SUMMARY OF THE INVENTION

[0009] The present invention refers to subject matter as defined in the attached set of claims. In accordance with certain examples of the present disclosure, there are described monoclonal antibodies, or fragments thereof, that bind to Olfml-3 and inhibit the activity of Olfml-3 in angiogenesis. Thus, in some examples, there is described an isolated or recombinant monoclonal antibody that specifically binds to an Olfml-3 polypeptide. In certain examples, an antibody competes for the binding of an Olfml-3 polypeptide with a 46A9BO, 9F8BO or Z14A7 monoclonal antibody. Preferred antibodies compete for binding of the Olfml-3 polypeptide with the 46A9BO monoclonal antibody. In certain examples, the antibody may comprise all or part of the heavy chain variable region and/or the light chain variable region of the 46A9BO, 9F8BO or Z14A7 monoclonal antibodies. In a further example, the antibody may comprise an amino acid sequence that corresponds to a first, second, and/or third complementarity determining region (CDR) from the light variable and/or heavy variable chain of the monoclonal antibodies of the present examples. In one example, there is disclosed an isolated monoclonal antibody, wherein the antibody comprises (a) a first VH CDR at least 80% identical to VH CDR1 of 46A9BO (SEQ ID NO: 7), 9F8BO (SEQ ID NO: 21), or Z14A7 (SEQ ID NO: 13); (b) a second VH CDR at least 80% identical to VH CDR2 of 46A9BO (SEQ ID NO: 8), 9F8BO (SEQ ID NO: 22), or Z14A7 (SEQ ID NO: 14); (c) a third VH CDR at least 80% identical to VH CDR3 of 46A9BO (SEQ ID NO: 9), 9F8BO (SEQ ID NO: 23), or Z14A7 (SEQ ID NO: 15); (d) a first VL CDR at least 80% identical to VL CDR1 of 46A9BO (SEQ ID NO: 10), 9F8BO (SEQ ID NO: 24), or Z14A7 (SEQ ID NO: 16);(e) a second VL CDR at least 80% identical to VL CDR2 of 46A9BO (SEQ ID NO: 11), 9F8BO (SEQ ID NO: 25), or Z14A7 (SEQ ID NO: 17); and (f) a third VL CDR at least 80% identical to VL CDR3 of 46A9BO (SEQ ID NO: 12), 9F8BO (SEQ ID NO: 26), or Z14A7 (SEQ ID NO: 18). In another example, there is disclosed a composition comprising an antibody as described herein in a pharmaceutically acceptable carrier. In a further example, there is disclosed an isolated polynucleotide molecule comprising a nucleic acid sequence encoding an antibody as described herein. In yet another example, there is disclosed a recombinant polypeptide comprising an antibody VH domain comprising CDRs 1-3 of the VH domain of 46A9BO (SEQ ID NOs: 7, 8 and 9); CDRs 1-3 of the VH domain of 9F8BO (SEQ ID NOs: 21, 22 and 23); or CDRs 1-3 of the VH domain of Z14A7 (SEQ ID NOs: 13, 14 and 15). In another example, there is disclosed a recombinant polypeptide comprising an antibody VL domain comprising CDRs 1-3 of the VL domain of 46A9BO (SEQ ID NOs: 10, 11 and 12); CDRs 1-3 of the VL domain of 9F8BO (SEQ ID NOs: 24, 25 and 26); or CDRs 1-3 of the VL domain

WHAT IS CLAIMED IS:

1. An isolated monoclonal antibody, wherein the antibody comprises:

(i) (a) a first VH CDR which is identical to SEQ ID NO: 7;
(b) a second VH CDR which is identical to SEQ ID NO: 8;
(c) a third VH CDR which is identical to SEQ ID NO: 9;
(d) a first VL CDR which is identical to SEQ ID NO: 10;
(e) a second VL CDR which is identical to SEQ ID NO: 11; and
(f) a third VL CDR which is identical to SEQ ID NO: 12; or

(ii) (a) a first VH CDR which is identical to SEQ ID NO: 21;
(b) a second VH CDR which is identical to SEQ ID NO: 22;
(c) a third VH CDR which is identical to SEQ ID NO: 23;
(d) a first VL CDR which is identical to SEQ ID NO: 24;
(e) a second VL CDR which is identical to SEQ ID NO: 25; and
(f) a third VL CDR which is identical to SEQ ID NO: 26.

2. The isolated antibody of claim 1, wherein the antibody comprises:
(a) a first VH CDR which is identical to SEQ ID NO: 7;
(b) a second VH CDR which is identical to SEQ ID NO: 8;
(c) a third VH CDR which is identical to SEQ ID NO: 9;
(d) a first VL CDR which is identical to SEQ ID NO: 10;
(e) a second VL CDR which is identical to SEQ ID NO: 11; and
(f) a third VL CDR which is identical to SEQ ID NO: 12.

3. The isolated antibody of claim 1, wherein the antibody comprises:
(a) a first VH CDR which is identical to SEQ ID NO: 21;
(b) a second VH CDR which is identical to SEQ ID NO: 22;
(c) a third VH CDR which is identical to SEQ ID NO: 23;
(d) a first VL CDR which is identical to SEQ ID NO: 24;
(e) a second VL CDR which is identical to SEQ ID NO: 25; and
(f) a third VL CDR which is identical to SEQ ID NO: 26.

