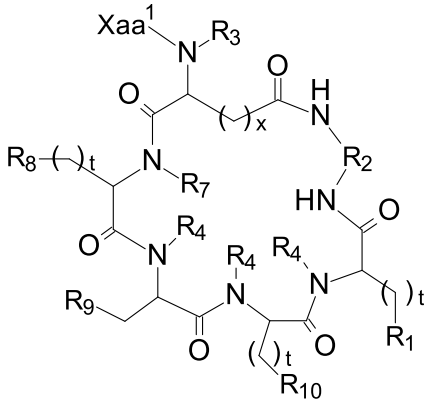
CLAIMS

We claim:

1. A cyclic peptide of formula II:



(II)

including all enantiomers, stereoisomers or diastereomers thereof, or a pharmaceutically acceptable salt of any of the foregoing,

wherein:

Xaa^1 is $-R_5-R_6$;

R_1 is substituted or unsubstituted indole, phenyl or naphthyl;

R_2 is $–(CH_2)_u-$ or $–(CH_2)_v-O-(CH_2)_w-$;

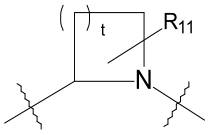
R_3 is H or a C_1 to C_9 linear or branched aliphatic chain, optionally comprising one or more C=C double bonds;

R_4 is -H or $-CH_3$;

R_5 is optionally present, and if present, is from one to three L- or D-isomer amino acids, or a combination thereof, wherein any backbone nitrogen atom is optionally methylated;

R_6 is H or a C_1 to C_{17} acyl group comprising optionally substituted linear or branched alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl or heteroaryl;

R_7 is -H, $-CH_3$ or $-CH_2-$, and if it is $-CH_2-$ forms with R_8 a ring of the general structure



;

R_8 is -H if R_8 forms the ring with R_7, or R_8 is

$-(CH_2)_3$,

$-N(R_{12a})(R_{12b})$,

$-NH-(CH_2)_z-N(R_{12a})(R_{12b})$,

$-C(=O)-N(R_{12a})(R_{12b})$,

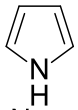
$-O-(R_{12a})$,

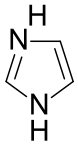
$-S-(=O)_2-CH_3$,

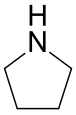
$-S-(=O)-CH_3$,

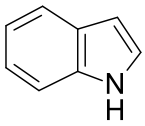
substituted or unsubstituted phenyl,

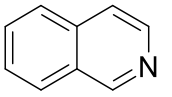
-O-CH_2-phenyl, where phenyl is substituted or unsubstituted,

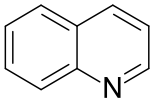

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,


, or


;

R_9 is substituted or unsubstituted phenyl or naphthyl;

R_{10} is

-N(R_{12a})(R_{12b}),

-NH-$(CH_2)_z$-N(R_{12a})(R_{12b}),

-NH-C(=NH)-N(R_{12a})(R_{12b}),

-NH-C(=O)-N(R_{12a})(R_{12b}),

-O(R_{12a}),

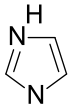
-C_1 to C_{17} linear, branched or cyclic alkyl chain,

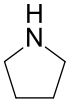
-S(=O)$_2$-CH_3,

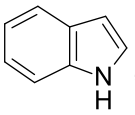
-S(=O)-CH_3,

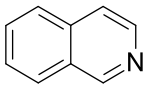
-C(=O)-O(R_{12a}),

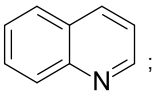

,


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,


,


, or


;

R_{11} is -O-CH_2-phenyl, where phenyl is substituted or unsubstituted;

R_{12a} and R_{12b} are each independently and independently in each instance H or a C_1 to C_4 linear, branched or cyclic alkyl chain;

t is in each instance independently from 1 to 4;

x is from 1 to 5;

u is from 2 to 8;

v and w are each independently from 2 to 5; and

z is from 1 to 3.

