Claims

1. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain binds PDGF-BB in PBS with a Kd below 10^{-7}M.

2. The binding protein of claim 1, wherein said ankyrin repeat domain inhibits the binding of PDGF-BB to PDGFRbeta in PBS with an IC_{50} value below 10^{-7}M.

3. The binding protein of claim 1 or 2, wherein said ankyrin repeat domain inhibits the PDGF-BB stimulated proliferation of 3T3 fibroblasts with an IC_{50} value below 10^{-7}M.

4. The binding protein of any one of claims 1 to 3, wherein said ankyrin repeat domain competes for binding to PDGF-BB with an ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60.

5. The binding protein of any one of claims 1 to 4, wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 70% amino acid sequence identity with one ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60,
wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing; and
L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

6. The binding protein of claim 5 , wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 76% amino acid sequence identity with one ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60,
wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing; and
L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

7. The binding protein of claim 5 , wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 70% amino acid sequence identity in its framework positions with one ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60,

wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing; and
L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

8. The binding protein of claim 5 , wherein said ankyrin repeat domain is selected from the group consisting of SEQ ID NOs:23 to 60
wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing; and
L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

9. The binding protein of any one of claims 1 to 8, wherein said ankyrin repeat domain attaches to the same epitope as an ankyrin repeat domain selected from the group consisting of SEQ ID NOs:23 to 60.

10. The binding protein of any one of claims 1 to 7 or 9, wherein said ankyrin repeat domain comprises an ankyrin repeat module having an amino acid sequence selected from the group consisting of SEQ ID NO:12, 14, 15, 17, 18 and 19 and sequences, wherein up to 9 amino acids in SEQ ID NO:12, 14, 15, 17, 18 and 19 are exchanged by any amino acid.

11. The binding protein of claim 10, wherein said ankyrin repeat domain comprises an ankyrin repeat module having an amino acid sequence selected from the group consisting of SEQ ID NO:12, 14, 15, 17, 18 and 19 and sequences, wherein up to 2 amino acids in SEQ ID NO:12, 14, 15, 17, 18 and 19 are exchanged by any amino acid.

12. The binding protein of claim 10, wherein said ankyrin repeat domain comprises an ankyrin repeat module having an amino acid sequence selected from the group consisting of SEQ ID NO:12, 14, 15, 17, 18 and 19 and sequences, wherein up to 8 amino acids in the framework positions of SEQ ID NO:12, 14, 15, 17, 18 and 19 are exchanged by any amino acid.

13. The binding protein of claim 10, wherein said ankyrin repeat module has the amino acid sequence
KDEEGTTPLHYAAVWGHLEIVEVLLKAGADVNA (SEQ ID NO:12)

and sequences, wherein up to 9 amino acids in SEQ ID NO:12 are exchanged by any amino acid and wherein

E at position 3 is optionally exchanged by an amino acid selected from the group consisting of D, W, Q, I and Y;

E at position 4 is optionally exchanged by an amino acid selected from the group consisting of T, D, Y, and S;

T at position 6 is optionally exchanged by an amino acid selected from the group consisting of S and F;

Y at position 11 is optionally exchanged by F;

V at position 14 is optionally exchanged by an amino acid selected from the group consisting of A, Y and T;

W at position 15 is optionally exchanged by an amino acid selected from the group consisting of F, K, V, and Y.

14. The binding protein of claim 13, wherein said ankyrin repeat module has the amino acid sequence

KDEEGTTPLHYAAVWGHLEIVEVLLKAGADVNA (SEQ ID NO:12)

wherein up to 8 amino acids in framework positions of SEQ ID NO:12 are exchanged by any amino acid and wherein

E at position 3 is optionally exchanged by an amino acid selected from the group consisting of D, W, Q, I and Y;

E at position 4 is optionally exchanged by an amino acid selected from the group consisting of T, D, Y, and S;

T at position 6 is optionally exchanged by an amino acid selected from the group consisting of S and F;

Y at position 11 is optionally exchanged by F;

V at position 14 is optionally exchanged by an amino acid selected from the group consisting of A, Y and T;

W at position 15 is optionally exchanged by an amino acid selected from the group consisting of F, K, V, and Y.

