[Document Name] Claims

[Claim 1]

An antibody having properties described in the following (I) to (III) or a functional fragment thereof:

(I) binding to the ROBO4 protein with a K_D value of 1×10^{-8} or lower;

(II) suppressing or inhibiting vascular endothelial cell migration in the absence of a cross-linking antibody *in vitro*; and

(III) suppressing or inhibiting angiogenesis *in vivo*.

[Claim 2]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is the human ROBO4 protein.

[Claim 3]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is a protein consisting of an amino acid sequence of amino acid Nos. 1 to 1007 of SEQ ID NO: 2 .

[Claim 4]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is a protein consisting of an amino acid sequence of amino acid Nos. 46 to 1007 of SEQ ID NO: 2 .

[Claim 5]

The antibody or the functional fragment thereof according to claim 3 or 4, wherein the antibody or the functional fragment thereof binds to a site consisting of an amino acid sequence of amino acid Nos. 132 to 209 of SEQ ID NO: 2 .

[Claim 6]

The antibody or the functional fragment thereof according to claim 1, wherein the antibody or the functional fragment thereof is a monoclonal antibody or a functional fragment thereof.

[Claim 7]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody consists of a heavy chain comprising CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 44 (Figure 25) , CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 46 (Figure 26) or an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 46 by the substitution of one amino acid, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 48 (Figure 27) , and a light chain comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 50 (Figure 28) or an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 50 by the substitution of one to three amino acid(s), CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 52 (Figure 29) , and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 54 (Figure 30) .

[Claim 8]

The antibody or the functional fragment thereof according to any one of claims 1 to 7, wherein the antibody consists of a heavy chain comprising CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 44 (Figure 25) , CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 46 (Figure 26) or the amino acid sequence represented by SEQ ID NO: 68 (Figure 44) , and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 48 (Figure 27) , and a light chain comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 50 (Figure 28) or the amino acid sequence represented by SEQ ID NO: 70 (Figure 46) , CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 52 (Figure 29) , and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 54 (Figure 30) .

[Claim 9]

The antibody or the functional fragment thereof according to any one of claims 1 to 7, wherein the antibody comprises a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 31 (Figure 16), and a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 33 (Figure 18).

[Claim 10]

The antibody or the functional fragment thereof according to any one of claims 1 to 8, wherein the antibody comprises any one heavy chain variable region selected from the following a) to d) and a light chain variable region selected from e) and f):

a) a heavy chain (hMAb1-H1-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 56 (Figure 32) ,

b) a heavy chain (hMAb1-H2-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34) ,

c) a heavy chain (hMAb1-H3-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 60 (Figure 36) , and

d) a heavy chain (hMAb1-H4-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38) ; and

e) a light chain (hMAb1-L1-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40) , and

f) a light chain (hMAb1-L2-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42) .

[Claim 11]

The antibody or the functional fragment thereof according to any one of claims 1 to 8, wherein the antibody comprises any one of the following combinations 1) to 6) of a heavy chain variable region and a light chain variable region:

1) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34) and a light

chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64(Figure 40) ,

2) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42) ,

3) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42) .

4) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40) ,

5) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 56 (Figure 32) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40) , and

6) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 60 (Figure 36) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40) ,

[Claim 12]

The antibody or the functional fragment thereof according to any one of claims 1 to 11, wherein the antibody or the functional fragment thereof is a chimeric antibody or a functional fragment thereof.

[Claim 13]

The antibody or the functional fragment thereof according to any one of claims 1 to 11, wherein the antibody or the functional fragment thereof is a humanized antibody or a functional fragment thereof.

[Claim 14]

The antibody or the functional fragment thereof according to any one of claims 1 to 13, wherein the antibody comprises a human IgG1 or human IgG2 heavy chain constant region.

[Claim 15]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody or the functional fragment thereof binds to a site on an antigen recognized by the antibody according to claims 7 to 14.

[Claim 16]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody or the functional fragment thereof competes with any one antibody according to claims 7 to 14 for the binding to ROBO4 protein.