2. The cyclic peptide of claim 1 wherein:

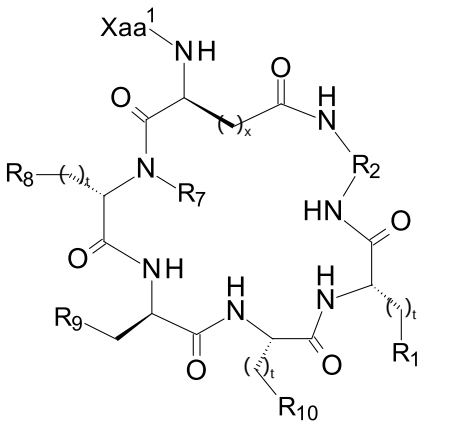
(a) R_9 is unsubstituted naphthyl; or

(b) any substituted phenyl or naphthyl is in each instance independently substituted with between one and three ring substituents wherein the substituents are the same or different, and are each independently halo, (C_1-C_{10})alkyl-halo, (C_1-C_{10})alkyl, (C_1-C_{10})alkoxy, (C_1-C_{10})alkylthio, aryl, (C_1-C_{10})alkylaryl, aryloxy, nitro, nitrile, sulfonamide, amino, monosubstituted amino, disubstituted amino, hydroxy, carbamoyl, carboxy, carbamoyl, alkoxy-carbonyl, or aryloxy-carbonyl; or

(c) R_5 comprises at least one L- or D-isomer amino acid; optionally wherein R_5 is a single L- or D-isomer amino acid with an aliphatic side chain; optionally wherein the aliphatic side chain is -$(CH_2)_3$-CH_3; or

(d) R_5 is a single L- or D-isomer amino acid with a side chain comprising at least one nitrogen atom; optionally wherein R_5 is an L- or D-isomer of Arg, Lys, Orn, Dab, Dap or Cit.

3. The cyclic peptide of claim 1 wherein the cyclic peptide of formula II is a cyclic peptide of the formula:



4. The cyclic peptide of claim 1 or 3 wherein Xaa^1 is Ac-Arg, Ac-D-Arg, Ac-Nle, Ac-D-Nle, Ac-Trp, cyclopentyl acetyl, hexanoyl, 3-phenylpropanoyl, cyclopentylacetyl, acetyl, 2-naphthylacetyl, or 3-(1-naphthyl)propanoyl.

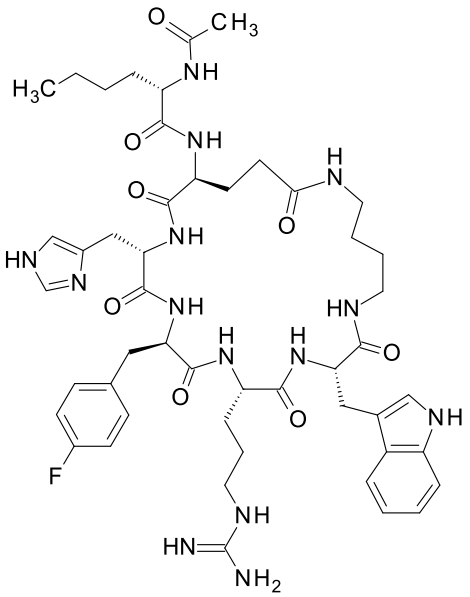
5. The cyclic peptide of claim 1 or 3 wherein:

(a) R_1 is indole or naphthalene; or

(b) R_7 and R_8 comprise pyrrolidine; optionally wherein pyrrolidine is substituted; optionally wherein the substituent is -O-CH_2-phenyl, where phenyl is substituted or unsubstituted; or

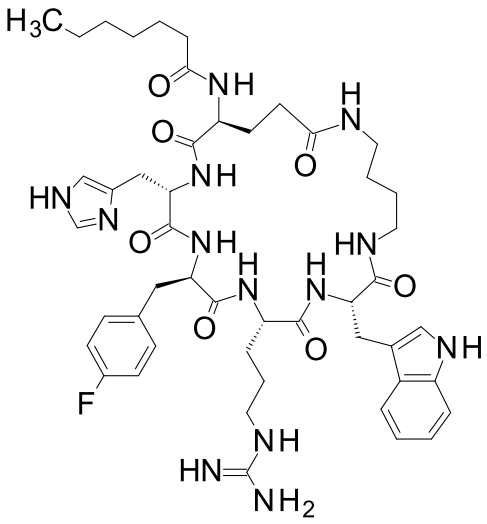
(c) R_9 is substituted phenyl.

