

WHAT IS CLAIMED IS:

1. A fusion protein comprising:

an integrin binding peptide comprising disintegrin targeting at least integrins $\alpha v\beta 3$ and $\alpha 5\beta 1$ or its integrin binding fragments,

5 the integrin binding peptide comprising at least one mutation on a RGD motif or within 15-20 amino acids from the RGD motif;

other protein binding peptide targeting an angiogenic factor,

the angiogenic factor comprising Angiopoietin (ANG), Ephrin (Eph),
 Fibroblast Growth Factor (FGF), Neuropilin (NRP), Plasminogen Activators,
 10 urokinase-type plasminogen activator receptor (uPAR), Platelet-Derived Growth
 Factor (PDGF), Placental growth factor (PlGF), Tumor Growth Factor beta (TGF- β),
 Vascular Endothelial Growth Factor (VEGF), Vascular Endothelial cadherin
 (VE-cadherin), Insulin-like Growth Factor (IGF), Connective-Tissue Growth Factor
 (CTGF), Tumor Necrosis Factor alpha (TNF- α), Interleukin 1 (IL-1), Interleukin 6
 15 (IL-6), Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF), and
 receptors thereof; and
 a Fc domain.

2. A fusion protein comprising:

20 an integrin binding peptide targeting at least integrins $\alpha v\beta 3$ and $\alpha 5\beta 1$, having an
 amino acid sequence selected from a group consisting of SEQ ID NO: 1, SEQ ID NO: 2,
 SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7, or
 amino acid sequence having at least 85% sequence identity to SEQ ID NO: 1, SEQ ID NO:
 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7;

25 other protein binding peptide comprising extracellular domains of VEGF receptors;
 and

a Fc domain;

wherein the integrin binding peptide has at least one mutation on a RGD motif or within
 15-20 amino acids from the RGD motif.

3. A fusion protein comprising:

an integrin binding peptide comprising disintegrin targeting at least integrins $\alpha v\beta 3$ and $\alpha 5\beta 1$ or its integrin binding fragments;

other protein binding peptide comprising extracellular domains of VEGF receptors; and
5 a Fc domain;

wherein the integrin binding peptide comprises at least one mutation on a RGD motif or within 15-20 amino acids from the RGD motif.

4. A fusion protein comprising:

10 an integrin binding portion targeting at least integrins $\alpha v\beta 3$ and $\alpha 5\beta 1$, selected from a group consisting of an amino acid sequence of SEQ ID NO: 1 with at least one mutation on a RGD motif or within 15-20 amino acids from the RGD motif, an amino acid sequence having at least 85% sequence identity to the amino acid of SEQ ID NO: 1 with at least one mutation, and an amino acid sequence of SEQ ID NO: 2;

15 a human or humanized constant sub-region comprising an immunoglobulin CH2 domain and a CH3 domain;

other protein binding peptide having an Ig-like domain D2 of a VEGFR1 and an Ig-like domain D3 of a VEGFR2.

20 5. The fusion protein according to claims 1, 2 or 3 comprising the integrin binding peptide, the Fc domain and the other protein binding peptide from C-terminus to N-terminus.

25 6. The fusion protein according to claims 1, 2 or 3 comprising the integrin binding peptide, the Fc domain and the other protein binding peptide from N-terminus to C-terminus.

7. The fusion protein according to any of claims 1-4, wherein the integrin binding peptide has at least 85% sequence identity to SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7.
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8. The fusion protein according to claim 7, wherein the integrin binding peptide has at least 85% sequence identity to SEQ ID NO: 2.

5 9. The fusion protein of any of claims 1-4 further comprising a linker sequence between the integrin binding peptide and the other protein binding peptide.

10. The fusion protein of any of claims 1-4 further comprising a signal peptide sequence upstream of the other protein binding peptide.

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11. The fusion protein according to claim 2 or 3, wherein the extracellular domains of VEGF receptors comprise an Ig-like domains D1-D7 of the VEGF receptors.

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12. The fusion protein according to claim 2 or 3, wherein extracellular domains of VEGF receptors comprising i) an Ig-like domain D2 of a VEGFR1 and an Ig-like domain D3 of a VEGFR2; ii) the amino acid sequence of SED ID NO: 10 or iii) an amino acid sequence having at least 90% identity to SEQ ID NO: 10.

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13. The fusion protein of any of claims 1-3 further comprising a GS or G₉ linker between the Fc domain and the integrin binding peptide or the other protein binding peptide.

14. A nucleic acid encoding the fusion protein of any of claims 1-4.

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15. A dimer of the fusion protein of any of claims 1-4.

16. A vector comprising a nucleotide sequence encoding the fusion protein of any of claims 1-4.

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17. A method of producing a fusion protein, comprising culturing a host cell comprising a nucleic acid encoding the fusion protein of any of claims 1-4 under a condition that produces the fusion protein, and recovering the fusion protein produced by the host cell.

18. A composition comprising the fusion protein according to any of claims 1-4 and a pharmaceutically acceptable adjuvant, carrier or excipient.

19. Use of the fusion protein of any one of claims 1-4 in the manufacture of a medicament for treating/preventing an angiogenic disease.

20. The use of claim 19, wherein the angiogenic disease comprises rheumatoid arthritis, inflammatory arthritis, osteoarthritis, ocular and systemic cancer, tumor related metastasis and invasion, ocular disease characterized by neovascularization or ischemia, uveitis, retinitis pigmentosa, age-related macular degeneration (AMD), diabetic retinopathy and diabetic macular edema (DME).

21. The use of claim 20, wherein the ocular disease characterized by neovascularization or ischemia is choroidal neovascularization.

22. Use of the fusion protein of any one of claims 1-4 in the manufacture of a medicament for treating/preventing systemic fibrosis diseases.

23. The use of claim 22, wherein the systemic fibrosis diseases include idiopathic lung fibrosis (IPF), nonalcoholic steatohepatitis (NASH) or liver fibrosis, diabetic nephropathy and/or kidney fibrosis, dermal fibrosis or keloid, cardio-fibrosis, and ischemia induced stroke.

24. Use of the fusion protein of any one of claims 1-4 in the manufacture of a medicament for wound healing.