

Name	Sequence Identifier No.	Sequence
Nucleic Acid Sequence encoding h11G2 VL (XC154)	SEQ ID NO:95	GACATCCAGATGACCCAGAGCCCTTCCAGCCTGAGCGCT TCCGTGGGAGATAGGGTGACCATCACCTGCAGGGCCAGC GAGTCCGTGGAGTACCACGGCACCAGCCTGATGCACTGG TACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATC TACGCCGCCAGCAACGTGGAGAGCGGCGTGCCTAGCAG ATTCAGCGGCAGCGGAAGCGGCACCGACTTCACCCTGAC CATTAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTA CTGTCAGCAGAGCAGGAAGGTGCCCTGGACCTTCGGCCA GGGCACCAAGGTCGAGATCAAG
Nucleic Acid Sequence encoding h11G2 VH (XC155)	SEQ ID NO:96	GAGGTGCAGCTGGTGGAGAGCGGAGGAGGACTGGTGCA GCCTGGCGGAAGCCTGAGACTGAGCTGCGCCGCCAGCG GCTTCACCTTTACCGACTTCTACATGAGCTGGGTGAGGCA GGCTCCCGGCAAAGGACTGGAGTGGGTGGGTTTCATCAG GAACAAGGCCAACGGCTACACCACCGAGTATAGCGCCTC CGTGAAGGGCAGGTTACCATCAGCAGGGACAACGCCAA GAACAGCCTGTACCTGCAGATGAACAGCCTGAGGGCCGA GGACACCGCCGTGTACTACTGCGCCAGAGTGTACGGCAG CACACTGCACTACTGGGGCCAGGGCACCCCTGGTGACCGT GAGCAGC

What is claimed is:

1. An isolated antibody, or antigen-binding fragment thereof, that specifically binds C-X-C-chemokine receptor 5 (CXCR5), wherein the antibody, or antigen-binding fragment thereof, is at least one antibody, or antigen-binding fragment thereof, selected from the group consisting of:

a) an antibody, or antigen-binding fragment thereof, comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:2; a CDR-L2 comprising the amino acid sequence of SEQ ID NO:3; a CDR-L3 comprising the amino acid sequence of SEQ ID NO:4; a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7; a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8; and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9;

b) an antibody, or antigen-binding fragment thereof, comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:2; a CDR-L2 comprising the amino acid sequence of SEQ ID NO:3; a CDR-L3 comprising the amino acid sequence of SEQ ID NO:4; a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7; a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8; and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:11;

c) an antibody, or antigen-binding fragment thereof, comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:14; a CDR-L2 comprising the amino acid sequence of SEQ ID NO:15; a CDR-L3 comprising the amino acid sequence of SEQ ID NO:16; a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19; a CDR-H2 comprising the amino acid sequence of SEQ ID NO:20; and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21;

d) an antibody, or antigen-binding fragment thereof, comprising a VL comprising an amino acid sequence encoded by the insert of the plasmid deposited with the ATCC and having

Accession Number PTA-124324 and a VH comprising an amino acid sequence encoded by the insert of the plasmid deposited with the ATCC having Accession Number PTA-124323;

e) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:1, and a VH comprising the amino acid sequence of SEQ ID NO:6;

f) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:13, and a VH comprising the amino acid sequence of SEQ ID NO:18;

g) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:47, and a VH comprising the amino acid sequence of SEQ ID NO:52;

h) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:5, and a VH comprising the amino acid sequence of SEQ ID NO:6;

i) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:5, and a VH comprising the amino acid sequence of SEQ ID NO:10;

j) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:13, and a VH comprising the amino acid sequence of SEQ ID NO:17;

k) an antibody, or antigen-binding fragment thereof, comprising a VL comprising the amino acid sequence of SEQ ID NO:1, and a VH comprising the amino acid sequence of SEQ ID NO:12;

l) an antibody, or antigen-binding fragment thereof, comprising a LC comprising the amino acid sequence of SEQ ID NO:22, and a HC comprising the amino acid sequence of SEQ ID NO:23;

m) an antibody, or antigen-binding fragment thereof, comprising a LC comprising the amino acid sequence of SEQ ID NO:24, and a HC comprising the amino acid sequence of SEQ ID NO:25;

n) an antibody, or antigen-binding fragment thereof, comprising a LC comprising the amino acid sequence of SEQ ID NO:26, and a HC comprising the amino acid sequence of SEQ ID NO:27;

o) an antibody, or antigen-binding fragment thereof, comprising a LC comprising the amino acid sequence of SEQ ID NO:28, and a HC comprising the amino acid sequence of SEQ ID NO:29.

