permeability of several organs such as kidney liver, heart and lung. Severe sepsis (sepsis with organ dysfunction) refers to sepsis with acute organ dysfunction caused by sepsis. Septic shock refers to persistent hypotension unexplained by other causes.

[0024] Thus, there is a need for high-affinity neutralizing antibody to ANGPT2 that will limit antagonistic binding of ANGPT2 to Tie2, Enhanced Tie2 signaling is expected to have many beneficial effects including, for example, stabilizing the glomerular capillary structure, reducing endothelial activation, and restoring filtration barrier integrity. In total, these beneficial effects are expected to decrease proteinuria and preserve renal function resulting in a slowed disease progression in chronic kidney disease (CKD) patients.

[0025] The beneficial effects of a high-affinity neutralizing antibody to ANGPT2 are further expected to aid in the treatment of patients afflicted with vascular hyperpermeability of the lung and associated disorders.

~~BRIEF~~ SUMMARY ~~OF THE INVENTION~~

[0026] The present ~~invention~~disclosure provides monoclonal antibodies that specifically bind to human ANGPT2. ~~In one aspect of the invention, the~~The antibodies of the present ~~invention~~disclosure neutralize ANGPT2. Therefore, the antibodies of the ~~invention~~disclosure are useful, for example, for the treatment and/or prevention of diseases or disorders that can be alleviated by neutralizing ANGPT2.

[0027] ~~In another aspect, the~~The present ~~invention~~disclosure provides an anti-ANGPT2 antibody, in particular a humanized anti-ANGPT2 antibody, having one or more of the properties described herein below.

[0028] In one ~~embodiment~~aspect, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment ~~thereof~~ comprising:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3), and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 14 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 21 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 25 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

[0029] In another ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof comprising:

a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 3 and SEQ ID NO. 8, respectively,

or

a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 4 and SEQ ID NO. 9, respectively,

or

a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 5 and SEQ ID NO. 10, respectively, or

a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 6 and SEQ ID NO. 11, respectively, or

a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 7 and SEQ ID NO. 12, respectively.

[0030] In another ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof comprising:

a heavy chain comprising the amino acid sequence of SEQ ID NO. 31 and a light chain comprising the amino acid sequence of SEQ ID NO. 32,

or

a heavy chain comprising the amino acid sequence of SEQ ID NO. 33 and a light chain comprising the amino acid sequence of SEQ ID NO. 34,

or

a heavy chain comprising the amino acid sequence of SEQ ID NO. 35 and a light chain comprising the amino acid sequence of SEQ ID NO. 36,

or

a heavy chain comprising the amino acid sequence of SEQ ID NO. 37 and a light chain comprising the amino acid sequence of SEQ ID NO. 38,

or

a heavy chain comprising the amino acid sequence of SEQ ID NO. 39 and a light chain comprising the amino acid sequence of SEQ ID NO. 40.

[0030a] In another aspect, the present disclosure provides an anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 31 and a light chain comprising SEQ ID NO. 32.

[0030b] In another aspect, the present disclosure provides an anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 33 and a light chain comprising SEQ ID NO. 34.

[0030c] In another aspect, the present disclosure provides an anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 35 and a light chain comprising SEQ ID NO. 36.

[0030d] In another aspect, the present disclosure provides an anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 37 and a light chain comprising SEQ ID NO. 38.

[0030e] In another aspect, the present disclosure provides an anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 39 and a light chain comprising SEQ ID NO. 40.

[0031] In one ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof comprising:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3), or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 14 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3), or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3);

and

a heavy chain framework region comprising one to four amino acid sequences selected from the group consisting of the amino acid sequence of SEQ ID NO. 41 (H-FR1); amino acid sequence of SEQ ID NO. 42 (H-FR2); the amino acid sequence of SEQ ID NO. 43 (H-FR3); and the amino acid sequence of SEQ ID NO. 44 (H-FR4).

[0032] In another ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof comprising:

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3), or

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3), or

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3), or

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 21 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 25 (L-CDR3), or

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3);

and

a light chain framework region comprising one to four amino acid sequences selected from the group consisting of the amino acid sequence of SEQ ID NO. 45 (L-FR1); amino acid sequence of SEQ ID NO. 46 (L-FR2); the amino acid sequence of SEQ ID NO. 47 (L-FR3); and the amino acid sequence of SEQ ID NO. 48 (L-FR4).

