

SUMMARY ~~OF THE INVENTION~~

The present ~~invention~~disclosure provides compositions and methods for the amelioration of symptoms associated with the release of inflammatory cytokines. These cytokines are known to be a part of the etiology and pathology of many inflammatory disorders. The diseases and disorders amenable to treatment with the compositions of the ~~invention~~disclosure include but are not limited to inflammatory diseases of the eye, ear, lung, and bowel. The diseases and disorders amenable to treatment also include autoimmune diseases where the administration of the medicaments may be chronic administration in order to prevent exacerbations.

The present ~~invention~~disclosure is based in part on the finding in in-vitro and in-vivo models, that the peptides denoted ZEP3 and ZEP4 show unexpectedly strong activity in attenuating the expression and/or release of inflammatory and pro-inflammatory mediators, including the specific cytokines interferon gamma (IFN-gamma, IFN γ), interleukin 1 beta (IL-1 beta, IL-1 β), interleukin 10 (IL-10), tumor necrosis factor alpha (TNF alpha, TNF α), and interleukin 6 (IL-6), and the mediators reactive oxygen species (ROS) and RANTES (Regulated upon activation normal T cell expressed and presumably secreted).

It was surprisingly found that the activity of the peptides in inhibition of the inflammatory cascades, is exerted even when the peptides are administered before the inflammatory reaction is initiated. Thus, the peptides can ameliorate or suppress the symptoms induced in various inflammatory diseases and disorders and can be useful to eliminate the inflammatory reaction altogether. It is envisaged that the compositions of the present ~~invention~~disclosure can be useful to prevent exacerbations in chronic inflammatory diseases.

It is to be understood explicitly that use of the compositions of the ~~invention~~disclosure to treat inflammatory diseases does not include treatment of skin disorders or pain per se.

~~According to one aspect of the present invention there~~There is provided a pharmaceutical composition comprising as an active ingredient a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, wherein X₁ is a polar amino acid residue; X₂ is an aromatic or hydrophobic amino acid residue; and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue, or a pharmaceutically acceptable salt or derivative thereof; and a pharmaceutically acceptable carrier, for use in reducing the release or inhibiting the activity of an inflammatory cytokine.

According to some [embodimentsexamples](#), X₁ is selected from the group consisting of: Asn, Gln, His, Ser, Thr, Tyr, and Cys, X₂ is selected from Trp, Phe, Tyr, Ala, Ile, Leu, Met, Val, and Gly and X₃ is selected from Lys, Lys derivative, Arg, His, Asn, Gln, His, Ser, Thr, and Tyr.

5 According to yet other [embodimentsexamples](#), X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr.

According to some [embodimentsexamples](#), the peptide derivative comprises an alkyl group attached to a free functional group of the peptide sequence.

10 According to yet other [embodimentsexamples](#), the alkyl group is attached by an amide bond or linkage to a free amino group of a side chain or the N-terminal of the peptide.

According to some [embodimentsexamples](#), the alkyl a C4 to C30 alkyl.

15 According to some specific [embodimentsexamples](#), a C8 alkyl group (herein octanoyl), is attached by an amide linkage to the side chain of a Lys residue of the peptide sequence or a terminal amino group of the peptide. According to some [embodimentsexamples](#), the carboxy terminus of the peptide is modified, to form for example by an amide, alcohol or ester terminus,

20 According to some specific [embodimentsexamples](#), the peptide is selected from the group consisting of: pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1), pGlu-Asn-Trp-Thr-OH (SEQ ID NO: 2) and pharmaceutically acceptable derivatives and salts thereof.

According to some [embodimentsexamples](#), the inflammatory cytokine is selected from the group consisting of: TNF alpha, IL-1 beta, IL-6, IL-10 and IFN gamma.

The present [inventiondisclosure](#) provides, ~~according to yet another aspect~~, a pharmaceutical composition comprising as an active ingredient a peptide according to 25 Formula I: pGlu-X₁-X₂-X₃-OH, wherein X₁ is a polar amino acid residue; X₂ is an aromatic or hydrophobic amino acid residue; and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue, or a pharmaceutically acceptable salt or derivative thereof; and a pharmaceutically acceptable carrier, for use in reducing the release of an inflammatory mediator or chemokine, wherein the mediator or chemokine.

