CLAIMS

1. An isolated antibody that specifically binds human NOTCH2 and/or NOTCH3, wherein the antibody comprises:

(a) a heavy chain CDR1 comprising SSSGMS (SEQ ID NO:5), a heavy chain CDR2 comprising VIASSGSNTYYADSVKG (SEQ ID NO:6), and a heavy chain CDR3 comprising SIFYTT (SEQ ID NO:51) or GIFFAI (SEQ ID NO:7); and

(b) a light chain CDR1 comprising RASQSVRSNYLA (SEQ ID NO:8), a light chain CDR2 comprising GASSRAT (SEQ ID NO:9), and a light chain CDR3 comprising QQYSNFPI (SEQ ID NO:10).

2. The antibody of claim 1, which comprises a heavy chain CDR1 comprising SSSGMS (SEQ ID NO:5), a heavy chain CDR2 comprising VIASSGSNTYYADSVKG (SEQ ID NO:6), and a heavy chain CDR3 comprising SIFYTT (SEQ ID NO:51).

3. The antibody of claim 1, which comprises a heavy chain CDR1 comprising SSSGMS (SEQ ID NO:5), a heavy chain CDR2 comprising VIASSGSNTYYADSVKG (SEQ ID NO:6), and a heavy chain CDR3 comprising GIFFAI (SEQ ID NO:7).

4. An antibody that specifically binds human NOTCH2 and/or NOTCH3, wherein the antibody comprises:

(a) a heavy chain variable region having at least about 90% sequence identity to SEQ ID NO:50, SEQ ID NO:14, or SEQ ID NO:20; and

(b) a light chain variable region having at least about 90% sequence identity to SEQ ID NO:13 or SEQ ID NO:19.

5. The antibody of claim 4, which comprises:

(a) a heavy chain variable region having at least about 95% sequence identity to SEQ ID NO:50; and

(b) a light chain variable region having at least about 95% sequence identity to SEQ ID NO:13.

6. The antibody of claim 4, which comprises:

(a) a heavy chain variable region comprising SEQ ID NO:50; and

(b) a light chain variable region comprising SEQ ID NO:13.

7. The antibody of claim 4, which comprises:

(a) a heavy chain variable region having at least about 95% sequence identity to SEQ ID NO:14; and

(b) a light chain variable region having at least about 95% sequence identity to SEQ ID NO:13.

8. The antibody of claim 4, which comprises:

(a) a heavy chain variable region comprising SEQ ID NO:14; and

(b) a light chain variable region comprising SEQ ID NO:13.

9. An isolated antibody that specifically binds human NOTCH2 and/or human NOTCH3, wherein the antibody:

(a) binds at least part of the sequence HKGAL (SEQ ID NO:28) within the EGF repeat 10 of human NOTCH2; and/or

(b) binds at least part of the sequence HEDAI (SEQ ID NO:29) within the EGF repeat 9 of human NOTCH3.

10. An antibody that competes for specific binding to human NOTCH2 and/or human NOTCH3 with a second antibody in a competitive binding assay, wherein the second antibody comprises:

(a) a heavy chain variable region comprising SEQ ID NO:50 and a light chain variable region comprising SEQ ID NO:13; or

(b) a heavy chain variable region comprising SEQ ID NO:14 and a light chain variable region comprising SEQ ID NO:13.

11. An antibody that competes for specific binding to human NOTCH2 and/or human NOTCH3 with antibody 59R5 or antibody 59R1.

12. The antibody of any one of claims 1 to 11, which is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human antibody, a bispecific antibody, or an antibody fragment.

13. The antibody of claim 1 encoded by the polynucleotide deposited with the ATCC as PTA-10170.

14. The antibody of claim 1 encoded by the polynucleotide deposited with the ATCC as PTA-9547.

15. The antibody of any one of claims 1 to 11, 13, or 14, which is conjugated to a cytotoxic agent.

16. An isolated cell producing the antibody of any one of claims 1 to 15.

17. A pharmaceutical composition comprising the antibody of any one of claims 1 to 15 and a pharmaceutically acceptable carrier.

18. An isolated polynucleotide encoding the antibody of any one of claims 1 to 15.

19. A vector comprising the polynucleotide of claim 18.

20. An isolated cell comprising the polynucleotide of claim 18.

21. An isolated cell comprising the vector of claim19.

22. Use of the antibody of any one of claims 1 to 15, in the manufacture of a medicament for the treatment of cancer.

23. Use of the antibody of any one of claims 1 to 15, in the manufacture of a medicament for inhibiting tumor growth.

24. The use of claim 22 or claim 23, wherein the treatment of cancer or inhibiting tumor growth comprises use of the antibody in combination with a second therapeutic agent.