15. The binding protein of any one of claims 1 to 14, wherein said ankyrin repeat domain comprises a capping module having an amino acid sequence selected from the group consisting of SEQ ID NO:13 and 16 and sequences, wherein up to 8 amino acids in SEQ ID NO:13 and 16 are exchanged by any amino acid.

16. The binding protein of claim 15, wherein said ankyrin repeat domain comprises a capping module having an amino acid sequence selected from the group consisting of SEQ ID NO:13 and 16 and sequences, wherein up to 7 amino acids in framework positions of SEQ ID NO:13 and 16 are exchanged by any amino acid.

17. The binding protein of claim 15, wherein the ankyrin repeat domain with binding specificity to PDGF-BB comprises a C-terminal capping module with the amino acid sequence
QDIYGATPADLAALVGHEDIAEVLQKLN (SEQ ID NO:13)
and sequences, wherein up to 8 amino acids in SEQ ID NO:13 are exchanged by any amino acid and wherein
I at position 3 is optionally exchanged by an amino acid selected from the group consisting of K, L, A and V;
Y at position 4 is optionally exchanged by an amino acid selected from the group consisting of W. F and S;
A at position 6 is optionally exchanged by K;
L at position 14 is optionally exchanged by an amino acid selected from the group consisting of F, Y and D;
V at position 15 is optionally exchanged by an amino acid selected from the group consisting of L, I , A and N; and
V at position 23 is exchanged by an amino acid selected from the group consisting of I and L.

18. The binding protein of claim 15, wherein the ankyrin repeat domain with binding specificity to PDGF-BB comprises a C-terminal capping module with the amino acid sequence
QDIYGATPADLAALVGHEDIAEVLQKLN (SEQ ID NO:13)
wherein up to 7 amino acids in framework positions of SEQ ID NO:13 are exchanged by any amino acid and wherein
I at position 3 is optionally exchanged by an amino acid selected from the group consisting of K, L, A and V;
Y at position 4 is optionally exchanged by an amino acid selected from the group consisting of W. F and S;
A at position 6 is optionally exchanged by K;
L at position 14 is optionally exchanged by an amino acid selected from the group consisting of F, Y and D;

V at position 15 is optionally exchanged by an amino acid selected from the group consisting of L, I , A and N; and
V at position 23 is exchanged by an amino acid selected from the group consisting of I and L.

19. The binding protein of any one of claims 1 to 4, wherein said ankyrin repeat domain comprises the ankyrin repeat module of claim 13 and the C-terminal capping module of claim 17.

20. The binding protein of claim 19 wherein said ankyrin repeat domain comprises the ankyrin repeat module of SEQ ID NO:12 directly followed by the C-terminal capping module of SEQ ID NO:13.

21. The binding protein of any one of claims 1 to 7 and 9 to 19, wherein one or more of the amino acid residues of the ankyrin repeat modules of said ankyrin repeat domain are exchanged by an amino acid residue found at the corresponding position on alignment of an ankyrin repeat unit.

22. The binding protein of any one of claims 1 to 4, comprising a peptide of any one of the sequences SEQ ID NO:12 to 19 and 23 to 61.

23. A nucleic acid encoding a binding protein of any one of claims 1 to 22 .

24. A pharmaceutical composition comprising the binding protein of any one of claims 1 to 22 or the nucleic acid of claim 23 , and optionally a pharmaceutical acceptable carrier and/or diluent.

25. A method of treating a condition selected from exudative age-related macular degeneration, polypoidal choroidal neovascularization, and pathological myopia, the method comprising the step of administering, to a patient in need of such treatment, a therapeutically effect amount of a binding protein of any one of claims 1 to 22 .

26. A method of treating a condition selected from exudative age-related macular degeneration, polypoidal choroidal neovascularization, and pathological myopia, the method comprising the step of administering, to a patient in need of such treatment, a

therapeutically effect amount of a binding protein comprising an ankyrin repeat domain specifically binding PDGF-BB and an ankyrin repeat domain specifically binding VEGF-A.