30 According to some specific [embodimentsexamples](#), the peptide selected from the group consisting of: pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1), pGlu-Asn-Trp-Thr-OH (SEQ ID NO: 2) and pharmaceutically acceptable derivatives and salts thereof.

According to some [embodimentsexamples](#), the inflammatory mediator or cytokine is selected from the group consisting of reactive oxygen species (ROS) and RANTES (Regulated upon activation normal T cell expressed and presumably secreted).

~~According to another aspect of the present invention there~~ [There](#) is provided a method of reducing the release or inhibiting the activity of at least one inflammatory or pro-inflammatory cytokine, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, wherein X₁ is a polar amino acid residue; X₂ is an aromatic or hydrophobic amino acid residue; and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue, or a pharmaceutically acceptable salt or derivative thereof.

~~According to another aspect, there~~ [There](#) is provided a method of reducing the release of an inflammatory mediator or chemokine, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, wherein X₁ is a polar amino acid residue; X₂ is an aromatic or hydrophobic amino acid residue and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue, or a pharmaceutically acceptable salt or derivative thereof.

According to some [embodimentsexamples](#), the inflammatory mediator or chemokine is selected from the group consisting of ROS and RANTES.

~~According to yet another aspect, the~~ [The](#) present [inventiondisclosure](#) provides a method of treating an inflammatory disease or disorder. According to specific [embodimentsexamples](#) the inflammatory disease or disorder is selected from the group consisting of: an eye inflammatory disease or disorder, an ear inflammatory disease or disorder, a lung inflammatory disease or disorder, a bowel inflammatory disease or disorder, or an inflammatory autoimmune disease or disorder, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is a polar amino acid residue; X₂ is selected from an aromatic amino acid residue and a hydrophobic amino acid residue; and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue.

According to some [embodimentsexamples](#) the present [inventiondisclosure](#) provides methods of treating chronic inflammatory diseases. According to specific [embodimentsexamples](#) the step of

administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I is performed even before the symptoms have emerged or developed. These methods of treating chronic inflammatory diseases are effective to prevent exacerbations.

5 ~~According to yet another aspect, the~~The present ~~invention~~disclosure provides a method of treating an eye inflammatory disease or disorder, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is a polar amino acid residue; X₂ is an aromatic or
10 hydrophobic amino acid residue and X₃ is selected from a positively charged amino acid residue and a polar amino acid residue.

 According to some [embodimentsexamples](#), X₁ is selected from the group consisting of: Asn, Gln, His, Ser, Thr, Tyr and Cys; X₂ is selected from Trp, Phe, Tyr, Ala, Ile, Leu, Met, Val, and Gly; and X₃ is selected from Lys, Lys derivative, Arg, His, Asn, Gln, His,
15 Ser, Thr, and Tyr.

 According to yet other [embodimentsexamples](#), X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr.

 According to some specific [embodimentsexamples](#), the Lys derivative is Lys(Octanoyl).

20 According to some [embodimentsexamples](#), the peptide derivative comprises an alkyl group attached to a functional group of the peptide sequence.

 According to yet other [embodimentsexamples](#), the alkyl group is attached by an amide bond to an amino group of a side chain or a terminal of the peptide.

 According to some [embodimentsexamples](#), the alkyl is a C₄ to C₃₀ alkyl.

25 According to some specific [embodimentsexamples](#), a C₈ alkyl group (herein octanoyl), is attached by an amide bond to the side chain of a Lys residue or a terminal amino group of the peptide sequence.

 According to some specific [embodimentsexamples](#), the peptide is selected from the group consisting of: pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1), pGlu-Asn-Trp-
30 Thr-OH (SEQ ID NO: 2) and pharmaceutically acceptable salts or derivatives thereof.

Thus, in one aspect, the present disclosure provides use of a peptide selected from the group consisting of pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1), pGlu-Asn-Trp-Thr-OH (SEQ ID NO: 2), and pharmaceutically acceptable salts thereof in the manufacture of a pharmaceutical composition for treating an inflammatory disease or disorder selected from the group consisting of: an eye inflammatory disease or disorder, an ear inflammatory disease or disorder, a lung inflammatory disease or disorder, a bowel inflammatory disease or disorder, or an inflammatory autoimmune disease or disorder.

