WHAT IS CLAIMED IS:

1. An antibody that binds to Notch1, comprising:

a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3, wherein the heavy chain variable region is selected from the group consisting of SEQ ID NOS: 69 and 71, and

a light chain variable region comprising a CDR1, a CDR2, and a CDR3, wherein the light chain variable region is selected from the group consisting of SEQ ID NOS: 83, 85, 87, 89, 91, 93, 95, 97, 105, 107 and 109.

2. The antibody according to claim 1, comprising:

(a) a heavy chain variable region CDR1 as set forth in SEQ ID NO: 73,

(b) a heavy chain variable region CDR2 as set forth in SEQ ID NO: 77,

(c) a heavy chain variable region CDR3 as set forth in SEQ ID NO: 81,

(d) a light chain variable region CDR1 as set forth in SEQ ID NO: 99,

(e) a light chain variable region CDR2 as set forth in SEQ ID NO: 101, and

(f) a light chain variable region CDR3 as set forth in SEQ ID NO: 103.

3. An antibody that binds to Notch1, comprising:

a heavy chain variable region amino acid sequence that is at least 90% identical to SEQ ID NO: 71; and

a light chain variable region amino acid sequence that is at least 90% identical to SEQ ID NO: 97.

4. The antibody according to claim 3, comprising:

a heavy chain variable region amino acid sequence as set forth in SEQ ID NO: 71; and

a light chain variable region amino acid sequence as set forth in SEQ ID NO: 97.

5. An antibody that binds to Notch1, comprising:

a heavy chain amino acid sequence that is at least 90% identical to SEQ ID NO: 111; and

a light chain amino acid sequence that is at least 90% identical to SEQ ID NO: 113.

6. The antibody according to claim 5, comprising:

a heavy chain amino acid sequence as set forth in SEQ ID NO: 111; and

a light chain amino acid sequence as set forth in SEQ ID NO: 113.

7. An antibody that binds to Notch1, wherein the antibody binds an epitope comprising at least 7 amino acid residues selected from Asn 1461, Lys 1462, Val 1463, Cys 1464, Leu 1466, Leu 1580, Tyr 1621, Gly 1622, Met 1670, Asp 1671, Val 1672, Arg 1673, Leu 1707, Ala 1708, Leu 1710, Gly 1711, Ser 1712, Leu 1713, Pro 1716 and Lys 1718.

8. An antibody that binds to Notch1, comprising:

a heavy chain variable region comprising a CDR1, a CDR2, and a CDR3, wherein the heavy chain variable region is set forth in SEQ ID NO: 115, and

a light chain variable region comprising a CDR1, a CDR2, and a CDR3, wherein the light chain variable region is selected from the group consisting of SEQ ID NOS: 127, 129, 137, 139, 141, 143, 145 and 147.

9. The antibody according to claim 8, comprising:

(a) a heavy chain variable region CDR1 as set forth in SEQ ID NO: 117,
(b) a heavy chain variable region CDR2 as set forth in SEQ ID NO: 121,
(c) a heavy chain variable region CDR3 as set forth in SEQ ID NO: 125,
(d) a light chain variable region CDR1 as set forth in SEQ ID NO: 131,
(e) a light chain variable region CDR2 as set forth in SEQ ID NO: 133, and
(f) a light chain variable region CDR3 as set forth in SEQ ID NO: 135.

10. An antibody that binds to Notch1, comprising:

a heavy chain variable region amino acid sequence that is at least 90% identical to SEQ ID NO: 115; and

a light chain variable region amino acid sequence that is at least 90% identical to SEQ ID NO: 129.

11. The antibody according to claim 10, comprising:

a heavy chain variable region amino acid sequence as set forth in SEQ ID NO: 115; and

a light chain variable region amino acid sequence as set forth in SEQ ID NO: 129.

12. An antibody that binds to Notch1, comprising:

a heavy chain amino acid sequence that is at least 90% identical to SEQ ID NO: 149; and

a light chain amino acid sequence that is at least 90% identical to SEQ ID NO: 151.

13. The antibody according to claim 12, comprising:
a heavy chain amino acid sequence as set forth in SEQ ID NO: 149; and
a light chain amino acid sequence as set forth in SEQ ID NO: 151.

