

WHAT IS CLAIMED:

1. An antibody which immunospecifically binds to human KIT, comprising:

(i) a light chain variable region ("VL") comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, respectively;

(ii) a heavy chain variable region ("VH") comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7, respectively; and

(iii) a modified human IgG1 Fc region or domain which comprises non-naturally occurring amino acids 234A, 235Q and 322Q as numbered by the EU index as set forth in Kabat.

2. The antibody of claim 1, wherein the modified human IgG1 Fc region or domain further comprises non-naturally occurring amino acids 252Y, 254T and 256E as numbered by the EU index as set forth in Kabat.

3. The antibody of claim 1 or 2, wherein:

(i) the VL comprises the amino acid sequence:

DIVMTQSPSX_{K1}LSASVGDRVTTITCKASQNVRTNVAWYQQKPGKAPKX_{K2}LIYSASYR
YSGVPDRFX_{K3}GSGSGTDFTLTISSLQX_{K4}EDFAX_{K5}YX_{K6}CQQYNSYPRTFGGGTKVEIK
(SEQ ID NO: 17), wherein X_{K1} is an amino acid with an aromatic or aliphatic hydroxyl side chain, X_{K2} is an amino acid with an aliphatic or aliphatic hydroxyl side chain, X_{K3} is an amino acid with an aliphatic hydroxyl side chain, X_{K4} is an amino acid with an aliphatic hydroxyl side chain or is P, X_{K5} is an amino acid with a charged or acidic side chain and X_{K6} is an amino acid with an aromatic side chain; and

(ii) the VH comprises the amino acid sequence:

QVQLVQSGAEX_{H1}KKPGASVKX_{H2}SCKASGYTFTDYYINWVX_{H3}QAPGKGLEWIARIY
 PGSGNTYYNEKFKGRX_{H4}TX_{H5}TAX_{H6}KSTSTAYMX_{H7}LSSLRSEDX_{H8}AVYFCARGVY
 YFDYWGQGTTVTVSS (SEQ ID NO: 18), wherein X_{H1} is an amino acid with an aliphatic
 side chain, X_{H2} is an amino acid with an aliphatic side chain, X_{H3} is an amino acid with a polar
 or basic side chain, X_{H4} is an amino acid with an aliphatic side chain, X_{H5} is an amino acid with
 an aliphatic side chain, X_{H6} is an amino acid with an acidic side chain, X_{H7} is an amino acid
 with an acidic or amide derivative side chain, and X_{H8} is an amino acid with an aliphatic
 hydroxyl side chain.

4. The antibody of claim 3, wherein X_{K1} is the amino acid F or S, X_{K2} is the amino acid A
 or S, X_{K3} is the amino acid T or S, X_{K4} is the amino acid S or P, X_{K5} is the amino acid D or T,
 X_{K6} is the amino acid F or Y, X_{H1} is the amino acid L or V, X_{H2} is the amino acid L or V, X_{H3}
 is the amino acid K or R, X_{H4} is the amino acid V or A, X_{H5} is the amino acid L or I, X_{H6} is the
 amino acid E or D, X_{H7} is the amino acid Q or E, and X_{H8} is the amino acid S or T.

5. The antibody of any one of claims 1 to 4, wherein:

- i) the VL comprises the amino acid sequence of SEQ ID NO: 13, 14, 15 or 16, and
- ii) the VH comprises the amino acid sequence of SEQ ID NO: 8, 9, 10, 11 or 12.

6. The antibody of any one of claims 1 to 5, comprising:

- (i) a VL comprising an amino acid sequence of SEQ ID NO: 14;
- (ii) a VH comprising an amino acid sequence of SEQ ID NO: 10; and
- (iii) a modified human IgG1 Fc region or domain comprising non-naturally occurring
 amino acids 234A, 235Q and 322Q as numbered by the EU index as set forth in Kabat.

7. The antibody of any one of claims 1 to 5, comprising:

- (i) a VL comprising an amino acid sequence of SEQ ID NO: 14;
- (ii) a VH comprising an amino acid sequence of SEQ ID NO: 10; and

(iii) a modified human IgG1 Fc region or domain comprising non-naturally occurring amino acids 234A, 235Q, 322Q, 252Y, 254T and 256E as numbered by the EU index as set forth in Kabat.

