Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Xaa14

wherein:

Xaa1 is absent;

Xaa2 is absent;

Xaa3 and Xaa8 form a linkage Xaa3-Xaa8;

Xaa4 and Xaa14 form a linkage Xaa4-Xaa14;

Xaa5 is selected from: Asp, Gln, Glu, Arg, His and Lys;

Xaa6 is selected from: Pro and hydroxyproline;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Asn, Asp, Gln, Glu, Arg, His and Lys;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser, Thr, Arg, His and Lys;

wherein Xaa3 is~~the~~ an N-termin~~us~~al amino acid ~~is optionally modified~~; and

Xaa14 is a~~the~~ C-terminal~~us~~ amino acid~~is optionally modified~~.

[0004b] In another aspect, the present disclosure refers to a cosmetic composition comprising the muscle-type nicotinic acetylcholine receptor peptide antagonist as described here, for prevention or temporary improvement of the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity, in a subject.

[0004c] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the muscle-type nicotinic acetylcholine receptor peptide antagonist as described herein, for: prevention or temporary improvement of the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity; treatment of overactive bladder (OAB); treatment of urinary incontinence; prophylaxis of headaches; treatment of spasticity; treatment of cervical dystonia; treatment of hypersalivation; treatment of blepharospasm associated with dystonia; or treatment of strabismus, in a subject.

[0004d] In yet another aspect, the present disclosure refers to a method for preventing or temporarily improving the appearance in a subject for prevention or temporary improvement of

the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity, comprising applying an effective amount of the cosmetic composition as described herein to the skin of the subject.

~~**[0004e]** In yet another aspect, the present disclosure refers to a use of the pharmaceutical composition as described herein in the manufacture of a medicament for preventing or temporarily improving one or more of the appearance of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity; treatment of overactive bladder (OAB); treatment of urinary incontinence; prophylaxis of headaches; treatment of spasticity; treatment of cervical dystonia; treatment of hypersalivation; treatment of blepharospasm associated with dystonia; or treatment of strabismus; in a subject, wherein the pharmaceutical composition as described herein is to be administered an effective amount to the subject.~~

[0004e~~f~~] In yet another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use as a therapy.

[0005] The present disclosure includes a muscle-type nicotinic acetylcholine receptor peptide antagonist comprising an amino acid sequence Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Xaa14, wherein: Xaa1 is absent or selected from Ala,

CLAIMS

WHAT IS CLAIMED IS:

1. A muscle-type nicotinic acetylcholine receptor peptide antagonist comprising an amino acid sequence:

Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Xaa14

wherein:

Xaa1 is absent;

Xaa2 is absent;

Xaa3 and Xaa8 form a linkage Xaa3-Xaa8;

Xaa4 and Xaa14 form a linkage Xaa4-Xaa14;

Xaa5 is selected from: Asp, Gln, Glu, Arg, His and Lys;

Xaa6 is selected from: Pro and hydroxyproline;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Asn, Asp, Gln, Glu, Arg, His and Lys;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser, Thr, Arg, His and Lys;

wherein Xaa3 is ~~the~~an N-terminal~~us~~ amino acid ~~is optionally modified~~; and

Xaa14 is a~~the~~ C-terminal~~us~~ amino acid ~~is optionally modified~~.

2. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 1, wherein:

Xaa1 is absent;

Xaa2 is absent;

the Xaa3-Xaa8 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

the Xaa4-Xaa14 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

Xaa5 is selected from: Asp, Gln and Glu;

Xaa6 is selected from: Pro and hydroxyproline;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Arg, His, and Lys;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser, and Thr.

3. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 1, wherein:

Xaa1 is absent;

Xaa2 is absent;

the Xaa3-Xaa8 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

the Xaa4-Xaa14 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

Xaa5 is selected from: Arg, His and Lys;

Xaa6 is selected from: Pro and hydroxyproline;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Asn, Asp, Gln and Glu;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser and Thr.

4. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 1, wherein:

Xaa1 is absent;

Xaa2 is absent;

the Xaa3-Xaa8 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

the Xaa4-Xaa14 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

Xaa5 is selected from: Arg, His and Lys;

Xaa6 is selected from: Pro;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Arg, His and Lys;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser, and Thr.

5. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 1, wherein:

Xaa1 is absent;

Xaa2 is absent;

the Xaa3-Xaa8 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

the Xaa4-Xaa14 linkage is selected from: a Cys-Cys linkage, a Sec-Sec linkage, a cystathionine linkage, a lactam bridge, a thioether linkage, and a dicarba linkage;

Xaa5 is selected from: Arg, His and Lys;

Xaa6 is selected from: Pro and hydroxyproline;

Xaa7 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa9 is selected from: Ala, Gly, Val, Leu and Ile;

Xaa10 is selected from: Arg and His;

Xaa11 is selected from: Arg, His, Lys, Asn, Asp, Gln and Glu;

Xaa12 is selected from: Trp and Tyr; and

Xaa13 is selected from: Cys, Met, Sec, Ser and Thr.

6. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 1, wherein the Xaa3-Xaa8 linkage and the Xaa4-Xaa14 linkage are independently selected from:

(i) a Cys-Cys linkage;

(ii) a Sec-Sec linkage;

(iii) a cystathionine linkage;

(iv) a lactam bridge,

(v) a thioether linkage, and

(vi) a dicarba linkage.

7. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 6, wherein the thioether linkage is a lanthionine linkage.

8. The muscle-type nicotinic acetylcholine receptor peptide antagonist of any one of claims 1-7, wherein the N-terminus is modified to comprise C_1-C_6 acyl, C_1-C_8 alkyl, C_6-C_{12} aralkyl, C_5-C_{10} aryl, C_4-C_8 heteroaryl, formyl, or a lipid.

9. The muscle-type nicotinic acetylcholine receptor peptide antagonist of any one of claims 1-8, wherein the C-terminus is modified to comprise NH_2, amino-acyl, amino-C_1-C_8 alkyl, amino-C_6-C_{12}-aralkyl, amino-C_5-C_{10} aryl, amino-C_4-C_8 heteroaryl, or O-(C_1-C_8 alkyl).

10. The muscle-type nicotinic acetylcholine receptor peptide antagonist of any one of claims 1-9, wherein a lipid is covalently attached to a cysteine, serine, lysine, threonine or tyrosine.

11. The muscle-type nicotinic acetylcholine receptor peptide antagonist of any one of claims 1-10, wherein the antagonist selectively inhibits a muscle-type nicotinic acetylcholine receptor.

12. The muscle-type nicotinic acetylcholine receptor peptide antagonist of claim 11, wherein the IC_{50} is: ~~about~~ 1 millimolar to ~~about~~ 1 picomolar, less than ~~about~~ 200 nM, less than ~~about~~ 150 nM, or less than ~~about~~ 100 nM.

13. A cosmetic composition comprising the muscle-type nicotinic acetylcholine receptor peptide antagonist of any of claims 1-12, for prevention or temporary improvement of the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity, in a subject.

14. The cosmetic composition of claim 13, formulated for topical use.

15. A pharmaceutical composition comprising the muscle-type nicotinic acetylcholine receptor peptide antagonist of any of claims 1-12, for: prevention or temporary improvement of the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity; treatment of overactive bladder (OAB); treatment of urinary incontinence; prophylaxis of headaches; treatment of spasticity; treatment of cervical dystonia; treatment of hypersalivation; treatment of blepharospasm associated with dystonia; or treatment of strabismus, in a subject.

16. A method for preventing or temporarily improving the appearance in a subject for prevention or temporary improvement of the appearance of one or more of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity, comprising applying an effective amount of the cosmetic composition of claim 13 or 14 to the skin of the subject.

~~17. Use of the pharmaceutical composition of claim 15 in the manufacture of a medicament for preventing or temporarily improving one or more of the appearance of skin wrinkles, skin laxity, moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, moderate to severe lateral canthal lines associated with orbicularis oculi activity, and moderate to severe forehead lines associated with frontalis muscle activity; treatment of overactive bladder (OAB); treatment of urinary incontinence; prophylaxis of headaches; treatment of spasticity; treatment of cervical dystonia; treatment of hypersalivation; treatment of blepharospasm associated with dystonia; or treatment of strabismus; in a subject, wherein the pharmaceutical composition of claim 15 is to be administered an effective amount to the subject.~~

~~18~~17. The pharmaceutical composition of claim 15 for use as a therapy.