with high affinity and neutralize human Ang2, but do not bind with high affinity or neutralize human Ang1.

Summary

In one aspect of the present disclosure, there is provided an antibody that binds human Ang2 (SEQ ID NO: 7), comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 consisting of the amino acid sequences KASQDVYIAVA (SEQ ID NO: 8), YWASTRDT (SEQ ID NO: 9), and HQYSSYPPT (SEQ ID NO: 10), respectively, and wherein the heavy chain comprises heavy chain complementarity determining regions HCDR1, HCDR2, and HCDR3 consisting of the amino acid sequences GYSFTDYNMV (SEQ ID NO: 11), YIDPYNGGTGYNQKFEG (SEQ ID NO: 12), and ARTRDRYDVWYFDV (SEQ ID NO: 13), respectively.

In another aspect of the present disclosure, there is provided an antibody, comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR has the amino acid sequence given in SEQ ID NO: 3, and the HCVR has the amino acid sequence given in SEQ ID NO: 1.

In a further aspect of the present disclosure, there is provided a mammalian cell comprising a DNA molecule comprising a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 4 and a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 2, wherein the cell is capable of expressing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 4 and a heavy chain having an amino acid sequence of SEQ ID NO: 2.

In another aspect of the present disclosure, there is provided a process for producing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 4 and a heavy chain having an amino acid sequence of SEQ ID NO: 2, comprising cultivating the mammalian cell disclosed herein under conditions such that the antibody is expressed, and recovering the expressed antibody.

In a further aspect of the present disclosure, there is provided an antibody produced by the process disclosed herein.

In another aspect of the present disclosure, there is provided a pharmaceutical composition, comprising the antibody disclosed herein, and an acceptable carrier, diluent, or excipient.

In a further aspect of the present disclosure, there is provided a use of an antibody disclosed herein in the manufacture of a medicament for treating cancer.

In another aspect of the present disclosure, there is provided the antibody disclosed herein, for use in therapy.

In a further aspect of the present disclosure, there is provided the antibody disclosed herein, for use in the treatment of cancer.

Description

Accordingly, an embodiment of the present invention provides an antibody, comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR has the amino acid sequence given in SEQ ID NO: 3, and the HCVR has the amino acid sequence given in SEQ ID NO: 1.

Certain antibodies of the present invention bind human Ang-2 with a high affinity that is greater than human Ang2 antibodies known in the art. Furthermore, certain antibodies of the present invention demonstrate a positive response in tumor xenograft models, such as EL 1997 for triple negative breast cancer, SKOV3x.1 for ovarian cancer, and PC3 for prostate cancer, indicating potential as a cancer therapeutic. Additionally, certain antibodies of the invention selectively bind human Ang-2 over human Ang-1, and avoid potential off-target liabilities for human Ang1.

In a further embodiment, the present invention provides an antibody, wherein the LC has the amino acid sequence given in SEQ ID NO: 4, and the HC has the amino acid sequence given in SEQ ID NO: 2.

In a further embodiment, the present invention provides an antibody, comprising two light chains and two heavy chains, wherein each light chain has the amino acid

sequence given in SEQ ID NO: 4, and each heavy chain has the amino acid sequence given in SEQ ID NO: 2.

In a further embodiment, the present invention provides an antibody, wherein one of the heavy chains forms an inter-chain disulfide bond with one of the light chains, and the other heavy chain forms an inter-chain disulfide bond with the other light chain, and one of the heavy chains forms two inter-chain disulfide bonds with the other heavy chain.

In a further embodiment, the present invention provides an antibody, wherein the antibody is glycosylated.

In an embodiment, the present invention provides an antibody that binds human Ang2 (SEQ ID NO: 7), comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 consisting of the amino acid sequences KASQDVYIAVA (SEQ ID

6. The antibody of any one of Claims 1-5, wherein the antibody is glycosylated.
7. A mammalian cell comprising a DNA molecule comprising a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 4 and a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 2, wherein the cell is capable of expressing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 4 and a heavy chain having an amino acid sequence of SEQ ID NO: 2.
8. A process for producing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 4 and a heavy chain having an amino acid sequence of SEQ ID NO: 2, comprising cultivating the mammalian cell of Claim 7 under conditions such that the antibody is expressed, and recovering the expressed antibody.
9. An antibody produced by the process of Claim 8.
10. A pharmaceutical composition, comprising the antibody of any one of Claims 1-6 or 9, and an acceptable carrier, diluent, or excipient.
11. Use of an antibody of any one of Claims 1-6 or 9 in the manufacture of a medicament for treating cancer in a patient.
12. The use of Claim 11, wherein the cancer is breast cancer, ovarian cancer, gastric cancer, colorectal cancer, or hepatocellular carcinoma.
13. The use of Claim 11 or 12, wherein an effective amount of ramucirumab is to be further administered simultaneously, separately, or sequentially to the patient.
14. The antibody of any one of Claims 1-6 or 9, for use in therapy.
15. The antibody of any one of Claims 1-6 or 9, for use in the treatment of cancer.
16. The antibody for use of Claim 15, wherein the cancer is breast cancer, ovarian cancer, gastric cancer, colorectal cancer, or hepatocellular carcinoma.