Claims

1. An isolated polypeptide comprising an amino acid sequence that has at least 95% amino acid sequence identity to an amino acid sequence selected from the group of sequences of TABLE 1, wherein the polypeptide comprises an amino acid that is a polar amino acid other than K or R at position 423, as determined with reference to SEQ ID NO:1, and wherein the polypeptide has chondrogenic activity.

2. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

3. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

4. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

5. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58,

SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

6. The polypeptide of claim 1, wherein the polypeptide has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

7. The polypeptide of claim 1, wherein the polypeptide has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

8. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from the group of sequences of TABLE 1.

9. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

10. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

11. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is Q or S or the amino acid at position 423 is deleted.

12. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is Q.

13. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is S.

14. The polypeptide of any one of claims 1 to 11, wherein the polypeptide is PEGylated.

15. The polypeptide of any one of claims 1-14, wherein the polypeptide is fused to a heterologous peptide selected from any of human serum albumin (HSA), an immunoglobulin heavy chain constant region (Fc), a polyhistidine, a glutathione S transferase (GST), a thioredoxin, a protein A, a protein G, or a maltose binding protein (MBP), or a fragment thereof.

16. The polypeptide of any claim 15, wherein the heterologous peptide is fused at the amino-terminal end of the polypeptide.

17. The polypeptide of claim 15, wherein the heterologous peptide is fused at the carboxy-terminal end of the polypeptide.

18. A pharmaceutical composition comprising a polypeptide of any one of claims 1 to 17.

19. The pharmaceutical composition of claim 18, further comprising a hyaluronic acid or a derivative thereof.

20. The pharmaceutical composition of claim 18, further comprising an agent selected from the group consisting of oral salmon calcitonin, SD-6010 (iNOS inhibitor), vitamin D3 (choliecalciferol), collagen hydrolyzate, FGF18, BMP7, rusalatide acetate, avocado soy unsaponifiables (ASU), kartogenin, a steroid, and a non-steroidal anti-inflammatory agent (NSAID)

21. The pharmaceutical composition of claim 18 for use in treating, ameliorating or preventing arthritis or joint damage in a subject, wherein a therapeutically effective amount of the pharmaceutical composition of claim 18 is to be administered to a joint of the subject.

22. The polypeptide of any one of claims 1-17 for use in inducing differentiation of mesenchymal stem cells into chondrocytes, wherein mesenchymal stem cells are contacted with an effective amount of a polypeptide of any one of claims 1-17 to induce differentiation of the mesenchymal stem cells into chondrocytes.

23. The polypeptide for use according to claim 22, wherein the differentiation of the mesenchymal stem cells into chondrocytes is to be induced *in vivo* and the mesenchymal stem cells are present in a human subject.

24. The polypeptide for use according to claim 23, wherein the subject has or is at risk for, arthritis or joint damage.

25. The polypeptide of any one of claims 1-17 for use in treating a subject who has or is at risk of joint damage or arthritis, wherein a therapeutically effective amount of the polypeptide of any one of claims 1-17 is to be administered to the subject.

26. The pharmaceutical composition for use according to claim 21 or the polypeptide for use according to claim 24 or claim 25, wherein the arthritis is osteoarthritis, trauma arthritis, or autoimmune arthritis.

27. The pharmaceutical composition for use according to claim 21, further comprising hyaluronic acid.

28. The pharmaceutical composition for use according to claim 21 or the polypeptide for use according to claim 25, wherein the pharmaceutical composition or polypeptide is to be administered in conjunction with any one of bone marrow stimulation, cartilage replacement, autologous chondrocyte implantation (ACI), matrix-induced autologous chondrocyte implantation (MACI).

29. The pharmaceutical composition for use according to claim 21 or the polypeptide for use according to claim 25, wherein the pharmaceutical composition or polypeptide is to be administered in conjunction with or in addition to one or more additional chondrogenic factors.

30. The pharmaceutical composition for use according to claim 21 or the polypeptide for use according to claim 25, wherein the pharmaceutical composition or polypeptide is to be administered in a matrix or biocompatible scaffold.

Claims

1. An isolated polypeptide comprising an amino acid sequence that has at least 95% amino acid sequence identity to an amino acid sequence selected from the group of sequences of TABLE 1, wherein the polypeptide comprises an amino acid that is a polar amino acid other than K or R at position 423, as determined with reference to SEQ ID NO:1, and wherein the polypeptide has chondrogenic activity.

2. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

3. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

4. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

5. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

6. The polypeptide of claim 1, wherein the polypeptide has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

7. The polypeptide of claim 1, wherein the polypeptide has at least 95% sequence identity to an amino acid sequence of any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

8. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from the group of sequences of TABLE 1.

9. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from any one of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70.

10. The polypeptide of claim 1, wherein the polypeptide consists of an amino acid sequence selected from any one of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, or SEQ ID NO:64.

11. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is Q or S or the amino acid at position 423 is deleted.

12. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is Q.

13. The polypeptide of any one of claims 1-10, wherein the amino acid at position 423 is S.

14. The polypeptide of any one of claims 1 to 11, wherein the polypeptide is PEGylated.

15. The polypeptide of any one of claims 1-14, wherein the polypeptide is fused to a heterologous peptide selected from any of human serum albumin (HSA), an immunoglobulin heavy chain constant region (Fc), a polyhistidine, a glutathione S transferase (GST), a thioredoxin, a protein A, a protein G, or a maltose binding protein (MBP), or a fragment thereof.

16. The polypeptide of any claim 15, wherein the heterologous peptide is fused at the amino-terminal end of the polypeptide.

17. The polypeptide of claim 15, wherein the heterologous peptide is fused at the carboxy-terminal end of the polypeptide.

18. A pharmaceutical composition comprising a polypeptide of any one of claims 1 to 17 or 23.

19. The pharmaceutical composition of claim 18, further comprising a hyaluronic acid or a derivative thereof.

20. The pharmaceutical composition of claim 18, further comprising an agent selected from the group consisting of oral salmon calcitonin, SD-6010 (iNOS inhibitor), vitamin D3 (choliecalciferol), collagen hydrolyzate, FGF18, BMP7, rusalatide acetate, avocado soy unsaponifiables (ASU), kartogenin, a steroid, and a non-steroidal anti-inflammatory agent (NSAID).

21. The pharmaceutical composition of any one of claims 18-20 for use in treating, ameliorating or preventing arthritis or joint damage in a subject, wherein a therapeutically effective amount of the pharmaceutical composition of any one of claims 18-20 is to be administered to a joint of the subject.

22. The polypeptide of any one of claims 1-17 or 23 for use in treating, ameliorating or preventing arthritis or joint damage in a subject, wherein a therapeutically effective amount of the polypeptide of any one of claims 1-17 or 23 is to be administered to the subject.

23. The polypeptide of claim 1, wherein the polypeptide consists of SEQ ID NO: 28.