6. The cyclic peptide of claim 1 having the structure



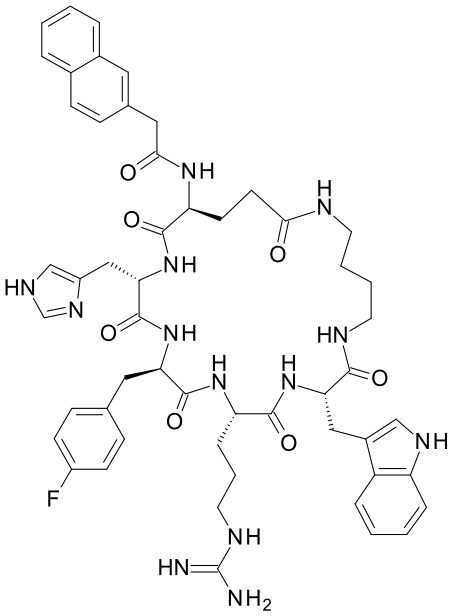
or a pharmaceutically acceptable salt thereof.

7. The cyclic peptide of claim 1 having the structure



or a pharmaceutically acceptable salt thereof.

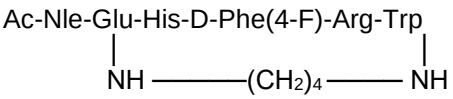
8. The cyclic peptide of claim 1 having the structure



or a pharmaceutically acceptable salt thereof.

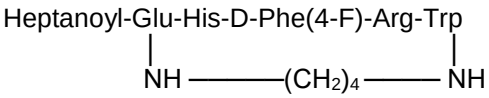
9. The cyclic peptide according to any of claims 6-8, which is an acetate salt or a trifluoroacetate salt.

10. The cyclic peptide of claim 1 which is



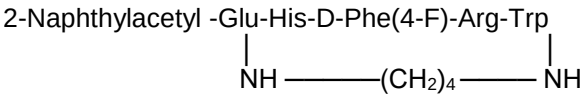
or a pharmaceutically acceptable salt thereof.

11. The cyclic peptide of claim 1 which is



or a pharmaceutically acceptable salt thereof.

12. The cyclic peptide of claim 1 which is



or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising the cyclic peptide according to any of claims 6-8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

14. The pharmaceutical composition of claim 13 for use in a method for treatment of:

(a) a melanocortin receptor-mediated disease, indication, condition or syndrome in a human or non-human mammal; or

(b) a condition responsive to changes in melanocortin receptor function in a human or non-human mammal; optionally

wherein the melanocortin receptor-mediated disease, indication, condition or syndrome in a human is ocular inflammation; optionally

wherein:

(i) the pharmaceutical composition is an aqueous pharmaceutical composition for administration to the surface of the eye; or

(ii) the inflammation is caused by an ocular condition, wherein the ocular condition is dry eye disease, corneal ulcer, corneal erosion, corneal abrasion, corneal degeneration, corneal perforation, corneal scarring, epithelial defect, keratoconjunctivitis, idiopathic uveitis, corneal transplantation, age-related macular degeneration, diabetic eye, blepharitis, glaucoma, ocular hypertension, post-operative eye pain and inflammation, posterior segment neovascularization, proliferative vitreoretinopathy, cytomegalovirus retinitis, endophthalmitis, choroidal neovascular membrane, vascular occlusive disease, allergic eye disease, tumor, retinitis pigmentosa, eye infection, scleritis, ptosis, miosis, eye pain, mydriasis, neuralgia, cicatrizing ocular surface disease, ocular infection, inflammatory ocular disease, ocular surface disease, corneal disease, retinal disease, ocular manifestations of systemic diseases, hereditary eye condition, ocular tumor, increased intraocular pressure, herpetic infection, pterygium, a wound sustained to ocular surface, post-photorefractive keratotomy eye pain and inflammation, thermal or chemical burn to the cornea, scleral wound, keratoconus or conjunctival wound; optionally

