO:32), H-Gly-Ala-Glu-Leu-Ser-Asn-Glu-Glu-Arg-NH_2 (SEQ ID NO:33), H-Nva-Ala-Glu-Nle-Ser-Asn-Glu-Glu-Orn-NH_2 (SEQ ID NO:34), and H-βAla-Ala-Glu-Leu-DSer-Asn-Glu-Glu-NMeArg-NH_2 (SEQ ID NO:35), an analogue thereof, a variant thereof, and a derivative thereof; optionally wherein the peptide is a synthetic peptide.

3. The composition of any one of claims 1 to 2, wherein (i) a polynucleotide sequence encodes the peptide of any one of SEQ ID NO:1 to SEQ ID NO:35, an analogue thereof, a variant thereof, or a derivative thereof; and/or (ii) wherein the polynucleotide encoding the peptide is the DNA form or DNA/RNA hybrid forms thereof; and any complementary sequence thereof.

4. A pharmaceutical composition of claims 1 or 2, and a pharmaceutically acceptable excipient.

5. The pharmaceutical composition of claim 5 wherein (i) the peptide is present in an amount sufficient to improve tear film stability in the dry eye when the pharmaceutical composition is to be administered to the subject in need thereof; and/or wherein (ii) the pharmaceutically acceptable excipient comprises at least one

of a solvent, a buffering agent, a preservative, a chelating agent, an antioxidant, a stabilizer, an emulsifying agent, a suspending agent, and a diluent.

6. The composition of any one of claims 1 to 5, further comprising 1.0% to 10.0% Lifitegrast or a salt thereof.

7. Use of an ophthalmic composition of any one of claims 1 to 6 in the manufacture of a medicament for treating dry eye, wherein the medicament is to be administered via topical treatment, intravitreal injection, subconjunctival injection, conjunctival injection, intramuscular injection, subcutaneous injection, intravenous injection, intracameral injection, and implantation into a subject's eye.

8. The use of claim 7, wherein (i) the dry eye presents at least one symptom or clinical sign of dry eye selected from the group consisting of a change in tear secretion, a change in tear clearance, ocular surface damage, corneal epithelial defects, a change in ocular surface cells, a change in tear film stability, a change in tear volume, a change in tear film composition, a change in tear osmolarity, and any combination thereof; or wherein (ii) the dry eye presents at least one symptom or clinical sign of dry eye selected from the group consisting of hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens-Johnson syndrome, ocular pemphigoid blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact lens wearing-associated dry eye; or wherein (iii) the dry eye is an ocular disease associated with inflammation selected from the group consisting of uveitis, scleritis, post-eye surgery inflammation, corneal transplantation, corneal wound healing, conjunctivitis, retinal disease, glaucoma, ocular hypertension, pterygium and a combination thereof.

9. The composition of any one of claims 1 to 6 or the use according to any one of claims 7 to 8, wherein the peptide is present in an amount between about 0.01% (wt) to about 5.0% (wt) of the final composition.

10. The composition of any one of claims 1 to 6 and 9, or the use according to any one of claims 7 to 9, wherein (i) the composition or the medicament is to be administered to a subject in need thereof once a day, two times a day, three times a day or more often; and/or (ii) wherein the composition or the medicament is to be administered to the subject in need thereof every other day or less often.

11. The composition of any one of claims 1 to 7, 9 and 10, or the use according to any one of claims 7 to 10, wherein the composition is in a formulation selected from the group consisting of a solution, suspension, syrup, liquid, gel, hydrogel, emulsion,

liposome, aerosol, mist, film, suspension, plug, polymer, implant, contact lens, ocular insert, nanoparticle, microparticle, a sustained release formulation, and a formulation suitable for an ocular medical device.

12. The use according to any one of claims 7 to 11, wherein the use further comprises a composition comprising cyclosporin, artificial tears, a corticosteroid, an anti-inflammatory agent, or any combination thereof to be administered to a subject in need thereof.

13. The composition of any one of claims 1 to 6 and 9 to 11, or the use of any one of claims 7 to 12, wherein the composition further comprises two or more different peptides or analogues thereof.

14. Use of a composition comprising a peptide of claims 1 or 2 and a pharmaceutically acceptable excipient in the manufacture of a medicament treating dry eye in a subject in need thereof.

15. The use of claim 14, wherein (i) the peptide is to be administered topically, by intravitreal injection, by subconjunctival injection, by conjunctival injection, by intramuscular injection, by subcutaneous injection, by intravenous injection, by intracameral injection, or by implantation into the subject's eye; and/or wherein (ii) the dry eye is selected from the group consisting of hypolacrimation, tear deficiency, xerophthalmia, Sjogren's syndrome dry eye, non-Sjogren's syndrome dry eye, keratoconjunctivitis sicca, aqueous tear-deficiency dry eye (ADDE), evaporative dry eye (EDE), environmental dry eye, Stevens-Johnson syndrome, ocular pemphigoid blepharitis marginal, eyelid-closure failure, sensory nerve paralysis, allergic conjunctivitis-associated dry eye, post-viral conjunctivitis dry eye, post-cataract surgery dry eye, VDT operation-associated dry eye, and contact lens wearing-associated dry eye.

16. The use of any one of claims 14-15, further comprising about 1.0% to about 10.0% Lifitegrast.

17. The use of any one of claims 14-16, wherein (i) the composition is to be administered to the subject once a day, two times a day, three times a day or more often; and/or wherein (ii) the composition is to be administered every other day or less often.

18. The use of any one of claims 14-17, wherein the peptide is present in an amount between about 0.01% (wt) to about 5.0% (wt) of the final composition.

19. The use of any one of claims 14-18, wherein the composition is in a formulation selected from the group consisting of a solution, suspension, syrup, liquid, gel, hydrogel, emulsion, liposome, aerosol, mist, film, suspension, plug, polymer, implant,

contact lens, ocular insert, nanoparticle, microparticle, a sustained release formulation, and a formulation suitable for an ocular medical device.

20. The use of any one of claims 14- 19, further comprising a composition comprising cyclosporin (0.1 to 1.0 mg/ml), artificial tears, a corticosteroid, an anti-inflammatory agent, or any combination thereof to be administered.