

Claims:

Claim 1. An antigen-binding molecule, optionally isolated, which binds to VEGFA, wherein the antigen-binding molecule comprises a single domain antibody sequence incorporating the following CDRs:

(a) CDR1 having the amino acid sequence of SEQ ID NO:13
CDR2 having the amino acid sequence of SEQ ID NO:14
CDR3 having the amino acid sequence of SEQ ID NO:15; or

(b) CDR1 having the amino acid sequence of SEQ ID NO:2
CDR2 having the amino acid sequence of SEQ ID NO:3
CDR3 having the amino acid sequence of SEQ ID NO:4; or

(c) CDR1 having the amino acid sequence of SEQ ID NO:6
CDR2 having the amino acid sequence of SEQ ID NO:7
CDR3 having the amino acid sequence of SEQ ID NO:8.

Claim 2. The antigen-binding molecule according to claim 1, wherein the antigen-binding molecule comprises, or consists of, an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:16, SEQ ID NO:1 or SEQ ID NO:5.

Claim 3. The antigen-binding molecule according to claim 1 or claim 2, wherein the antigen-binding molecule comprises a single domain antibody sequence incorporating the following FRs:

FR1 having the amino acid sequence of SEQ ID NO:9
FR2 having the amino acid sequence of SEQ ID NO:10
FR3 having the amino acid sequence of SEQ ID NO:11
FR4 having the amino acid sequence of SEQ ID NO:12.

~~4. The antigen-binding molecule according to any one of claims 1 to 3, wherein the antigen-binding molecule comprises a single domain antibody sequence incorporating the following CDRs:~~

~~CDR1 having the amino acid sequence of SEQ ID NO:2
CDR2 having the amino acid sequence of SEQ ID NO:3
CDR3 having the amino acid sequence of SEQ ID NO:4.~~

~~5. The antigen-binding molecule according to any one of claims 1 to 4, wherein the antigen-binding molecule comprises, or consists of, an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:1.~~

~~6. The antigen-binding molecule according to any one of claims 1 to 3, wherein the antigen-binding molecule comprises a single domain antibody sequence incorporating the following CDRs:~~

~~CDR1 having the amino acid sequence of SEQ ID NO:6
CDR2 having the amino acid sequence of SEQ ID NO:7
CDR3 having the amino acid sequence of SEQ ID NO:8.~~

~~7. The antigen-binding molecule according to any one of claims 1 to 3 or claim 6, wherein the antigen-binding molecule comprises, or consists of, an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:5.~~

Claim 48. The antigen-binding molecule according to any one of claims 1 to 73, wherein the antigen-binding molecule inhibits interaction between VEGFA and VEGFR.

5 Claim 59. The antigen-binding molecule according to any one of claims 1 to 84, wherein the antigen-binding molecule is a multispecific antigen-binding molecule, further comprising an antigen-binding domain specific for a target antigen other than VEGFA; optionally wherein the multispecific antigen-binding molecule is a bispecific antibody.

10 Claim 640. A chimeric antigen receptor (CAR) comprising an antigen-binding molecule according to any one of claims 1 to 95.

15 Claim 744. A nucleic acid, optionally isolated, encoding an antigen-binding molecule according to any one of claims 1 to 95, or a CAR according to claim 406.

20 Claim 842. An expression vector comprising a nucleic acid according to claim 447.

25 Claim 943. A cell comprising an antigen-binding molecule according to any one of claims 1 to 95, a CAR according to claim 406, a nucleic acid according to claim 447, or an expression vector according to claim 428.

30 Claim 1044. A method for producing an antigen-binding molecule which binds to VEGFA, comprising culturing a cell according to claim 43-9 under conditions suitable for expression of an antigen-binding molecule or CAR by the cell.

35 Claim 1145. A composition comprising an antigen-binding molecule according to any one of claims 1 to 95, a CAR according to claim 406, a nucleic acid according to claim 447, an expression vector according to claim 428, or a cell according to claim 439, and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

40 Claim 1246. An antigen-binding molecule according to any one of claims 1 to 95, a CAR according to claim 406, a nucleic acid according to claim 447, an expression vector according to claim 428, a cell according to claim 439, or a composition according to claim 4511, for use in a method of medical treatment or prophylaxis.

45 ~~17. An antigen-binding molecule according to any one of claims 1 to 9, a CAR according to claim 10, a nucleic acid according to claim 11, an expression vector according to claim 12, a cell according to claim 13, or a composition according to claim 15, for use in a method of treatment or prevention of a disease in which VEGFA/VEGFR-mediated signalling is pathologically implicated.~~

Claim 1318. Use of an antigen-binding molecule according to any one of claims 1 to 95, a CAR according to claim 406, a nucleic acid according to claim 447, an expression vector according to claim 428, a cell according to claim 439, or a composition according to claim 4511, in the manufacture of a medicament for treating or preventing a disease in which VEGFA/VEGFR-mediated signalling is pathologically-implicated.

19. ~~A method of treating or preventing a disease in which VEGFA/VEGFR mediated signalling is pathologically implicated, comprising administering to a subject a therapeutically or prophylactically-effective amount of an antigen-binding molecule according to any one of claims 1 to 9, a CAR according to claim 10, a nucleic acid according to claim 11, an expression vector according to claim 12, a cell according to claim 13, or a composition according to claim 15.~~

Claim 1420. The ~~antigen-binding molecule, CAR, nucleic acid, expression vector, cell or composition for use according to claim 17, the~~ use according to claim ~~1813, or the method according to claim 19,~~ wherein the disease is selected from: a disease characterised by pathological angiogenesis, a cancer, a VEGFA-expressing cancer, a VEGFR-expressing cancer, an ocular disease, retinopathy, diabetic retinopathy, macular degeneration, age-related macular degeneration, wet age-related macular degeneration, retinal vein occlusion, myopic choroidal neovascularisation, retinopathy of prematurity, neovascular glaucoma, central serous retinopathy, ocular tumor, corneal neovascularisation, an inflammatory disease, an autoimmune disease, arthritis, rheumatoid arthritis, osteoarthritis, psoriasis, multiple sclerosis, sepsis, motor neuron disease and amyotrophic lateral sclerosis.

Claim 1524. An *in vitro* complex, optionally isolated, comprising an antigen-binding molecule according to any one of claims 1 to 9-5 bound to VEGFA.

Claim 1622. A method for detecting VEGFA in a sample, comprising contacting a sample containing, or suspected to contain, VEGFA with an antigen-binding molecule according to any one of claims 1 to 95, and detecting the formation of a complex of the antigen-binding molecule with VEGFA.

Claim 1723. Use of an antigen-binding molecule according to any one of claims 1 to 9-5 in a method for detecting, localizing or imaging VEGFA, or cells comprising or expressing VEGFA; or as an *in vitro* or *in vivo* diagnostic or prognostic agent.

Claim 1824. A method of selecting or stratifying a subject for treatment with a VEGFA-targeted agent, the method comprising contacting, *in vitro*, a sample from the subject with an antigen-binding molecule according to any one of claims 1 to 95, and detecting the formation of a complex of the antigen-binding molecule with VEGFA.

~~25. — Use of an antigen-binding molecule according to any one of claims 1 to 9 as an *in vitro* or *in vivo* diagnostic or prognostic agent.~~

Claim 1926. Use of an antigen-binding molecule according to any one of claims 1 to 9-5 in a method for detecting, localizing or imaging a disease/condition characterised by expression of VEGFA.