[Claim 17]

The antibody according to any one of claims 1 to 8, wherein the antibody comprises any one of the following combinations 1) to 6) of a heavy chain and a light chain:

1) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 58 (Figure 34) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-1140),

2) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 58 (Figure 34) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 66 (Figure 42) (H-1143),

3) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 62 (Figure 38) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 66 (Figure 42) (H-2143).

4) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 62 (Figure 38) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-2140),

5) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 56 (Figure 32) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-1040), and

6) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 60 (Figure 36) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-2040).

[Claim 18]

An antibody comprising a modified form of a heavy chain of any one antibody according to claim 17, wherein said modified form lacks one to several carboxyl-terminal amino acid(s) of said heavy chain.

[Claim 19]

The antibody according to any one of claims 1 to 6, wherein the antibody is 95% or more identical in the amino acid sequence to any one antibody according to claim 17; has a K_D value of 1×10^{-8} or lower for a human ROBO4; suppresses or inhibits vascular endothelial cell migration in the absence of a cross-linking antibody *in vitro*; and suppresses or inhibits angiogenesis *in vivo*.

[Claim 20]

The antibody or the functional fragment thereof according to claim 15, wherein the antibody or the functional fragment thereof is a human antibody or a functional fragment thereof.

[Claim 21]

A nucleotide sequence selected from the group consisting of the following (I) to (III):

(I) a nucleotide sequence comprising a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 20,

(II) a nucleotide sequence consisting of a nucleotide sequence comprising a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 20, and

(III) a nucleotide sequence consisting of a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 20.

[Claim 22]

A recombinant vector containing an insert of a nucleotide sequence according to claim 21.

[Claim 23]

A recombinant cell containing a nucleotide sequence according to claim 21 or a recombinant vector according to claim 22 introduced therein.

[Claim 24]

A cell producing an antibody according to any one of claims 1 to 20.

[Claim 25]

A method for producing an antibody or a functional fragment thereof according to any one of claims 1 to 20, comprising the following steps (I) and (II):

(I) culturing a cell according to claim 23 or 24; and

(II) collecting the antibody or the functional fragment thereof according to any one of claims 1 to 20 from the culture obtained in the step (I).

[Claim 26]

An antibody or a functional fragment thereof produced by a production method according to claim 25.

[Claim 27]

A modified form of an antibody or a functional fragment thereof according to any one of claims 1 to 20 and 26.

[Claim 28]

A pharmaceutical composition comprising an antibody or a functional fragment thereof according to any one of claims 1 to 20 and 26 or a modified form according to claim 27 as an active ingredient.

[Claim 29]

The pharmaceutical composition according to claim 28, wherein the pharmaceutical composition is for use in treating or preventing an angiogenic disease.

[Claim 30]

The pharmaceutical composition for the use according to claim 29, wherein the angiogenic disease is exudative age-related macular degeneration, diabetic retinopathy, macular edema, benign or malignant tumor, atherosclerosis, retrolental fibroplasia, angioma, chronic inflammation, ocular neovascular disease, proliferative retinopathy, neovascular glaucoma, immune rejection of a corneal tissue transplant or other tissue transplants, rheumatoid arthritis, psoriasis, acute inflammation, sepsis, or obesity.

[Claim 31]

The pharmaceutical composition for the use according to claim 29, wherein the angiogenic disease is exudative age-related macular degeneration, diabetic retinopathy,

macular edema, retrolental fibroplasia, ocular neovascular disease, proliferative retinopathy, neovascular glaucoma, or immune rejection of a corneal tissue transplant.

[Claim 32]

An angiogenesis inhibitor comprising an antibody or a functional fragment thereof according to any one of claims 1 to 20 and 26 or a modified form according to claim 27 as an active ingredient.

[Claim 33]

A method for treating or preventing an angiogenic disease comprising administering to a subject in need thereof an effective amont of an antibody or a functional fragment thereof according to any one of claims 1 to 20 and 26 or a modified form according to claim 27, or the composition according to any one of claims 28 to 31.

[Claim 34]

The pharmaceutical composition according to any one of claims 28 to 31, wherein said composition is used in combination with a further therapeutic or prophylactic agent.