According to some ~~embodiments~~examples, the peptide has an amino acid sequence as set forth in SEQ ID NO: 1. In another aspect, the present disclosure provides an isolated sodium salt of a peptide having a sequence as set forth in SEQ ID NO: 1.

According to some [embodimentsexamples](#), the peptide has an amino acid sequence as set forth in SEQ ID NO: 2.

According to some [embodimentsexamples](#), the pharmaceutical composition comprises a derivative or a salt of a peptide having an amino acid sequence set forth in a sequence selected from SEQ ID NO: 1 and SEQ ID NO: 2.

According to some [embodimentsexamples](#), the method comprises administering a derivative or a salt of a peptide having an amino acid sequence set forth in a sequence selected from SEQ ID NO: 1 and SEQ ID NO: 2.

According to some [embodimentsexamples](#), the pharmaceutical composition comprises a sodium salt of a peptide set forth in any one of SEQ ID NO: 1 and SEQ ID NO: 2.

According to some [embodimentsexamples](#), the pharmaceutical composition is formulated for an administration via a route selected from the group consisting of: topical administration, ophthalmic administration, oral administration, nasal administration, and parenteral administration.

According to various [embodimentsexamples](#), formulations for topical administration may be selected from a cream, an ointment, a paste, a lotion, a gel or in the form of eyedrops.

According to some specific [embodimentsexamples](#), a cream formulation is provided comprising a peptide selected from SEQ ID NOs: 1 and 2, or a pharmaceutically acceptable salt thereof, for use in topical administration.

According to some [embodimentsexamples](#), the cream composition comprises 0.1-5% w/w of the peptide. According to other [embodimentsexamples](#), the composition comprises 0.5-2% of the peptide. According to yet other [embodimentsexamples](#), the composition comprises about 1% of the peptide.

According to some [embodimentsexamples](#), a composition according to the present [inventiondisclosure](#), has a pH of about 4 to about 8. According to some [embodimentsexamples](#), the composition has a pH of about 4.5 to about 6.5. According to yet other [embodimentsexamples](#), the composition has a pH of about 7 to about 9.

According to some [embodimentsexamples](#), the pharmaceutical composition comprises at least one excipient selected from the group consisting of: polysorbate 80, edetate disodium (EDTA), silicon dioxide, methylparaben, white petrolatum, isopropyl myristate, cetyl alcohol and glyceryl monostearate.

According to other [embodimentexamples](#), the composition for administration to a subject having a disease or injury of the eye is formulated in a form selected from the group consisting of a liquid solution or suspension for use as eyedrops, an emulsion, a cream, an ointment, a spray and a gel.

5 According to some [embodimentexamples](#), the disease or injury of the eye is an inflammatory disease or disorder selected from the group consisting of: uveitis, dry eye syndrome, inflammatory symptoms associated with an infectious eye disease, an allergic eye disease, keratitis, conjunctivitis, meibomian gland dysfunction and Sjogren syndrome.

10 According to still further [embodimentexamples](#), the pharmaceutical composition is formulated as eye drops, eye ointment, eye spray, ophthalmic suspension, ophthalmic emulsion, ophthalmic solution, ophthalmic gel, or intravitreal injection.

According to still further [embodimentexamples](#) the inflammatory disease or disorder in an autoimmune disease or disorder.

15 According to still further [embodimentexamples](#) the autoimmune disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, lupus, and Sjogren syndrome.

According to still further [embodimentexamples](#) the inflammatory disease or disorder is an inflammatory bowel disease.

20 According to still further [embodimentexamples](#) the inflammatory bowel disease is selected from the group consisting of Crohn's disease, ulcerative colitis and celiac disease.

According to still further [embodimentexamples](#) the inflammatory disease or disorder is an inflammatory disease or disorder of the lung.

25 According to still further [embodimentexamples](#) the inflammatory disease or disorder of the lung is selected from the group consisting of asthma, bronchitis, pleurisy, alveolitis, vasculitis, pneumonia, chronic bronchitis, bronchiectasis, diffuse panbronchiolitis, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis and cystic fibrosis.

