Claims

1. A recombinant binding protein comprising an ankyrin repeat domain and a polyethylene glycol moiety of at least 5 kDa molecular weight, wherein said ankyrin domain binds VEGF-Axxx with a Kd below 10^{-9}M and inhibits VEGF-Axxx binding to VEGFR-2.

2. The binding protein of claim 1, which has an apparent molecular weight of at least 100 kDa when analyzed at a concentration of 0.1 mM in PBS at room temperature by size exclusion chromatography using globular proteins as molecular weight standards.

3. The binding protein of claim 1, wherein the N-terminal capping module of said ankyrin repeat domain comprises an Asp residue at position 5.

4. The binding protein of claim 1, wherein said ankyrin repeat domain competes for binding to VEGF-Axxx with the ankyrin repeat domains of SEQ ID NO:1 or 3.

5. The binding protein of claim 1, wherein said ankyrin repeat domain is selected from the group consisting of the ankyrin repeat domains of SEQ ID NO:1 to 7.

6. The binding protein of any one of claims 1 to 5, wherein said ankyrin repeat domain is conjugated at its C-terminus via a peptide bond to a polypeptide linker and a C-terminal Cys residue, wherein the thiol of said C-terminal Cys is further conjugated to a maleimide-coupled polyethylene glycol.

7. The binding protein of claim 6, wherein said maleimide-coupled polyethylene glycol is α-[3-(3-maleimido-1-oxopropyl)amino]propyl-ω-methoxy-polyoxyethylene.

8. The binding protein of claim 1, wherein said binding protein is an ankyrin repeat protein selected from the group consisting of the ankyrin repeat proteins of SEQ ID NO:2, 3, 5, 6 or 7.

9. The binding protein of any one of claims 6 to 8, wherein said polyethylene glycol moiety has a molecular weight of around 20 kDa.

10. The binding protein of claim 1 comprising the ankyrin repeat protein of SEQ ID NO:3 wherein the thiol of the C-terminal Cys of said ankyrin repeat protein is further conjugated to a maleimide-coupled polyethylene glycol.

11. The binding protein of claim 10 wherein said maleimide-coupled polyethylene glycol is α-[3-(3-maleimido-1-oxopropyl)amino]propyl-ω-methoxy-polyoxyethylene, and wherein the polyethylene glycol moiety has a molecular weight of at least 10 kDa.

12. A pharmaceutical composition comprising the binding protein of any one of claims 1 to 11 and optionally a pharmaceutical acceptable carrier and/or diluent.

13. A pharmaceutical composition according to claim 12 for use in the treatment of an eye disease.

14. A pharmaceutical composition according to claim 12 for use in the treatment of an eye disease by intravitreal injection.

15. Use of a compound according to claims 1 to 11 for the manufacture of a pharmaceutical composition for the treatment of pathological angiogenesis.

Claims

1. A recombinant binding protein comprising an ankyrin repeat domain comprising the amino acid sequence 1 to 126 of SEQ ID NO: 3 and a polyethylene glycol moiety of at least 5 kDa molecular weight.

2. The binding protein of claim 1, wherein said ankyrin repeat domain is conjugated at its C-terminus via a peptide bond to a polypeptide linker consisting of 2 to 24 amino acids and having a C-terminal Cys residue, wherein the thiol of said C-terminal Cys is further conjugated to a maleimide-coupled polyethylene glycol.

3. The binding protein of claim 2, wherein said maleimide-coupled polyethylene glycol is α-[3-(3-maleimido-1-oxopropyl)amino]propyl-ω-methoxy-polyoxyethylene.

4. The binding protein of any one of claims 2 to 4, wherein said polyethylene glycol moiety has a molecular weight of around 20 kDa.

5. The binding protein of claim 1 comprising the amino acid sequence of SEQ ID NO:3 wherein the thiol of the C-terminal Cys of SEQ ID NO:3 is further conjugated to a maleimide-coupled polyethylene glycol.

6. The binding protein of claim 5 wherein said maleimide-coupled polyethylene glycol is α-[3-(3-maleimido-1-oxopropyl)amino]propyl-ω-methoxy-polyoxyethylene, and wherein the polyethylene glycol moiety has a molecular weight of at least 10 kDa.

7. A pharmaceutical composition comprising the binding protein of any one of claims 1 to 6 and optionally a pharmaceutical acceptable carrier and/or diluent.

8. A pharmaceutical composition according to claim 7 for use in the treatment of an eye disease.

9. A pharmaceutical composition according to claim 7 for use in the treatment of an eye disease by intravitreal injection.

10. Use of a compound according to claims 1 to 6 for the manufacture of a pharmaceutical composition for the treatment of pathological angiogensis.