CLAIMS

[Claim 1]

An antibody having properties described in the following (I) to (III) or a functional fragment thereof:

(I) binding to the ROBO4 protein with a K_D value of 1×10^{-8} M or lower;
(II) suppressing or inhibiting vascular endothelial cell migration in the absence of a cross-linking antibody in vitro; and
(III) suppressing or inhibiting angiogenesis in vivo,
wherein the antibody consists of a heavy chain comprising CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 44 (Figure 25), CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 46 (Figure 26) or an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 46 by the substitution of one amino acid, and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 48 (Figure 27), and a light chain comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 50 (Figure 28) or an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 50 by the substitution of one to three amino acid(s), CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 52 (Figure 29), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 54 (Figure 30).

[Claim 2]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is the human ROBO4 protein.

[Claim 3]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is a protein consisting of an amino acid sequence of amino acid Nos. 1 to 1007 of SEQ ID NO: 2.

[Claim 4]

The antibody or the functional fragment thereof according to claim 1, wherein the ROBO4 protein is a protein consisting of an amino acid sequence of amino acid Nos. 46 to 1007 of SEQ ID NO: 2.

[Claim 5]

The antibody or the functional fragment thereof according to claim 3 or 4, wherein the antibody or the functional fragment thereof binds to a site consisting of an amino acid sequence of amino acid Nos. 132 to 209 of SEQ ID NO: 2.

[Claim 6]

The antibody or the functional fragment thereof according to claim 1, wherein the antibody or the functional fragment thereof is a monoclonal antibody or a functional fragment thereof.

[Claim 7]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody consists of a heavy chain comprising CDRH1 consisting of the amino acid sequence represented by SEQ ID NO: 44 (Figure 25), CDRH2 consisting of the amino acid sequence represented by SEQ ID NO: 46 (Figure 26) or the amino acid sequence represented by SEQ ID NO: 68 (Figure 44), and CDRH3 consisting of the amino acid sequence represented by SEQ ID NO: 48 (Figure 27), and a light chain comprising CDRL1 consisting of the amino acid sequence represented by SEQ ID NO: 50 (Figure 28) or the amino acid sequence represented by SEQ ID NO: 70 (Figure 46), CDRL2 consisting of the amino acid sequence represented by SEQ ID NO: 52 (Figure 29), and CDRL3 consisting of the amino acid sequence represented by SEQ ID NO: 54 (Figure 30).

[Claim 8]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody comprises a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 31 (Figure 16), and a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 33 (Figure 18).

[Claim 9]

The antibody or the functional fragment thereof according to any one of claims 1 to 7, wherein the antibody comprises any one heavy chain variable region selected from the following a) to d) and a light chain variable region selected from e) and f):

a) a heavy chain (hMAb1-H1-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 56 (Figure 32),
b) a heavy chain (hMAb1-H2-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34),
c) a heavy chain (hMAb1-H3-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 60 (Figure 36), and
d) a heavy chain (hMAb1-H4-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38); and
e) a light chain (hMAb1-L1-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40), and
f) a light chain (hMAb1-L2-type) variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42).

[Claim 10]

The antibody or the functional fragment thereof according to any one of claims 1 to 7, wherein the antibody comprises any one of the following combinations 1) to 6) of a heavy chain variable region and a light chain variable region:

1) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40),

2) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 58 (Figure 34) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42),

3) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 66 (Figure 42),

4) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 62 (Figure 38) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40),

5) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 56 (Figure 32) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40), and

6) a heavy chain variable region consisting of an amino acid sequence represented by amino acid Nos. 20 to 137 of SEQ ID NO: 60 (Figure 36) and a light chain variable region consisting of an amino acid sequence represented by amino acid Nos. 21 to 134 of SEQ ID NO: 64 (Figure 40).

[Claim 11]

The antibody or the functional fragment thereof according to any one of claims 1 to 10, wherein the antibody or the functional fragment thereof is a chimeric antibody or a functional fragment thereof.