[0033] In one ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or antigen-binding fragment thereof that binds to at least one amino acid residue within amino acid regions 117-148 of the carboxy-terminal fibrinogen-like domain (FLD) region of human ANGPT2 with the SEQ ID NO. 50.

[0034] In another ~~embodiment~~example, the ~~invention~~disclosure relates to an ANGTP2 antibody or antigen-binding fragment thereof that binds to SEQ ID NO: 51.

[0035] In one ~~embodiment~~example, the anti-ANGPT2 antibody is a humanized anti-ANGPT2 antibody.

[0036] In another ~~embodiment~~example, the anti-ANGPT2 antibody is a chimeric anti-ANGPT2 antibody.

[0037] ~~In one embodiment, the~~The present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof for use in medicine.

[0038] In one ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof for use in the treatment of kidney diseases.

[0039] In one ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof for use in the treatment of liver diseases.

[0040] ~~In one embodiment, the~~The present ~~invention~~disclosure provides a pharmaceutical composition comprising an anti-ANGPT2 antibody or an antigen-binding fragment thereof and a pharmaceutically acceptable carrier. In another aspect, the present disclosure provides a pharmaceutical composition comprising the anti-ANGPT2 antibody or the antigen-binding fragment as described herein, and a pharmaceutically acceptable carrier.

[0041] In one ~~embodiment~~example, the present ~~invention~~disclosure provides an anti-ANGPT2 antibody or an antigen-binding fragment thereof or a pharmaceutical composition comprising the anti-ANGPT2 antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof is administered by a parenteral route, intravenous route, intravitreal route or subcutaneous route of administration.

[0042] ~~In one embodiment, the~~The present ~~invention~~disclosure provides an isolated polynucleotide or polynucleotides comprising a sequence encoding a light chain or light chain variable region of an antibody or antigen-binding fragment thereof and a heavy chain or heavy chain variable region of an antibody or antigen-binding fragment thereof.

[0043] ~~In one embodiment, the~~The present ~~invention~~disclosure provides an expression vector comprising an isolated polynucleotide or polynucleotides encoding a light chain or light chain variable region of an antibody or antigen-binding fragment thereof and a heavy chain or heavy chain variable region of an antibody or antigen-binding fragment thereof.

[0044] ~~In one embodiment, the~~The present ~~invention~~disclosure provides a viral vector comprising an isolated polynucleotide or polynucleotides encoding a light chain or light chain variable region of an antibody or antigen-binding fragment thereof and a heavy chain or heavy chain variable region of an antibody or antigen-binding fragment thereof.

[0045] ~~In one embodiment, the~~The present ~~invention~~disclosure provides a host cell comprising an expression vector or an isolated polynucleotide or polynucleotides encoding a light chain or light chain variable region of an antibody or antigen-binding fragment thereof and a heavy chain or heavy chain variable region of an antibody or antigen-binding fragment thereof.

[0046] ~~In one embodiment, the~~The present ~~invention~~disclosure provides a method for producing an anti-ANGPT2 antibody or an antigen-binding fragment thereof comprising:

obtaining a host cell comprising an expression vector or an isolated polynucleotide or polynucleotides encoding a light chain or light chain variable region of an antibody or antigen-binding fragment thereof and a heavy chain or heavy chain variable region of an antibody or antigen-binding fragment thereof; and cultivating the host cell.

[0047] In one ~~embodiment~~example, the method for producing an anti-ANGPT2 antibody or antigen-binding fragment thereof further comprises recovering and purifying the anti-ANGPT2 antibody or antigen-binding fragment thereof.

[0048] In another ~~embodiment~~example, the present ~~invention~~disclosure relates to an isolated polynucleotide or polynucleotides comprising:

a sequence encoding a heavy chain as shown in SEQ ID NO: 31 or a heavy chain variable region as shown in SEQ ID NO: 3; and a sequence encoding a light chain as shown in SEQ ID NO. 32 or a light chain variable region as shown in SEQ ID NO: 8, or

an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 33 or a heavy chain variable region as shown in SEQ ID NO: 4; and a sequence encoding a light chain as shown in SEQ ID NO. 34 or a light chain variable region as shown in SEQ ID NO: 9,

or

an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 35 or a heavy chain variable region as shown in SEQ ID NO: 5; and a sequence encoding a light chain as shown in SEQ ID NO. 36 or a light chain variable region as shown in SEQ ID NO: 10,

or

an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 37 or a heavy chain variable region as shown in SEQ ID NO: 6; and a sequence encoding a light chain as shown in SEQ ID NO. 38 or a light chain variable region as shown in SEQ ID NO: 11,

or

an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 39 or a heavy chain variable region as shown in SEQ ID NO: 7; and a sequence encoding a light chain as shown in SEQ ID NO. 40 or a light chain variable region as shown in SEQ ID NO: 12.