According to still further [embodimentexamples](#) the inflammatory disease or disorder is an inflammatory disease or disorder of the ear.

30 According to still further [embodimentexamples](#) the inflammatory disease or disorder of the ear is selected from the group consisting of inflammatory symptoms associated with ear infection, otitis media, otitis externa, mastoiditis and otomastoiditis.

According to still further features [embodimentsexamples](#) the administration is ophthalmic administration.

According to still further [embodimentsexamples](#) the administration is oral administration.

According to still further [embodimentsexamples](#) the administration is nasal administration.

According to still further [embodimentsexamples](#) the administration is parenteral administration.

The present [inventiondisclosure](#) successfully addresses the shortcomings of the presently known configurations by providing pharmaceutical compositions for use in reducing the release or inhibiting the activity of inflammatory cytokines and mediators and for the treatment of diseases or disorders associated with inflammatory cytokines and mediators.

Unless otherwise defined, all technical and/or scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the [inventiondisclosure](#) pertains. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of [embodimentsexamples](#) of the [inventiondisclosure](#), exemplary methods and/or materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be necessarily limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

Some embodiments of the invention are herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of embodiments of the invention. In this regard, the description taken with the drawings makes apparent to those skilled in the art how embodiments of the invention may be practiced.

In the drawings:

Figure 1 is a bar graph illustrating the effect of ZEP4 (Z), concentration range: 3.125 – 100 µg/ml, on the amount of TNFα produced by inflammation-induced macrophage cells. Lines marked by **** represent statistically significant difference at $p < 0.0001$.

Figure 2 is a bar graph illustrating the effect of ZEP4 (Z), (50 µg/ml) on the amount of TNFα produced by inflammation-induced macrophage cells, treated with

CLAIMS:

1. ~~A pharmaceutical composition comprising as an active ingredient a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr, and a pharmaceutically acceptable carrier, for use in reducing the release or inhibiting the activity of at least one inflammatory cytokine.~~
2. ~~The pharmaceutical composition for use according to claim 1, wherein the at least one inflammatory cytokine is selected from the group consisting of: interferon gamma (IFN gamma), interleukin 1 beta (IL-1 beta), interleukin 10 (IL-10), tumor necrosis factor alpha (TNF alpha), and interleukin 6 (IL-6).~~
3. ~~The pharmaceutical composition for use according to claim 1, wherein the at least one inflammatory cytokine is selected from the group consisting of: TNF alpha, IL-1 beta and IL-6.~~
4. ~~A pharmaceutical composition comprising as an active ingredient a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr, and a pharmaceutically acceptable carrier, for use in reducing the release of at least one inflammatory mediator or chemokine.~~
5. ~~The pharmaceutical composition for use according to claim 4, wherein the at least one inflammatory mediator or chemokine is selected from the group consisting of reactive oxygen species (ROS) and RANTES (Regulated upon activation normal T-cell expressed and presumably secreted).~~
6. ~~The pharmaceutical composition according to any one of claims 1 to 5, wherein the peptide derivative comprises an alkyl group attached to an amino group of a side chain or a terminal amino group of the peptide.~~
7. ~~The pharmaceutical composition according to claim 6, wherein the alkyl group is attached by an amide linkage.~~
8. ~~The pharmaceutical composition according to claim 6 or 7, wherein the alkyl is a C₄ to C₃₀ alkyl.~~