[Claim 12]

The antibody or the functional fragment thereof according to any one of claims 1 to 10, wherein the antibody or the functional fragment thereof is a humanized antibody or a functional fragment thereof.

[Claim 13]

The antibody or the functional fragment thereof according to any one of claims 1 to 12, wherein the antibody comprises a human IgG1 or human IgG2 heavy chain constant region.

[Claim 14]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody or the functional fragment thereof binds to a site on an antigen recognized by the antibody according to claims 9 or 10.

[Claim 15]

The antibody or the functional fragment thereof according to any one of claims 1 to 6, wherein the antibody or the functional fragment thereof competes with any one antibody according to claims 9 or 10 for the binding to ROBO4 protein.

[Claim 16]

The antibody according to any one of claims 1 to 7, wherein the antibody comprises any one of the following combinations 1) to 6) of a heavy chain and a light chain:

1) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 58 (Figure 34) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-1140),

2) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 58 (Figure 34) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 66 (Figure 42) (H-1143),

3) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 62 (Figure 38) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 66 (Figure 42) (H-2143).

4) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 62 (Figure 38) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-2140),

5) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 56 (Figure 32) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-1040), and

6) a heavy chain consisting of an amino acid sequence represented by amino acid Nos. 20 to 463 of SEQ ID NO: 60 (Figure 36) and a light chain consisting of an amino acid sequence represented by amino acid Nos. 21 to 239 of SEQ ID NO: 64 (Figure 40) (H-2040).

[Claim 17]

An antibody comprising a light chain and modified form of a heavy chain as defined in claim 16, wherein said modified form lacks one to ten carboxyl-terminal amino acid(s) of said heavy chain.

[Claim 18]

The antibody according to any one of claims 1 to 6, wherein the antibody is 95% or more identical in the amino acid sequence to any one antibody according to claim 16; has a K_D value of 1×10^{-8} M or lower for a human ROBO4; suppresses or inhibits vascular endothelial cell migration in the absence of a cross-linking antibody in vitro; and suppresses or inhibits angiogenesis in vivo.

[Claim 19]

The antibody or the functional fragment thereof according to claim 14, wherein the antibody or the functional fragment thereof is a human antibody or a functional fragment thereof.

[Claim 20]

A nucleotide sequence selected from the group consisting of the following (I) to (III):

(I) a nucleotide sequence comprising a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 19,

(II) a nucleotide sequence consisting of a nucleotide sequence comprising a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 19, and

(III) a nucleotide sequence consisting of a nucleotide sequence encoding the partial or whole amino acid sequence of the heavy chain or light chain of an antibody according to any one of claims 1 to 19.

[Claim 21]

A recombinant vector containing an insert of a nucleotide sequence according to claim 20.

[Claim 22]

A pharmaceutical composition comprising an antibody or a functional fragment thereof according to any one of claims 1 to 19 as an active ingredient.

[Claim 23]

The pharmaceutical composition according to claim 22, wherein the pharmaceutical composition is for use in treating or preventing an angiogenic disease.

[Claim 24]

The pharmaceutical composition for the use according to claim 23, wherein the angiogenic disease is exudative age-related macular degeneration, diabetic retinopathy, macular edema, benign or malignant tumor, atherosclerosis, retrolental fibroplasia, angioma, chronic inflammation, ocular neovascular disease, proliferative retinopathy, neovascular glaucoma, immune rejection of a corneal tissue transplant or other tissue transplants, rheumatoid arthritis, psoriasis, acute inflammation, sepsis, or obesity.

[Claim 25]

The pharmaceutical composition for the use according to claim 23, wherein the angiogenic disease is exudative age-related macular degeneration, diabetic retinopathy, macular edema, retrolental fibroplasia, ocular neovascular disease, proliferative retinopathy, neovascular glaucoma, or immune rejection of a corneal tissue transplant.

[Claim 26]

An angiogenesis inhibitor comprising an antibody or a functional fragment thereof according to any one of claims 1 to 19 as an active ingredient.

[Claim 27]

The pharmaceutical composition according to any one of claims 22 to 25, wherein said composition is used in combination with a further therapeutic or prophylactic agent.