[0049] Non-limiting examples of diseases, disorders, or conditions that can be alleviated by the anti-ANGPT2 antibodies of the ~~invention~~disclosure include cardiac hypertrophy, myocardial infarction, ischemia, ischemic reperfusion injury, stroke hypertension, pulmonary arterial hypertension, idiopathic pulmonary arterial hypertension, trauma induced brain disorders,

CLAIMS

What is claimed is:

1. An anti-ANGPT2 antibody or an antigen-binding fragment comprising:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3), and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 14 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 17 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 21 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 25 (L-CDR3),

or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO. 16 (H-CDR3); and

a light chain variable region comprising the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

2. The anti-ANGPT2 antibody of claim 1, wherein said antibody comprises a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO. 3 and SEQ ID NO. 8, respectively; SEQ ID NO. 4 and SEQ ID NO. 9, respectively; SEQ ID NO. 5 and SEQ ID NO. 10, respectively; SEQ ID NO. 6 and SEQ ID NO. 11, respectively; or SEQ ID NO. 7 and SEQ ID NO. 12, respectively.

3. The anti-ANGPT2 antibody of claim 1, wherein said antibody comprises a heavy chain and a light chain comprising SEQ ID NO. 31 and SEQ ID NO. 32, respectively; SEQ ID NO. 33 and SEQ ID NO. 34, respectively; SEQ ID NO. 35 and SEQ ID NO. 36; respectively; SEQ ID NO. 37 and SEQ ID NO. 38; respectively; or SEQ ID NO. 39 and SEQ ID NO. 40.

4. A pharmaceutical composition comprising the anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3, and a pharmaceutically acceptable carrier.

~~5. An anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 for use as a medicament.~~

~~6. A method of treating diseases or disorders that can be alleviated by treatment with an anti-ANGPT2 antibody, the method comprising administering to a patient in need thereof a pharmaceutically effective amount of the anti-ANGPT2 antibody or the antigen-binding fragment according to any one of claims 1 to 3.~~

7. An anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 for use in treating diseases or disorders that can be alleviated by treatment with an anti-ANGPT2 antibody.

8. Use of the anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 in manufacture of a medicament for treating diseases or disorders that can be alleviated by treatment with an anti-ANGPT2 antibody.

9. The method of claim 6, the anti-ANGPT2 antibody or the antigen-binding fragment of claim 7, or the use of the anti-ANGPT2 antibody or the antigen-binding fragment of claim 8, wherein the disease or disorder is selected from the group consisting of cardiac hypertrophy, myocardial infarction, ischemia, ischemic reperfusion injury, stroke hypertension, pulmonary arterial hypertension, idiopathic pulmonary arterial hypertension, trauma induced brain disorders, asthma, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, preeclampsia and pregnancy-induced hypertension, sepsis, severe sepsis, septic shock, non-alcoholic steatohepatitis (NASH), cirrhosis, minimal change disease, focal segmental glomerulosclerosis (FSGS), nephrotic syndrome, diabetic kidney disease (DKD), chronic kidney disease (CKD), diabetic renal insufficiency, end stage renal disease, ischemia or an ischemic reperfusion injury, cancer, hepatocellular carcinoma, idiopathic pulmonary fibrosis (IPF), emphysema, acute lung injury (ALI), acute respiratory disease syndrome (ARDS), severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), vascular hyperpermeability (and associated disorders), acute kidney injury, renal cell carcinoma, heart failure, lupus nephritis, Raynaud's, pancreatitis, peripheral artery disease, congenital heart disease, Dengue virus, malaria, hantavirus, edema, regeneration, lupus, interstitial lung disease, scleroderma, retinopathies, diabetic nephropathy, portal hypertension, varices growth, and liver transplantation.

10. The method of claim 9, the anti-ANGPT2 antibody or the antigen-binding fragment of claim 9, or the use of the anti-ANGPT2 antibody or the antigen-binding fragment of claim 9, wherein the disease or disorder is selected from the group consisting of chronic kidney disease, non-alcoholic steatohepatitis (NASH), diabetic nephropathy, sepsis and vascular hyperpermeability.