CLAIMS

1. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB and wherein said ankyrin repeat domain comprises an ankyrin repeat module having an amino acid sequence selected from the group consisting of SEQ ID NO: 12, 14, 15, 17, 18 and 19 and sequences, wherein

(1) up to 6 amino acids in SEQ ID NO:12 are exchanged by another amino acid, wherein the up to 6 amino acid exchanges are:

E at position 3 is optionally exchanged by an amino acid selected from the group consisting of D, W, Q, I and Y;

E at position 4 is optionally exchanged by an amino acid selected from the group consisting of T, D, Y, and S;

T at position 6 is optionally exchanged by an amino acid selected from the group consisting of S and F;

Y at position 11 is optionally exchanged by F;

V at position 14 is optionally exchanged by an amino acid selected from the group consisting of A, Y and T; and

W at position 15 is optionally exchanged by an amino acid selected from the group consisting of F, K, V, and Y; or

(2) up to 6 amino acids in SEQ ID NO:15 are exchanged by another amino acid, wherein the up to 6 amino acid exchanges are:

Q at position 3 is optionally exchanged by A;

E at position 4 is optionally exchanged by D;

T at position 6 is optionally exchanged by E;

F at position 11 is optionally exchanged by Y;

S at position 14 is optionally exchanged by V; and

V at position 15 is optionally exchanged by W; or

(3) up to 2 amino acids in SEQ ID NO:17 are exchanged by another amino acid, wherein the up to 2 amino acid exchanges are:

K at position 1 is optionally exchanged by Q or I; and

L at position 3 is optionally exchanged by N; or

(4) up to 3 amino acids in SEQ ID NO:18 are exchanged by another amino acid, wherein the up to 3 amino acid exchanges are:

K at position 1 is optionally exchanged by Q;

W at position 14 is optionally exchanged by H; and

A at position 15 is optionally exchanged by V; or

(5) up to 4 amino acids in SEQ ID NO:19 are exchanged by another amino acid, wherein the up to 4 amino acid exchanges are:

K at position 1 is optionally exchanged by N;

A at position 12 is optionally exchanged by T;

A at position 13 is optionally exchanged by T; and

E at position 22 is optionally exchanged by D.

2. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDEEGTTPLHYAAVWGHLEIVEVLLKAGADVNA (SEQ ID NO:12).

3. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDEEGTTPLHYAAVWGHLEIVEVLLKAGADVNA (SEQ ID NO:12), wherein up to 6 amino acids in SEQ ID NO:12 are exchanged by another amino acid, wherein the up to 6 amino acid exchanges are:

E at position 3 is optionally exchanged by an amino acid selected from the group consisting of D, W, Q, I and Y;

E at position 4 is optionally exchanged by an amino acid selected from the group consisting of T, D, Y, and S;

T at position 6 is optionally exchanged by an amino acid selected from the group consisting of S and F;

Y at position 11 is optionally exchanged by F;

V at position 14 is optionally exchanged by an amino acid selected from the group consisting of A, Y and T; and

W at position 15 is optionally exchanged by an amino acid selected from the group consisting of F, K, V, and Y.

4. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDKSGHTPLHLAAYSGHLEIVEVLLKAGADVNA (SEQ ID NO:14).

5. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDQEGTTPLHFAASVGHLEIVEVLLKAGADVNA (SEQ ID NO:15).

6. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDQEGTTPLHFAASVGHLEIVEVLLKAGADVNA (SEQ ID NO:15), wherein up to 6 amino acids in SEQ ID NO:15 are exchanged by another amino acid, wherein the up to 6 amino acid exchanges are:

Q at position 3 is optionally exchanged by A;

E at position 4 is optionally exchanged by D;

T at position 6 is optionally exchanged by E;

F at position 11 is optionally exchanged by Y;

S at position 14 is optionally exchanged by V; and

V at position 15 is optionally exchanged by W.

7. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDLNGQTPLHLAADIGHLEIVEVLLKAGADVNA (SEQ ID NO:17).

8. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDLNGQTPLHLAADIGHLEIVEVLLKAGADVNA (SEQ ID NO:17), wherein up to 2 amino acids in SEQ ID NO:17 are exchanged by another amino acid, wherein the up to 2 amino acid exchanges are:

K at position 1 is optionally exchanged by Q or I; and

L at position 3 is optionally exchanged by N.

9. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDYAGSTPLRLAAWAGHLEIVEVLLKAGADVNA (SEQ ID NO:18).

10. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDYAGSTPLRLAAWAGHLEIVEVLLKAGADVNA (SEQ ID NO:18), wherein up to 3 amino acids in SEQ ID NO:18 are exchanged by another amino acid, wherein the up to 3 amino acid exchanges are:

K at position 1 is optionally exchanged by Q;

W at position 14 is optionally exchanged by H; and

A at position 15 is optionally exchanged by V.

11. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDYFGYTPLHLAAYFGHLEIVEVLLKAGADVNA (SEQ ID NO:19).

12. The recombinant binding protein of claim 1, wherein said ankyrin repeat module has the amino acid sequence KDYFGYTPLHLAAYFGHLEIVEVLLKAGADVNA (SEQ ID NO:19), wherein up to 4 amino acids in SEQ ID NO:19 are exchanged by another amino acid, wherein the up to 4 amino acid exchanges are:

K at position 1 is optionally exchanged by N;

A at position 12 is optionally exchanged by T;

A at position 13 is optionally exchanged by T; and
E at position 22 is optionally exchanged by D.

13. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB and wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 90% amino acid sequence identity with one ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60, wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing, and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

14. The recombinant binding protein of claim 13, wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 95% amino acid sequence identity with one ankyrin repeat domain selected from the group consisting of SEQ ID NOs: 23 to 60, wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing, and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

15. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB and wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 85% amino acid sequence identity with SEQ ID NO: 24, wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing, and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

16. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB and wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 85% amino acid sequence identity with SEQ ID NO: 45, wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing, and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

17. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB and wherein said ankyrin repeat domain comprises an amino acid sequence that has at least 85% amino acid sequence identity with SEQ ID NO: 50, wherein G at position 1 and/or S at position 2 of said

ankyrin repeat domain are optionally missing, and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

18. The recombinant binding protein of claim 1, wherein said ankyrin repeat domain binds PDGF-BB in PBS with a Kd below 10^{-7}M.

19. The recombinant binding protein of claim 1, wherein said ankyrin repeat domain inhibits the binding of PDGF-BB to PDGFRbeta in PBS with an IC_{50} value below 10^{-7}M.

20. The recombinant binding protein of claim 1, wherein said ankyrin repeat domain inhibits the PDGF-BB stimulated proliferation of 3T3 fibroblasts with an IC_{50} value below 10^{-7}M.

21. The binding protein of claim 1, wherein said ankyrin repeat domain comprises a capping module having an amino acid sequence selected from the group consisting of SEQ ID NO:13 and 16 and sequences, wherein up to 8 amino acids in SEQ ID NO:13 and 16 are exchanged by any amino acid.

22. A nucleic acid encoding a binding protein of claim 1.

23. A pharmaceutical composition comprising the binding protein of claim 1, and optionally a pharmaceutical acceptable carrier and/or diluent.

24. A pharmaceutical composition comprising the nucleic acid of claim 22, and optionally a pharmaceutical acceptable carrier and/or diluent.

25. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain binds PDGF-BB in PBS, wherein said ankyrin repeat domain is selected from the group consisting of SEQ ID NOs:23 to 60 wherein G at position 1 and/or S at position 2 of said ankyrin repeat domain are optionally missing; and L at the second last position and/or N at the last position of said ankyrin repeat domain are optionally exchanged by A.

26. A recombinant binding protein comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain binds PDGF-BB in PBS and comprises the ankyrin repeat module of SEQ ID NO:12 directly followed by the C-terminal capping module of SEQ ID NO:13.

27. A recombinant binding protein, comprising at least one ankyrin repeat domain, wherein said ankyrin repeat domain specifically binds PDGF-BB, and wherein said recombinant binding protein comprises a peptide of any one of the sequences SEQ ID NO:12 to 19 and 23 to 61.

28. The binding protein of claim 1 for use in the treatment of a medical condition selected from exudative age-related macular degeneration, polypoidal choroidal neovascularization, and pathological myopia.

29. The binding protein of claim 27 for use in the treatment of a medical condition selected from exudative age-related macular degeneration, polypoidal choroidal neovascularization, and pathological myopia.