14. An antibody that binds to Notch1, wherein the antibody binds an epitope comprising at least 8 amino acid residues selected from Asp 1458, Asn 1461, Val 1463, Cys 1464, Leu 1466, Leu 1580, Met 1581, Pro 1582, Tyr 1621, Gly 1622, Arg 1623, Asp 1671, Val 1672, Arg 1673, Gly 1674, Leu 1710, Gly 1711, Ser 1712, Leu 1713, Asn 1714, Ile 1715, Pro 1716 and Lys 1718.

15. The antibody according to any one of claims 1-14, wherein the antibody is an IgA, IgD, IgE, IgG, or IgM molecule, or is derived therefrom.

16. The antibody according to claim 15, wherein the antibody is an IgG, having a subclass selected from the group consisting of IgG1, IgG2, IgG3 and IgG4, or is derived therefrom.

17. The antibody according to claim 16, wherein the subclass is IgG1.

18. The antibody according to any one of claims 8-17, wherein the antibody demonstrates higher inhibition of Notch1 activation of a mutant Notch1 receptor compared to inhibition of Notch1 activation of a native Notch1 receptor.

19. An antibody that binds to Notch1 and competes for binding to Notch1 with the antibody of any one of claims 1-18.

20. A nucleic acid that encodes the antibody according to any one of claims 1-19.

21. A nucleic acid comprising a sequence that is selected from the group consisting of SEQ ID NOS: 72, 98, 112, and 114.

22. A nucleic acid comprising a sequence that is selected from the group consisting of SEQ ID NOS: 116, 130, 150 and 152.

23. A vector comprising the nucleic acid of any of any one of claims 20-22.

24. A host cell comprising the vector of claim 23.

25. A process for producing an antibody, comprising cultivating the host cell of claim 24 and recovering the antibody from the culture media.

26. A host cell that recombinantly produces the antibody according to any one of claims 1-19.

27. A pharmaceutical composition comprising the antibody according to any one of claims 1-19 and a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for treating a disorder associated with abnormal activation of Notch1 in a subject, comprising the antibody according to any one of claims 1-19 and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition for treating a disorder selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer in a subject, comprising the antibody according to any one of claims 1-19 and a pharmaceutically acceptable carrier.

30. The antibody of any one of claims 1-19 for use in therapy.

31. The use of an antibody of any one of claims 1-19 for the manufacture of a medicament.

32. The use according to claim 30, wherein the use is for the treatment of cancer.

33. The use according to claim 32, wherein the cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer.

34. Use of an antibody according to any one of claims 1-19 for the manufacture of a medicament for the treatment of a disorder.

35. Use of a pharmaceutical composition according to any one of claims 27-29, for the manufacture of a medicament for the treatment of a disorder.

36. The use of claim 34 or 35, wherein said disorder is associated with abnormal activation of Notch1.

37. The use of claim 35, wherein said disorder is cancer.

38. The use of claim 37, wherein the cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer.

WHAT IS CLAIMED IS:

1. An antibody that binds to Notch1, comprising:
   (a) a heavy chain variable region CDR1 as set forth in SEQ ID NO: 73,
   (b) a heavy chain variable region CDR2 as set forth in SEQ ID NO: 77,
   (c) a heavy chain variable region CDR3 as set forth in SEQ ID NO: 81,
   (d) a light chain variable region CDR1 as set forth in SEQ ID NO: 99,
   (e) a light chain variable region CDR2 as set forth in SEQ ID NO: 101, and
   (f) a light chain variable region CDR3 as set forth in SEQ ID NO: 103.

2. The antibody according to claim 1, comprising:
   a heavy chain variable region selected from the group consisting of SEQ ID NOS: 69 and 71, and
   a light chain variable region selected from the group consisting of SEQ ID NOS: 83, 85, 87, 89, 91, 93, 95, 97, 105, 107 and 109.

3. The antibody according to claim 1, comprising:
   a heavy chain variable region amino acid sequence as set forth in SEQ ID NO: 71; and
   a light chain variable region amino acid sequence as set forth in SEQ ID NO: 97.

4. The antibody according to claim 1, comprising:
   a heavy chain amino acid sequence as set forth in SEQ ID NO: 111; and
   a light chain amino acid sequence as set forth in SEQ ID NO: 113.

