Claims:

1. A polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO: 1 or 25 for use in ameliorating or preventing arthritis or joint injury in a mammal.

2. Use of a polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO: 1 or 25 in the manufacture of a medicament for ameliorating or preventing arthritis or joint injury in the mammal.

3. The use of claim 1 or the use of claim 2, wherein the polypeptide is PEGylated.

4. The use of any one of claims 1 to 3, wherein the polypeptide is fused to a 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).

5. The use of any one of claims 1 to 4, wherein the polypeptide comprises 1, 2, 3, 4, or more unnatural amino acids.

6. The use of any one of the preceding claims, wherein (a) the individual has arthritis or joint injury or (b) the individual does not have, but is at risk for, arthritis or joint injury.

7. The use of any one of the preceding claims, wherein:
(a) the polypeptide comprises SEQ ID NO: 1 or 25; or
(b) the amino acid sequence has at least 95% identity to SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or
(c) the amino acid sequence comprises SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or
(d) the amino acid sequence is at least 80% identical to SEQ ID NOs: 5, 9, 13, 17, or 21; or 32

(e) the amino acid sequence comprises SEQ ID NOs: 5, 9, 13, 17, or 21.

8. The use of any one of the preceding claims, wherein :
(a) the arthritis is selected from the group consisting of osteoarthritis, trauma arthritis, and autoimmune arthritis; and/or
(b) the mammal is a human, a dog, or a cat; or
(c) the composition further comprises hyaluronic acid.

9. An *in vitro* method of inducing differentiation of mesenchymal stem cells into chondrocytes, the method comprising contacting mesenchymal stem cells with a sufficient amount of a polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO: 1 or 25 to induce differentiation of the stem cells into chondrocytes.

10. A polypeptide for use in a method of inducing differentiation of mesenchymal stem cells into chondrocytes in a mammal, wherein the method comprises contacting mesenchymal stem cells in the mammal with a sufficient amount of a polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO: 1 or 25 to induce differentiation of the stem cells into chondrocytes.

11. The method or the polypeptide for use in a method of claim 9 or claim 10, wherein the polypeptide is PEGylated.

12. The method or the polypeptide for use in a method any one of claims 9 to 11, wherein the polypeptide is fused to a 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).

13. The method or the polypeptide for use in a method any one of claims 9 to 12, wherein the polypeptide comprises 1, 2, 3, 4, or more unnatural amino acids.

14. The polypeptide for use in a method of any one of claims 10 to 13, wherein the mammal is a human, a dog, or a cat.

15. The method or the polypeptide for use in a method of any one of the preceding claims, wherein:
(a) the polypeptide comprises SEQ ID NO: 1 or 25; or
(b) the amino acid sequence has at least 95% identity to SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or
(c) the amino acid sequence comprises SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or
(d) the amino acid sequence is at least 80% identical to SEQ ID NOs: 5, 9, 13, 17, or 21; or
(e) the amino acid sequence comprises SEQ ID NOs: 5, 9, 13, 17, or 21.

16. A pharmaceutical composition for intra-articular delivery, the composition comprising a pharmaceutically effective amount of a polypeptide comprising an amino acid sequence having at least 95% identity to SEQ ID NO:1 or 25.

17. The composition of claim 16, wherein the polypeptide is PEGylated.

18. The composition of claim 17, wherein the polypeptide is fused to a 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).

19. The composition of any one of claims 16 to 18, wherein the polypeptide comprises 1, 2, 3, 4, or more unnatural amino acids.

20. The composition of any one of claims 16 to 19, further comprising hyaluronic acid.

21. The composition of any one of claims 16 to 19, wherein:

(a) the polypeptide comprises SEQ ID NO: 1 or 25; or 34

(b) the amino acid sequence has at least 95% identity to SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or

(c) the amino acid sequence comprises SEQ ID NOs: 2, 3, 4, 26, 27, or 28; or

(d) the amino acid sequence is at least 80% identical to SEQ ID NOs: 5, 9, 13, 17, or 21; or

(e) the amino acid sequence comprises SEQ ID NOs: 5, 9, 13, 17, or 21.

CLAIMS

1. An *in vitro* method of inducing differentiation of mesenchymal stem cells into chondrocytes, the method comprising, contacting mesenchymal stem cells with a sufficient amount of a polypeptide consisting of an ANGPTL3 C-terminal fibrinogen domain peptide comprising an amino acid sequence selected from:

(a) a polypeptide consisting of any one of SEQ ID NO:1, 2, 3, 27, 26, or 25;

(b) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(c) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(d) a polypeptide consisting of an amino acid sequence of SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(e) a polypeptide consisting of any one of SEQ ID NO:1, 2, 3, 27, 26, or 25 fused to a 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);

(f) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

(g) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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

(h) a polypeptide consisting of an amino acid sequence of SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

wherein said polypeptide has chondrogenic activity to induce differentiation of the stem cells into chondrocytes.

2. Use of a polypeptide consisting of an ANGPTL3 C-terminal fibrinogen domain peptide comprising an amino acid sequence selected from:

(a) a polypeptide consisting of an amino acid sequence of any one of SEQ ID Nos: 1, 2, 3, 25, 26, or 27;

(b) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(c) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(d) a polypeptide consisting of an amino acid sequence of SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23,

(e) a polypeptide consisting of any one of SEQ ID NO:1, 2, 3, 27, 26, or 25 fused to a 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);

(f) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

(g) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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

(h) a polypeptide consisting of an amino acid sequence of SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

in the manufacture of a medicament for ameliorating or preventing arthritis or joint injury in a mammal, wherein said polypeptide has chondrogenic activity.

3. A pharmaceutical composition for intra-articular delivery, the composition comprising a pharmaceutically effective amount of a polypeptide consisting of an ANGPTL3 C-terminal fibrinogen domain peptide comprising an amino acid sequence selected from:

(a) a polypeptide consisting of any one of SEQ ID NO:1, 2, 3, 27, 26, or 25;

(b) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(c) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(d) a polypeptide consisting of an amino acid sequence of SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23;

(e) a polypeptide consisting of any one of SEQ ID NO:1, 2, 3, 27, 26, or 25 fused to a 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);

(f) a polypeptide consisting of an amino acid sequence having at least 95% identity to SEQ ID NOs: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

(g) a polypeptide consisting of an Angptl3 variant amino acid sequence substantially identical to SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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

(h) a polypeptide consisting of an amino acid sequence of SEQ ID Nos: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22 or 23 fused to a 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);

wherein said polypeptide has chondrogenic activity.

4. The use of claim 2, wherein the arthritis is selected from the group consisting of osteoarthritis, trauma arthritis, and autoimmune arthritis.

5. The composition of claim 3, wherein the composition further comprises hyaluronic acid.

6. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the polypeptide is PEGylated.

7. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the polypeptide comprises 1, 2, 3, 4, or more unnatural amino acids.

8. The method of claim 1, or the use of claim 2, wherein the mammal is a human, a dog, or a cat.

9. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the polypeptide is SEQ ID NO:1 or SEQ ID NO:25.

10. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the amino acid sequence is SEQ ID NO: 2 or SEQ ID NO:26.

11. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the amino acid sequence is SEQ ID NO: 3 or SEQ ID NO:27.

12. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the amino acid sequence is at least 95% identical to SEQ ID NO: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, or 23.

13. The method of claim 1, or the use of claim 2, or the composition of claim 3, wherein the amino acid sequence is SEQ ID NO: 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, or 23.