11. The method of claim 9, the anti-ANGPT2 antibody or the antigen-binding fragment of claim 9, or the use of the anti-ANGPT2 antibody or the antigen-binding fragment of claim 9, wherein the

~~disease or disorder is selected from the group consisting of ALI, ARDS, SARS, MERS, and vascular hyperpermeability (and associated disorders).~~

~~12. The method of claim 6 or 9, further comprising administering a second therapeutic agent.~~

~~13. The method of claim 6 or 9, wherein said antibody is administered by a parenteral route, intravenous route or subcutaneous route of administration.~~

~~14. A method of blocking the function of human ANGPT2 in a human patient, comprising administering to said human patient a composition comprising the anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 in an amount sufficient to block an ANGPT2 mediated response in said human patient.~~

~~15. An anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 for use in blocking the function of human ANGPT2.~~

~~16. Use of the anti-ANGPT2 antibody or the antigen-binding fragment according to any of claims 1 to 3 in manufacture of a medicament for blocking the function of human ANGPT2.~~

~~17. An isolated polynucleotide encoding a heavy chain variable region amino acid sequence or a light chain variable region, wherein the heavy chain variable region amino acid sequence comprises any of SEQ ID NOs: 3 to 7, SEQ ID NOs: 13 to 17; SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, or SEQ ID NO: 39; a and the light chain variable region amino acid sequence comprises any of SEQ ID NOs: 8 to 12, SEQ ID NOs: 19 to 26, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, or SEQ ID NO: 40.~~

5. The anti-ANGPT2 antibody or an antigen-binding fragment of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO.17 (H-CDR3), and

the light chain variable region comprises the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

6. The anti-ANGPT2 antibody or an antigen-binding fragment of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO. 14 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO.17 (H-CDR3), and

the light chain variable region comprises the amino acid sequence of SEQ ID NO. 19 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

7. The anti-ANGPT2 antibody or an antigen-binding fragment of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO.16 (H-CDR3), and

the light chain variable region comprises the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

8. The anti-ANGPT2 antibody or an antigen-binding fragment of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO.16 (H-CDR3), and

the light chain variable region comprises the amino acid sequence of SEQ ID NO. 21 (L-CDR1); the amino acid sequence of SEQ ID NO. 23 (L-CDR2); and the amino acid sequence of SEQ ID NO. 25 (L-CDR3).

9. The anti-ANGPT2 antibody or an antigen-binding fragment of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO. 13 (H-CDR1); the amino acid sequence of SEQ ID NO. 15 (H-CDR2); and the amino acid sequence of SEQ ID NO.16 (H-CDR3), and

the light chain variable region comprises the amino acid sequence of SEQ ID NO. 20 (L-CDR1); the amino acid sequence of SEQ ID NO. 22 (L-CDR2); and the amino acid sequence of SEQ ID NO. 24 (L-CDR3).

10. The anti-ANGPT2 antibody of claim 2, wherein the variable heavy chain comprises the amino acid sequence of SEQ ID NO. 3 and the variable light chain comprises the amino acid sequence of SEQ ID NO. 8.

11. The anti-ANGPT2 antibody of claim 2, wherein the variable heavy chain comprises the amino acid sequence of SEQ ID NO. 4 and the variable light chain comprises the amino acid sequence of SEQ ID NO. 9.

12. The anti-ANGPT2 antibody of claim 2, wherein the variable heavy chain comprises the amino acid sequence of SEQ ID NO. 5 and the variable light chain comprises the amino acid sequence of SEQ ID NO. 10.

13. The anti-ANGPT2 antibody of claim 2, wherein the variable heavy chain comprises the amino acid sequence of SEQ ID NO. 6 and the variable light chain comprises the amino acid sequence of SEQ ID NO. 11.

14. The anti-ANGPT2 antibody of claim 2, wherein the variable heavy chain comprises the amino acid sequence of SEQ ID NO. 7 and the variable light chain comprises the amino acid sequence of SEQ ID NO. 12.

15. An anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 31 and a light chain comprising SEQ ID NO. 32.

16. An anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 33 and a light chain comprising SEQ ID NO. 34.

17. An anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 35 and a light chain comprising SEQ ID NO. 36.

18. An anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 37 and a light chain comprising SEQ ID NO. 38.

19. An anti-ANGPT2 antibody comprising a heavy chain comprising SEQ ID NO. 39 and a light chain comprising SEQ ID NO. 40.