Claims

1. A bispecific binding molecule comprising

- ~~at least one~~a VEGF-binding ~~component~~ immunoglobulin single variable domain,

- ~~at least one~~a serum albumin binding ~~component~~ immunoglobulin single variable domain, and

- ~~at least one~~an Ang2-binding ~~component~~ immunoglobulin single variable domain, ~~wherein said Ang2-binding component~~

~~binds to Ang2 with a potency at least 5,000 times higher than to Ang1 or to Ang4, and~~

wherein

- said VEGF-binding immunoglobulin single variable domain has the following CDR sequences:

CDR1: SYSMG

CDR2: AISKGGYKYDAVSLEG

CDR3: SRAYGSSRLRLADTYEY,

said serum albumin binding immunoglobulin single variable domain has the following CDR sequences:

CDR1: SFGMS (SEQ ID NO:255)

CDR2: SISGSGSDTLYADSVKG (SEQ ID NO:256)

CDR3: GGSLSR (SEQ ID NO:257)

said Ang2-binding immunoglobulin single variable domain has the following CDR sequences:

CDR1: DYAIG (SEQ ID NO:248)

CDR2: AIRSSGGSTYYADSVKG (SEQ ID NO:249)

CDR3: VPAGRLRYGEQWYPIYEYDA (SEQ ID NO:250)

~~, serum albumin and Ang2-binding components are immunoglobulin single variable domains, each immunoglobulin single variable domain consisting of four framework regions and three complementarity determining regions (CDRs), and wherein said bispecific binding molecule is selected from the group consisting of bispecific binding molecules having~~

~~(i) the CDR sequences as present in VEGFANGBII00022 (SEQ ID NO: 207),~~

~~(ii) the CDR sequences as present in VEGFANGBII00025 (SEQ ID NO: 210), and~~

~~(iii) the CDR sequences as present in VEGFANGBII00028 (SEQ ID NO: 213).~~

2. The bispecific binding molecule of claim 1, wherein said immunoglobulin single variable domains are VHHs.

3. The bispecifc binding molecule of claim 2, wherein
- said VEGF binding VHH has the following CDR sequences:
CDR1: SYSMG
CDR2: AISKGGYKYDAVSLEG
CDR3: SRAYGSSRLRLADTYEY,
- said serum albumin binding VHH is the Alb11 VHH domain (SEQ ID NO: 254), and
- said Ang2-binding VHH is the ANGBII00938 domain (SEQ ID NO: 222).

~~3~~4. The bispecific binding molecule of claim ~~2~~3, ~~selected from the group consisting of bispecific binding molecules (i) to (iii),~~wherein
~~the molecules (i) comprising~~
- ~~a~~ said VEGF binding ~~domain comprising the CDRs 1 to 3 of~~VHH is the VEGFBII00038 ~~VHH~~ domain (SEQ ID NO:57)~~,~~.
~~- the Alb11 VHH domain (SEQ ID NO: 254) as the serum albumin binding component, and~~
~~- the ANGBII00938 VHH domain (SEQ ID NO: 222) as the Ang2-binding domain, in this order;~~
~~the molecules (ii) comprising~~
~~- a VEGF binding domain comprising the CDRs 1 to 3 of the VEGFBII00038 VHH domain (SEQ ID NO:57),~~

~~- the Alb11 VHH domain (SEQ ID NO: 254) as the serum albumin binding component, and~~

~~- two ANGBII00921 VHH domains (SEQ ID NO: 220) as the Ang2-binding domains, in this order;~~

~~and~~

~~the molecules (iii) comprising~~

~~- a VEGF binding domain comprising the CDRs 1 to 3 of the VEGFBII00038 VHH domain (SEQ ID NO:57),~~

~~- the Alb11 VHH domain (SEQ ID NO: 254) as the serum albumin binding component, and~~

~~- two ANGBII00956 VHH domains (SEQ ID NO: 223) as the Ang2-binding domains,~~

~~in this order.~~

45. ~~The~~ A bispecific binding molecule ~~of claim 3, selected from the group consisting of (i)~~ VEGFANGBII00022 (SEQ ID NO: 207)~~,~~

~~(ii) VEGFANGBII00025 (SEQ ID NO: 210), and~~

~~(iii) VEGFANGBII00028 (SEQ ID NO: 213)~~.

56. A nucleic acid molecule encoding a bispecific binding molecule of any one of claims 1 to 45.

67. A vector containing a nucleic acid molecule of claim ~~5~~6.

78. A host cell containing ~~a nucleic acid molecule of claim 5 or~~ a vector of claim ~~6~~7.

89. A pharmaceutical composition containing at least one bispecific binding molecule of any one of claims 1 to ~~4~~5 as the active ingredient.

~~9. The pharmaceutical composition of claim 8 for the treatment of a disease that is associated with VEGF- and/or Ang2-mediated effects on angiogenesis.~~

10. The pharmaceutical composition of claim ~~8 or~~ 9 for use in the treatment of cancer and cancerous diseases.

11. The pharmaceutical composition of claim ~~8 or~~ 9 for use in the treatment of eye diseases.

12. A method of manufacturing a bispecific binding molecule of any one of claims 1 to 5 comprising the steps of:
- culturing host cells according to claim 8 under conditions that allow expression of said bispecific binding molecule; and
- recovering or isolating said bispecific binding molecule expressed by said host cells from the culture.

13. The method of claim 12, additionally comprising the step of:
- further purifying or modifying or formulating said bispecific binding molecule.