8. The antibody of any one of claims 1 to 5, which comprises a heavy chain comprising the amino acid sequence:

QVQLVQSGAEVKKPGASVKLSCKASGYTFTDYYINWVRQAPGKGLEWIARIYPGSG
NTYYNEKFKGRATLTADKSTSTAYMQLSSLRSEDNAVYFCARGVYYFDYWGQGTT
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP
CPAPEAQGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG (SEQ ID
NO: 21).

9. The antibody of any one of claims 1 to 5, which comprises a light chain comprising the amino acid sequence:

DIVMTQSPSSLSASVGDRVTITCKASQNVRTNVAWYQQKPGKAPKALIYSASYRYS
VPDRFTGSGSGTDFTLTISSLQPEDFADYFCQQYNSTYPRTFGGGTKEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 22).

10. The antibody of any one of claims 1 to 5, which comprises a heavy chain comprising the amino acid sequence:

QVQLVQSGAEVKKPGASVKLSCKASGYTFTDYYINWVRQAPGKGLEWIARIYPGSG
NTYYNEKFKGRATLTADKSTSTAYMQLSSLRSEDNAVYFCARGVYYFDYWGQGTT
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP
CPAPEAQGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL

DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 21); and a light chain comprising the amino acid sequence:

DIVMTQSPSSLSASVGDRVITITCKASQNVRTNVAWYQQKPGKAPKALIYSASYRYS
VPDRFTGSGSGTDFTLTISLQPEDFADYFCQQYNSYPRTFGGGTKVEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDST
YLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 22).

11. A conjugate comprising the antibody of any one of claims 1 to 10 linked to an agent.
12. A pharmaceutical composition comprising the antibody of any one of claims 1 to 10, or the conjugate of claim 11, and a pharmaceutically acceptable carrier.
13. A polynucleotide or combination of polynucleotides comprising nucleotide sequences encoding the antibody of any one of claims 1 to 10, or the VH and VL of said antibody.
14. A vector or combination of vectors comprising the polynucleotide or combination of polynucleotides of claim 13.
15. A host cell comprising the vector or combination of vectors of claim 14 or the polynucleotide or combination of polynucleotides of claim 13.
16. A kit comprising the antibody of any one of claims 1 to 10, the conjugate of claim 11, or the pharmaceutical composition of claim 12.
17. Use of an antibody of any one of claims 1 to 10, the conjugate of claim 11, or the pharmaceutical composition of claim 12 in the manufacture of a medicament for protecting against, treating or managing a KIT-associated disorder in a subject in need thereof, wherein a therapeutically effective amount of the antibody of any one of claims 1 to 10, the conjugate of claim 11, or the pharmaceutical composition of claim 12 is to be administered to the subject.
18. The use of claim 17, wherein the KIT-associated disorder is a mast cell related disorder, an eosinophil related disorder, a cancer, asthma, an inflammatory condition, rheumatoid arthritis, an allergic inflammation, inflammatory bowel disease, a gastrointestinal disorder, or fibrosis.
19. The use of claim 18, wherein the KIT-associated disorder is a mast cell related disorder.

20. The use of claim 19, wherein the mast cell related disorder is chronic urticaria.
21. The use of claim 20, wherein the chronic urticaria is chronic inducible urticaria.
22. The use of claim 21, wherein the chronic inducible urticaria is cold urticaria.
23. The use of claim 21, wherein the chronic inducible urticaria is symptomatic dermographism.
24. The use of claim 21, wherein the chronic inducible urticaria is cholinergic urticaria.
25. The use of claim 20, wherein the chronic urticaria is chronic spontaneous urticaria.
26. The use of claim 18, wherein the KIT-associated disorder is an eosinophil related disorder.
27. The use of any one of claims 17 to 26, wherein the medicament is to be administered with a second therapeutic agent.
28. The use of claim 27, wherein said second therapeutic agent is a chemotherapeutic agent, a histone deacetylase inhibitor, an antibody, a cytokine, a tyrosine kinase inhibitor, an antihistamine, a leukotriene receptor antagonist, an immunomodulator, or an anti-inflammatory agent.
29. An *in vitro* method for inhibiting KIT activity in a cell expressing KIT, comprising contacting the cell with an effective amount of the antibody of any one of claims 1 to 10, the conjugate of claim 11, or the pharmaceutical composition of claim 12.
30. The method of claim 29, wherein the method inhibits KIT activity by at least about 10% in the cell expressing KIT.
31. An *in vitro* method for diagnosing a subject with a KIT-associated disorder, wherein the method comprises contacting cells or a sample obtained from the subject with the antibody of any one of claims 1 to 10 and detecting the expression level of KIT in the cells or the sample.
32. A method of making an antibody, wherein said method comprises culturing, and/or expressing the antibody using, the host cell of claim 15.