4. The antibody of claim 1, wherein the antibody comprises:

(i) a VH domain at least about 80% identical to the VH domain of 46A9BO (SEQ ID NO: 1) and a VL domain at least about 80% identical to the VL domain of 46A9BO (SEQ ID NO: 2); or

(ii) a VH domain at least about 80% identical to the VH domain of 9F8BO (SEQ ID NO: 19) and a VL domain at least about 80% identical to the VL domain of 9F8BO (SEQ ID NO: 20).

5. The antibody of claim 4, wherein the antibody comprises a VH domain identical to the VH domain of 46A9BO (SEQ ID NO: 1) and a VL domain identical to the VL domain of 46A9BO (SEQ ID NO: 2).

6. The antibody of claim 4, wherein the antibody comprises a VH domain identical to the VH domain of 9F8BO (SEQ ID NO: 19) and a VL domain identical to the VL domain of 9F8BO (SEQ ID NO: 20).

7. The antibody of claim 4, wherein the antibody is the 46A9BO, or 9F8BO antibody.

8. The antibody of any one of claims 1-7, wherein the antibody is recombinant.

9. The antibody of any one of claims 1-3, wherein the antibody is an IgG, IgM, IgA or an antigen binding fragment thereof.

10. The antibody of any one of claims 1-3, wherein the antibody is a Fab', a F(ab')2, a F(ab')3, a monovalent scFv, a bivalent scFv, or a single domain antibody.

11. The antibody of any one of claims 1-7, wherein the antibody is a human, humanized antibody or de-immunized antibody.

12. The antibody of any one of claims 1-7, wherein the antibody is conjugated to an imaging agent, a chemotherapeutic agent, a toxin or a radionuclide.

13. A composition comprising an antibody of any one of claims 1-12 in a pharmaceutically acceptable carrier.

14. An isolated polynucleotide molecule comprising a nucleic acid sequence encoding an antibody of any one of claims 1-11.

15. A recombinant polypeptide comprising an antibody VH domain comprising CDRs 1-3 of the VH domain of 46A9BO (SEQ ID NOs: 7, 8 and 9) and VL domain comprising CDRs 1-3 of the VL domain of 46A9BO (SEQ ID NOs: 10, 11 and 12)

16. A recombinant polypeptide comprising an antibody VH domain comprising CDRs 1-3 of the VH domain of 9F8BO (SEQ ID NOs: 21, 22 and 23) and VL domain comprising CDRs 1-3 of the VL domain of 9F8BO (SEQ ID NOs: 24, 25 and 26).

17. An isolated polynucleotide molecule comprising a nucleic acid sequence encoding a polypeptide of claim 15 or 16.

18. A host cell comprising one or more polynucleotide molecule(s) encoding an antibody of any one of claims 1-7 or a recombinant polypeptide of claim 15 or 16.

19. The host cell of claim 18, wherein the host cell is a mammalian cell, a yeast cell, a bacterial cell, a ciliate cell or an insect cell.

20. A method of manufacturing an antibody comprising:

(a) expressing one or more polynucleotide molecule(s) encoding a VL and VH chain of an antibody of any one of claims 1-7 in a cell; and

(b) purifying the antibody from the cell.

21. Use of an antibody in accordance with any one of claims 1-12 in the manufacture of a medicament for treating a cancer in a subject.

22. The use of claim 21, wherein the cancer is a solid tumor, a metastatic tumor, or a non-metastatic tumor.

23. The use of claim 21, wherein the cancer is a breast cancer, lung cancer, head & neck cancer, prostate cancer, esophageal cancer, tracheal cancer, skin cancer brain cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer.

24. The use of claim 21, wherein the antibody is to be administered systemically.

25. The use of claim 21, wherein the antibody is to be administered intravenously, intradermally, intratumorally, intramuscularly, intraperitoneally, subcutaneously, or locally.

26. The use of claim 21, further comprising at least a second anticancer therapy to be administered to the subject.

27. The use of claim 26, wherein the second anticancer therapy is a surgical therapy, chemotherapy, radiation therapy, cryotherapy, hormonal therapy, immunotherapy or cytokine therapy.

28. The use of claim 21, wherein the subject is a human subject.

29. A composition comprising an antibody in accordance with any one of claims 1-12 for use in treating a cancer in a subject.

30. The composition of claim 29, wherein the cancer is a solid tumor, a metastatic tumor, or a non-metastatic tumor.

31. The composition of claim 29, wherein the cancer is a breast cancer, lung cancer, head & neck cancer, prostate cancer, esophageal cancer, tracheal cancer, skin cancer brain cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer.

32. The composition of claim 29, wherein the composition is to be administered systemically.

33. The composition of claim 29, wherein the composition is formulated to be administered intravenously, intradermally, intratumorally, intramuscularly, intraperitoneally, subcutaneously, or locally.

34. The composition of claim 29, further comprising at least a second anticancer agent.

35. The composition of claim 29, wherein the subject is a human subject.