25. The use of claim 24, wherein the second therapeutic agent is a chemotherapeutic agent, a second antibody, or an anti-angiogenesis agent.

26. Use of the antibody of any one of claims 1 to 15, in the manufacture of a medicament for inhibiting angiogenesis.

27. The use of claim 26, wherein the angiogenesis is tumor angiogenesis.

28. A polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:50, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:49.

29. The antibody of any one of claims 1-15, for use in the treatment of cancer.

30. The antibody of any one of claims 1-15, for use in inhibiting tumor growth.

31. The antibody of any one of claims 1-15, for use in inhibiting angiogenesis.

CLAIMS

1. An isolated antibody that specifically binds human Notch2 and Notch3, comprising:

   (a) a heavy chain CDR1 comprising SSSGMS (SEQ ID NO:5), a heavy chain CDR2 comprising VIASSGSN-TYYADSVKG (SEQ ID NO:6), and a heavy chain CDR3 comprising SIFYTT (SEQ ID NO:51) or SEQ ID NO: 30; and
   (b) a light chain CDR1 comprising RASQSVRSNYLA (SEQ ID NO:8), a light chain CDR2 comprising GASSRAT (SEQ ID NO:9), and a light chain CDR3 comprising QQYSNFPI (SEQ ID NO: 10).

2. An antibody according to claim 1, wherein the heavy chain CDR3 comprises SIFYTT (SEQ ID NO:51).

3. An antibody according to claim 2, comprising heavy chain variable region SEQ ID NO: 50 and light chain variable region SEQ ID NO: 13.

4. An antibody according to claim 1, wherein the heavy chain CDR3 comprises SIFYPT (SEQ ID NO: 22), SSFFAS (SEQ ID NO: 23), SSFYAS (SEQ ID NO: 24), SSFFAT (SEQ ID NO: 25), SIFYPS (SEQ ID NO: 26), SSFFAN (SEQ ID NO: 27) or GIFFAI (SEQ ID NO:7).

5. The antibody according to claim 1, claim 2 or claim 4, which comprises:

   (a) a heavy chain variable region having at least about 90% sequence identity to SEQ ID NO:50, SEQ ID NO:14, or SEQ ID NO:20; and
   (b) a light chain variable region having at least about 90% sequence identity to SEQ ID NO:13 or SEQ ID NO:19.

6. The antibody according to any one of claims 1 to 5, wherein the antibody is a recombinant antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a human antibody, an antibody fragment, a bispecific antibody, a monospecific antibody, an IgG1 antibody or an IgG2 antibody.

7. An antibody encoded by the polynucleotide deposited with the ATCC as PTA-10170 or by the polynucleotide deposited with the ATCC as PTA-9547.

8. A cell comprising or producing the antibody as defined in any one of claims 1 to 7.

9. An isolated polynucleotide comprising a polynucleotide encoding an antibody according to any of claims 1 to 7.

10. The antibody according to any one of claims 1 to 7 for use in the treatment of cancer.

11. The antibody according to any of claims 1 to 7 for use according to claim 10, wherein the treatment reduces the tumorigenicity of a tumor and/or reduces the frequency of cancer stem cells in the tumour.

12. The antibody according to any of claims 1 to 7 for use according to claim 10, wherein the cancer is colorectal cancer, breast cancer, pancreatic cancer, lung cancer or melanoma.

13. The antibody according to any of claims 1 to 7 for use according to claim 10, wherein the treatment comprises administering an effective amount of the antibody to a subject, and further comprises administering a therapeutically effective amount of a second agent to the subject, wherein the second agent is an anti-cancer agent and/or an anti-angiogenic agent.

14. The antibody according to any of claims 1 to 7 for use according to claim 13, wherein the second agent is a chemotherapeutic agent.

15. The antibody according to any of claims 1 to 7 for use according to claim 14, wherein the chemotherapeutic agent is paclitaxel, gemcitabine or irinotecan.

16. The antibody according to any of claims 1 to 7 for use according to claim 13 wherein the second agent is an antagonist of vascular endothelial cell growth factor (VEGF) or of a VEGF receptor.

17. The antibody according to any of claims 1 to 7 for use according to claim 13 wherein the second agent is an anti-DLL4 antibody.

18. Use of the antibody as defined in any one of claims 1 to 7 for the manufacture of a medicament for the treatment of cancer.

19. Use according to claim 18, wherein the treatment of cancer is treatment as defined in any of claims 11 to 17.