wherein the inflammation is caused by dry eye disease or keratoconjunctivitis sicca.

15. The pharmaceutical composition of claim 13 wherein the pharmaceutically acceptable carrier is an aqueous solution comprising about 2.79 mg/mL of trisodium citrate dihydrate, about 9 mg/mL of sodium chloride and about 1 mg/mL of polysorbate 80; optionally wherein:

the aqueous solution is at about pH 6.5, and the composition further comprises sodium hydroxide or hydrochloric acid as needed to adjust pH.

16. The pharmaceutical composition of claim 15 wherein the cyclic peptide is in a trifluoroacetic acid salt form at a concentration of about 1.0 µg/mL.

17. The pharmaceutical composition of claim 16 further comprising about 0.10 mg/mL anhydrous citric acid.

18. The pharmaceutical composition of claim 16 for use in a method of treating dry eye disease or keratoconjunctivitis sicca comprising administering no more than about 50 µL of the pharmaceutical composition of claim 16 per eye no more often than about three times per day; optionally

wherein no more than about 150 ng of cyclic peptide or pharmaceutically acceptable salt thereof is administered per eye per day.

19. An aqueous solution of a melanocortin receptor-specific peptide with an EC_{50} value of less than 1 nM at each of MC1r and MC5r for use in a method of treating dry eye disease or keratoconjunctivitis sicca wherein the method comprises administering the aqueous solution of a melanocortin receptor-specific peptide with an EC_{50} value of less than 1 nM at each of MC1r and MC5r to the surface of each eye; optionally

wherein:

(a) no more than about 150 ng of the melanocortin receptor-specific peptide is administered per eye per day as an eye drop; or

(b) the melanocortin receptor-specific peptide has an EC_{50} value that at MC1r and MC5r is no greater than the EC_{50} value for at least one of MC3r or MC4r; optionally

wherein the melanocortin receptor-specific peptide has an EC_{50} value that is at least four times lower at MC1r and MC5r than at least one of MC3r or MC4r; optionally

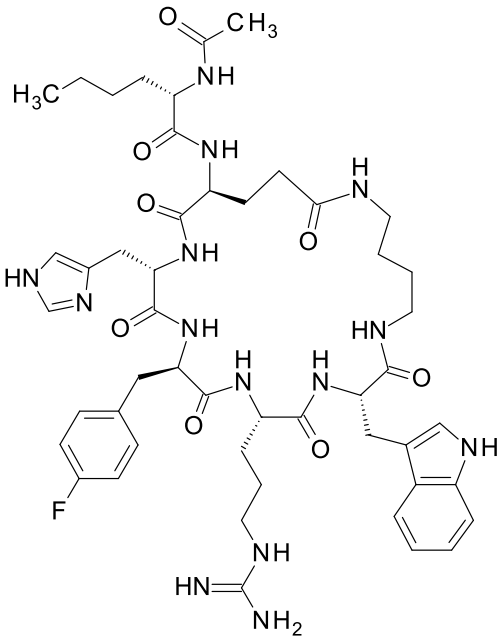
wherein the EC_{50} value is at least four times lower at MC1r and MC5r than at both MC3r and MC4r; or

(c) the peptide is either an agonist or partial agonist at each of MC1r and MC5r; or

(d) EC_{50} values are determined by cAMP production using the HTRF detection method as performed by CEREP; or

(e) the melanocortin receptor-specific peptide is a peptide of claim 1; optionally

wherein the melanocortin receptor-specific peptide is



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