[0010] One embodiment provides a recombinant modified FGF-1 polypeptide, comprising the following mutations of SEQ ID NO: 1: Cys16Ser, Ala66Cys, and Cys117Val, wherein the modified FGF-1 polypeptide comprises a methionine residue positioned upstream to the first residue of SEQ ID NO: 1, and at least one residue of the peptide ALTEK located between the N-terminal methionine and position 1 of SEQ ID NO: 1. In some embodiments, the modified FGF-1 polypeptide is not expressed with an extension peptide and is produced by a method that does not involve a step of removing an extension peptide.

[0010a] In one embodiment is provided a recombinant modified FGF-1 polypeptide comprising the sequence set forth as SEQ ID NO: 1 with (i) an N-terminal methionine residue positioned upstream to the first residue of SEQ ID NO: 1, and (ii) the mutations Cys16Ser, Ala66Cys, and Cys117Val with respect to the wild-type FGF-1 sequence of SEQ ID NO: 1.

[0011] In one embodiment is provided a pharmaceutical composition comprising the recombinant polypeptide of any one of the embodiments described above. In some embodiments, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier, excipient, or diluent. In some embodiments, the pharmaceutical composition is a liquid ophthalmic formulation. In some embodiments, the pharmaceutical formulation is administered topically, microneedle into the cornea, or intracamerally.

[0012] Provided herein in one embodiment is a method for producing a recombinant modified FGF-1 polypeptide, the method comprising: expressing the modified FGF-1 polypeptide in a host cell and maturing the expressed polypeptide in the cytoplasm of the host cell, wherein the modified FGF-1 polypeptide comprises one or more mutations of SEQ ID NO: 1, and is expressed with an N-terminal methionine residue positioned upstream to the first residue of SEQ ID NO: 1.

[0013] Provided herein in one embodiment is a method for producing a recombinant modified FGF-1 polypeptide, the method comprising: expressing the modified FGF-1 polypeptide in a host cell and maturing the expressed polypeptide in the cytoplasm of the host cell, wherein the modified FGF-1 polypeptide comprises one or more mutations of SEQ ID NO: 1, an extension

some embodiments, the herpetic keratopathy that is secondary to an infection by herpes simplex virus comprises neurotrophic keratopathy. In some embodiments, the modified FGF-1 polypeptide comprising a sequence as set forth in any one of SEQ ID Nos: 2 and 9-204, or a pharmaceutical composition comprising the same, is administered twice daily. In some embodiments, the modified FGF-1 polypeptide comprising a sequence as set forth in any one of SEQ ID Nos: 2 and 9-204, or a pharmaceutical composition comprising the same, is administered for a duration of 30 days. In some embodiments, administration of the modified FGF-1 polypeptide comprising a sequence as set forth in any one of SEQ ID Nos: 2 and 9-204, or a pharmaceutical composition comprising the same, results in healing of corneal ulcer, reduction of duration of pain and inflammation, reduction in pain and inflammation, reduction in corneal opacity, haze, scarring, or any combinations thereof. In some embodiments, the corneal ulcer comprises a herpetic corneal ulcer. In some embodiments, the mammal is a human.

[0031a] In one embodiment is provided a use of a recombinant modified FGF-1 polypeptide as described herein or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating or ameliorating a corneal disease, disorder or condition in a mammal.

[0031b] In one embodiment is provided a use of a recombinant modified FGF-1 polypeptide as described herein or a pharmaceutical composition as described herein in the manufacture of a medicament for treating or ameliorating herpetic keratopathy.

INCORPORATION BY REFERENCE

[0032] All publications and patent applications mentioned in this specification are herein incorporated by reference in their entireties to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF DRAWINGS

[0033] **Figure 1** illustrates the reaction of mustard gas with cysteine.

[0034] **Figure 2** illustrates the effect of exemplary modified FGF-1 polypeptides (TTHX1114 and TTHX1001) according to the present disclosure on the *in vitro* proliferation of human corneal endothelial cells. The dotted line corresponds to TTHX1114 and the dashed line corresponds to TTHX1001.

[0035] **Figure 3** illustrates an exemplary rabbit corneal organ culture model system.

CLAIMS

WHAT IS CLAIMED IS:

1. A recombinant modified FGF-1 polypeptide comprising the sequence set forth as SEQ ID NO: 1 with (i) an N-terminal methionine residue positioned upstream to the first residue of SEQ ID NO: 1, and (ii) the mutations Cys16Ser, Ala66Cys, and Cys117Val with respect to the wild-type FGF-1 sequence of SEQ ID NO: 1.

2. The recombinant modified FGF-1 polypeptide of claim 1, wherein the polypeptide further comprises an extension peptide positioned between the N-terminal methionine residue and the first residue of SEQ ID NO: 1.

3. The recombinant modified FGF-1 polypeptide of claim 2, wherein the extension peptide comprises one or more amino acid residues of SEQ ID NO: 3.

4. The recombinant modified FGF-1 polypeptide of claim 3, wherein the extension peptide comprises any one of the sequences set forth in SEQ ID NOS. 4-8.

5. The recombinant modified FGF-1 polypeptide of any one of claims 1-4, wherein the modified FGF-1 polypeptide comprises a sequence selected from SEQ ID NOS: 14-18.

6. The recombinant modified FGF-1 polypeptide of any one of claims 1-5, wherein the modified FGF-1 polypeptide further comprises a truncation of one or more of the first five residues of SEQ ID NO: 1.

7. The recombinant modified FGF-1 polypeptide of claim 6, wherein the modified FGF-1 polypeptide comprises a sequence selected from SEQ ID NOS: 118-141.

8. The recombinant modified FGF-1 polypeptide of claim 1 comprising a sequence as set forth in SEQ ID NO. 2.

9. The recombinant modified FGF-1 polypeptide of any one of claims 1-8, wherein the modified FGF-1 polypeptide is the mature form of the polypeptide.

10. The recombinant modified FGF-1 polypeptide of claim 1, wherein the modified FGF-1 polypeptide further comprises one or more mutations selected from the group consisting of: Lys12Val and Pro134Val.

11. The recombinant modified FGF-1 polypeptide of any one of claims 1-10, wherein the polypeptide is at least 141 amino acids in length.

12. A pharmaceutical composition comprising the recombinant polypeptide of any one of claims 1-11 and a pharmaceutically acceptable carrier, excipient, or diluent.

13. Use of a recombinant modified FGF-1 polypeptide according to any one of claims 1-11 or a pharmaceutical composition according to claim 12, in the manufacture of a medicament for treating or ameliorating a corneal disease, disorder or condition in a mammal.

14. The use of claim 13, wherein the corneal disease, disorder or condition comprises Fuch’s dystrophy or a chemical or vesicant induced injury.

15. Use of a recombinant modified FGF-1 polypeptide according to any one of claims 1-11 or a pharmaceutical composition according to claim 12 in the manufacture of a medicament for treating or ameliorating herpetic keratopathy.