9. ~~The pharmaceutical composition according to claim 8, wherein the alkyl is a C8 alkyl (octanoyl), attached to the side chain of a Lys residue via an amide linkage.~~
10. ~~The pharmaceutical composition according to any one of claims 1 to 5, wherein the peptide is selected from the group consisting of pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1) and pGlu-Asn-Trp-Thr-OH (SEQ ID NO: 2), and pharmaceutically acceptable salts and derivatives thereof.~~
11. ~~The pharmaceutical composition according to any one of claims 1 to 5, wherein said peptide has an amino acid sequence as set forth in SEQ ID NO: 1.~~
12. ~~The pharmaceutical composition according to any one of claims 1 to 5, wherein said peptide has an amino acid sequence as set forth in SEQ ID NO: 2.~~
13. ~~The pharmaceutical composition according to any one of the preceding claims having a pH in the range of about 4 to about 8.~~
14. ~~The pharmaceutical composition according to any one of the preceding claims, being formulated for an administration route selected from the group consisting of: topical administration, ophthalmic administration, oral administration, nasal administration, and parenteral administration.~~
15. ~~The pharmaceutical composition according to claim 14, for topical administration, wherein the composition is formulated as a cream, an ointment, a paste, a lotion, a gel or in the form of eyedrops.~~
16. ~~The pharmaceutical composition according to claim 15, formulated as a cream comprising 0.1-5% w/w of said peptide, derivative or pharmaceutically acceptable salt.~~
17. ~~The pharmaceutical composition according to claim 15, for administration to a subject having a disease or injury of the eye.~~
18. ~~The pharmaceutical composition according to claim 17, formulated in a form selected from the group consisting of a liquid solution or suspension for use as eyedrops, an emulsion, a cream, an ointment, a spray, a gel and an intravitreal injection.~~
19. ~~The pharmaceutical composition according to claim 17 or 18, wherein the disease or injury of the eye is an inflammatory disease or disorder selected from the group consisting of: uveitis, dry eye syndrome, inflammatory symptoms associated with an infectious eye disease, an allergic eye disease, keratitis, conjunctivitis, meibomian gland dysfunction, and ocular symptoms associated with Sjogren syndrome.~~

20. ~~The pharmaceutical composition according to claim 14, for administration to a subject having an inflammatory autoimmune disease or disorder.~~
21. ~~The pharmaceutical composition of claim 20, wherein said autoimmune disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis,~~
5 ~~psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and lupus.~~
22. ~~The pharmaceutical composition of claim 14, for administration to a subject having an inflammatory bowel disease.~~
23. ~~The pharmaceutical composition of claim 22, wherein said inflammatory bowel disease is selected from the group consisting of Crohn's disease and ulcerative colitis.~~
- 10 24. ~~The pharmaceutical composition of claim 14, for administration to a subject having an inflammatory disease or disorder of the lung.~~
25. ~~The pharmaceutical composition of claim 24, wherein said inflammatory disease or disorder of the lung is selected from the group consisting of asthma, bronchitis,~~
15 ~~pleurisy, alveolitis, vasculitis, pneumonia, chronic bronchitis, bronchiectasis, diffuse panbronchiolitis, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis and cystic fibrosis.~~
26. ~~The pharmaceutical composition of claim 14, for administration to a subject having an inflammatory disease or disorder of the ear.~~
27. ~~The pharmaceutical composition of claim 26, wherein said inflammatory disease or~~
20 ~~disorder of the ear is selected from the group consisting of inflammatory symptoms associated with ear infection, otitis media, otitis externa, mastoiditis and otomastoiditis.~~
28. ~~A method of reducing the release or inhibiting the activity of at least one inflammatory or pro-inflammatory cytokine, the method comprising administering to a subject in~~
25 ~~need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof,~~
~~wherein is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr.~~
29. ~~The method of claim 28 wherein the at least one inflammatory cytokine is selected~~
30 ~~from the group consisting of: interferon gamma (IFN gamma), interleukin 1 beta (IL-1 beta), interleukin 10 (IL-10), tumor necrosis factor alpha (TNF alpha), and interleukin 6 (IL-6).~~

30. ~~A method of reducing the release of an inflammatory mediator or chemokine, the method comprising administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr.~~

31. ~~The method of claim 30 wherein the inflammatory mediator or chemokine is selected from ROS and RANTES.~~

32.1. Use of a peptide selected from the group consisting of pGlu-Asn-Trp-Lys(Octanoyl)-OH (SEQ ID NO: 1), pGlu-Asn-Trp-Thr-OH (SEQ ID NO: 2), and pharmaceutically acceptable salts thereof in the manufacture of a pharmaceutical composition for
~~A method of treating an inflammatory disease or disorder selected from the group consisting of: an eye inflammatory disease or disorder, an ear inflammatory disease or disorder, a lung inflammatory disease or disorder, a bowel inflammatory disease or disorder, or an inflammatory autoimmune disease or disorder, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a peptide according to Formula I: pGlu-X₁-X₂-X₃-OH, or a pharmaceutically acceptable salt or derivative thereof, wherein X₁ is selected from Asn and Thr; X₂ is selected from Trp, Phe and Tyr; and X₃ is selected from Lys, Lys derivative and Thr, thereby treating the inflammatory disease or disorder.~~

33.2. The method use according to any one of claims 28 to 32.1, wherein the pharmaceutical composition is formulated for administration ~~is~~ via a route selected from the group consisting of topical, ophthalmic, oral, nasal, and parenteral administration.