33. The method of claim 32, further comprising purifying the antibody obtained from said host cell.

34. Use of (1) an antibody which immunospecifically binds to human KIT or an antigen binding fragment thereof, (2) a conjugate comprising the antibody or antigen binding fragment thereof linked to an agent, or (3) a pharmaceutical composition comprising the antibody or antigen binding fragment thereof or the conjugate, and a pharmaceutically acceptable carrier in the manufacture of a medicament for protecting against, treating or managing chronic urticaria in a subject, wherein a therapeutically effective amount of the antibody or the antigen binding fragment thereof, the conjugate, or the pharmaceutical composition, is to be administered to the subject in need thereof.

35. The use of claim 34, wherein the human KIT comprises the amino acid sequence of SEQ ID NO: 1.

36. The use of claim 34 or 35, wherein the antibody specifically binds to a D4 or D5 region of human KIT.

37. The use of any one of claims 34 to 36, wherein the antibody comprises a modified Fc region or domain.

38. The use of any one of claims 34 to 37, wherein the antibody comprises a modified human Fc region or domain.

39. The use of any one of claims 34 to 38, wherein the antibody has reduced Fc receptor binding activity.

40. The use of claim 39, wherein the antibody has reduced Fc γ R binding activity.

41. The use of any one of claims 34 to 40, wherein the antibody does not induce significant degranulation of Fc γ RI-expressing human mast cells.

42. The use of any one of claims 34 to 41, wherein the antibody does not show significant Fc receptor-dependent KIT agonist activity.

43. The use of any one of claims 34 to 42, wherein the antibody comprises:

(A) (i) a VL comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, respectively; and

(ii) a VH comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7, respectively;

(B) (i) a VL comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, respectively; and

(ii) a VH comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27, respectively;

(C) (i) a VL comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30, respectively; and

(ii) a VH comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 25, SEQ ID NO: 31, and SEQ ID NO: 32, respectively;

(D) (i) a VL comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, respectively; and

(ii) a VH comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 33, SEQ ID NO: 34, and SEQ ID NO: 27, respectively; or

(E) (i) a VL comprising VL CDR1, VL CDR2, and VL CDR3 having the amino acid sequences of SEQ ID NO: 35, SEQ ID NO: 36, and SEQ ID NO: 37, respectively; and

(ii) a VH comprising VH CDR1, VH CDR2, and VH CDR3 having the amino acid sequences of SEQ ID NO: 38, SEQ ID NO: 39, and SEQ ID NO: 40, respectively.

44. The use of claim 43, wherein the chronic urticaria is chronic inducible urticaria.

45. The use of claim 44, wherein the chronic inducible urticaria is cold urticaria.

46. The use of claim 44, wherein the chronic inducible urticaria is symptomatic dermographism.

47. The use of claim 44, wherein the chronic inducible urticaria is cholinergic urticaria.

48. The use of claim 43, wherein the chronic urticaria is chronic spontaneous urticaria.
49. The use of any one of claims 34 to 48, wherein the medicament is to be administered with a second therapeutic agent.
50. The use of claim 49, wherein said second therapeutic agent is a chemotherapeutic agent, a histone deacetylase inhibitor, an antibody, a cytokine, a tyrosine kinase inhibitor, an antihistamine, a leukotriene receptor antagonist, an immunomodulator, or an anti-inflammatory agent.