5. An isolated antibody that binds to human Notch1, wherein the antibody binds an epitope comprising amino acid residues Asn 1461, Lys 1462, Val 1463, Asp 1671, Arg 1673, Leu 1713, and Lys 1718.

6. An antibody that binds to Notch1, comprising:
   (a) a heavy chain variable region CDR1 as set forth in SEQ ID NO: 117,
   (b) a heavy chain variable region CDR2 as set forth in SEQ ID NO: 121,
   (c) a heavy chain variable region CDR3 as set forth in SEQ ID NO: 125,
   (d) a light chain variable region CDR1 as set forth in SEQ ID NO: 131,
   (e) a light chain variable region CDR2 as set forth in SEQ ID NO: 133, and
   (f) a light chain variable region CDR3 as set forth in SEQ ID NO: 135.

7. The antibody according to claim 6, comprising:

a heavy chain variable region set forth in SEQ ID NO: 115, and

a light chain variable region selected from the group consisting of SEQ ID NOS: 127, 129, 137, 139, 141, 143, 145 and 147.

8. The antibody according to claim 6, comprising:

a heavy chain variable region amino acid sequence as set forth in SEQ ID NO: 115; and

a light chain variable region amino acid sequence as set forth in SEQ ID NO: 129.

9. The antibody according to claim 6, comprising:

a heavy chain amino acid sequence as set forth in SEQ ID NO: 149; and

a light chain amino acid sequence as set forth in SEQ ID NO: 151.

10. An isolated antibody that binds to human Notch1, wherein the antibody binds an epitope comprising amino acid residues Asp 1458, Val 1463, Tyr 1621, Asp 1671, Val 1672, Arg 1673, Ser 1712 and Leu 1713.

11. The antibody according to any one of claims 1-10, wherein the antibody is an IgA, IgD, IgE, IgG, or IgM molecule, or is derived therefrom.

12. The antibody according to claim 11, wherein the antibody is an IgG, having a subclass selected from the group consisting of IgG1, IgG2, IgG3 and IgG4, or is derived therefrom.

13. The antibody according to claim 12, wherein the subclass is IgG1.

14. The antibody according to any one of claims 6-10, wherein the antibody demonstrates higher inhibition of Notch1 activation of a mutant Notch1 receptor compared to inhibition of Notch1 activation of a native Notch1 receptor.

15. A nucleic acid that encodes the antibody according to any one of claims 1-14.

16. A nucleic acid comprising a sequence that is selected from the group consisting of SEQ ID NOS: 72, 98, 112, and 114.

17. A nucleic acid comprising a sequence that is selected from the group consisting of SEQ ID NOS: 116, 130, 150 and 152.

18. A vector comprising the nucleic acid of any of any one of claims 15-17.

19. A host cell comprising the vector of claim 18.

20. A process for producing an antibody, comprising cultivating the host cell of claim 19 and recovering the antibody from the culture media.

21. A host cell that recombinantly produces the antibody according to any one of claims 1-14.

22. A pharmaceutical composition comprising the antibody according to any one of claims 1-14 and a pharmaceutically acceptable carrier.

23. A pharmaceutical composition for treating a disorder associated with abnormal activation of Notch1 in a subject, comprising the antibody according to any one of claims 1-14 and a pharmaceutically acceptable carrier.

24. A pharmaceutical composition for treating a disorder selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer in a subject, comprising the antibody according to any one of claims 1-14 and a pharmaceutically acceptable carrier.

25. The antibody of any one of claims 1-14 for use in therapy.

26. The antibody of any one of claims 1-14 for use as a medicament.

27. The antibody according to claim 26, wherein the antibody is for the treatment of cancer.

28. The antibody according to claim 27, wherein the cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer.

29. The use of an antibody according to any one of claims 1-14, in the manufacture of a medicament for the treatment of cancer.

30. The use of a pharmaceutical composition according to any one of claims 22-24, in the manufacture of a medicament for the treatment of cancer.

31. The use of claim 29 or 30, wherein said cancer is associated with abnormal activation of Notch1.

32. The use of claim 31, wherein the cancer is selected from the group consisting of T-cell acute lymphoblastic leukemia (T-ALL), non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colon cancer.