3. The use according to claim 2, wherein the pharmaceutical composition is formulated for topical administration as a cream, an ointment, a paste, a lotion, a gel or in the form of eyedrops.

4. The use according to claim 3, wherein the pharmaceutical composition is formulated as a cream comprising 0.1-5% w/w of said peptide or pharmaceutically acceptable salt.

5. The use according to claim 2, wherein the pharmaceutical composition is formulated for administration to a subject having a disease or injury of the eye.

6. The use according to claim 5, wherein the pharmaceutical composition is formulated in a form selected from the group consisting of a liquid solution or suspension for use

as eyedrops, an emulsion, a cream, an ointment, a spray, a gel and an intravitreal injection.

34.7. The ~~method of use according to~~ claim ~~32~~ 1, wherein the inflammatory disease or disorder of the eye is selected from the group consisting of uveitis, dry eye syndrome, inflammatory symptoms associated with an infectious eye disease, an allergic eye disease, keratitis, conjunctivitis, meibomian gland dysfunction and Sjogren syndrome.

35.8. The ~~method of use according to~~ claim ~~32~~ 1, wherein the inflammatory autoimmune disease or disorder is selected from the group consisting of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, Sjogren syndrome and lupus.

36.9. The ~~method of use according to~~ claim ~~32~~ 1, wherein the bowel inflammatory disease or disorder is selected from the group consisting of Crohn's disease and ulcerative colitis.

37.10. The ~~method of use according to~~ claim ~~32~~ 1, wherein the inflammatory disease or disorder of the lung is selected from the group consisting of asthma, bronchitis, pleurisy, alveolitis, vasculitis, pneumonia, chronic bronchitis, bronchiectasis, diffuse panbronchiolitis, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis and cystic fibrosis.

38.11. The ~~method of use according to~~ claim ~~32~~ 1, wherein the inflammatory disease or disorder of the ear is selected from the group consisting of inflammatory symptoms associated with ear infection, otitis media, otitis externa, mastoiditis and otomastoiditis.

~~39. The method according to any one of claims 28 to 38, wherein the peptide derivative comprises an alkyl group attached via an amide bond to an amino group of a side chain or a terminal amine of the peptide.~~

~~40. The method according to claim 39, wherein the alkyl is a C4 to C30 alkyl.~~

~~41. The method according to claim 40, wherein the alkyl is a C8 alkyl (octanoyl), attached to the side chain of a Lys residue.~~

~~42. The method according to any one of claims 28 to 38, wherein said peptide is selected from a peptide of SEQ ID NO: 1, a peptide of SEQ ID NO: 2, and salts and derivatives thereof.~~

12. The use according to any one of claims 1 to 11, wherein said peptide has an amino acid sequence as set forth in SEQ ID NO: 1.

13. The use according to any one of claims 1 to 11, wherein said peptide is the sodium salt of the peptide set forth in SEQ ID NO: 1.
14. The use according to any one of claims 1 to 11, wherein said peptide has an amino acid sequence as set forth in SEQ ID NO: 2.
- 5 15. The use according to any one of claims 1 to 11, wherein said peptide is the sodium salt of the peptide set forth in SEQ ID NO: 2.
16. The use according to any one of claims 1 to 15, wherein the pharmaceutical composition has a pH in the range of 4 to 8.
- 10 17. The use according to any one of claims 1 to 16, wherein treating an inflammatory disease or disorder comprises reducing the release or inhibiting the activity of at least one inflammatory cytokine selected from the group consisting of: TNF alpha, IL-1-beta and IL-6.
18. An isolated sodium salt of a peptide having a sequence as set forth in SEQ ID NO: 1.