2. The antibody, or antigen-binding fragment thereof, of claim 1, wherein said antibody, or antigen-binding fragment thereof, exhibits at least one of the following biological activities:

a) binds CXCR5+ human B cells with an apparent affinity of an EC50 of less than about 26 pM, but does not bind cells expressing CXCR5 mouse, rat or rabbit orthologs;

b) antagonizes CXCL13 inhibition of cAMP release triggered by forskolin;

c) triggers ADCC of CXCR5-expressing cells in human donor and cynomolgus PBMCs and human donor TMCs;

d) binds human CXCR5 but does not bind human chemokine receptors CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CMKLR1, CXCR3R1, CXCR1, CXCR2, CXCR3, CXCR4, CXCR6, CXCR7, or XCR1;

e) depletes B cells in the peripheral blood;

- f) depletes Tfh-like cells in the peripheral blood;
 - g) depletes bona fide Tfh cells in the spleen; and
 - h) impairs a humoral immune memory response.
3. The antibody, or antigen-binding fragment thereof, of claim 1, wherein said antibody, or antigen-binding fragment thereof, is afucosylated.
4. An isolated nucleic acid encoding the antibody, or antigen-binding fragment thereof, of claim 1.
5. A pharmaceutical composition comprising the antibody, or antigen-binding fragment thereof, of claim 1, and a pharmaceutically acceptable carrier or excipient.
6. The antibody, or antigen-binding fragment thereof, of claim 1, comprising a VL comprising the amino acid sequence of SEQ ID NO:1, and a VH comprising the amino acid sequence of SEQ ID NO:6.
7. The antibody, or antigen-binding fragment thereof, of claim 1, comprising a LC comprising the amino acid sequence of SEQ ID NO:28, and a HC comprising the amino acid sequence of SEQ ID NO:29.
8. An isolated antibody that specifically binds CXCR5 comprising a LC consisting of the

amino acid sequence of SEQ ID NO:28, and a HC consisting of the amino acid sequence of SEQ ID NO:29.

9. The antibody of claim 8, wherein the antibody is afucosylated.

10. An isolated antibody that specifically binds CXCR5 comprising: an antibody VL region comprising the first, second and third CDRs from the VL region comprising the amino acid sequence of SEQ ID NO:1; and an antibody VH region comprising the first, second and third CDRs from the VH region comprising the amino acid sequence of SEQ ID NO:6.

11. The antibody of claim 10, wherein the antibody is afucosylated.

12. An isolated antibody that specifically binds CXCR5 comprising: a) an antibody VL region comprising the first, second and third CDRs from the VL region comprising the amino acid sequence of SEQ ID NO:1; an antibody VH region comprising the first, second and third CDRs from the VH region comprising the amino acid sequence of SEQ ID NO:6; an antibody constant light (CL) region comprising the amino acid sequence of SEQ ID NO:30; and an antibody constant heavy (CH) region comprising the amino acid sequence of SEQ ID NO:31; or b) an antibody VL region at least 95% identical to the amino acid sequence of SEQ ID NO: 1 and comprising a CDR-L1 consisting of the amino acid sequence of SEQ ID NO:2; a CDR-L2 consisting of the amino acid sequence of SEQ ID NO:3; a CDR-L3 consisting of the amino acid sequence of SEQ ID NO:4; and an antibody VH region at least 95% identical to the amino acid sequence of SEQ ID NO:6 and a CDR-H1 consisting of the amino acid sequence of SEQ ID NO:7; a CDR-H2 consisting of the

amino acid sequence of SEQ ID NO:8; and a CDR-H3 consisting of the amino acid sequence of SEQ ID NO:9.

13. The antibody of claim 12, wherein the antibody is afucosylated.

14. An isolated antibody, or antigen-binding fragment thereof, that specifically binds C-X-C-chemokine receptor 5 (CXCR5), wherein the antibody, or antigen-binding fragment thereof, comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:2; a CDR-L2 comprising the amino acid sequence of SEQ ID NO:3; a CDR-L3 comprising the amino acid sequence of SEQ ID NO:4; a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7; a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8; and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9.

15. The antibody, or antigen-binding fragment thereof of claim 14, wherein said antibody, or antigen-binding fragment thereof, exhibits at least one of the following biological activities:

a) binds hCXCR5 expressed on human B cells with an apparent affinity of an EC₅₀ of about 6.60 pM with a standard deviation of about plus or minus 2.33 pM;

b) binds hCXCR5 expressed on human circulating follicular T helper-like cells with an apparent affinity of an EC₅₀ of about 5.89 pM with a standard deviation of about plus or minus 1.40 pM;

c) binds hCXCR5 expressed on human follicular T helper (T_{fh}) cells with an apparent affinity of an EC₅₀ of about 10.6 pM;

d) binds cynoCXCR5 expressed on cynomolgus monkey B cells with an apparent affinity of an EC50 of about 1.32 pM;

e) binds cynoCXCR5 expressed on cynomolgus monkey Tfh-like cells with an apparent affinity of an EC50 of about 10.5 pM;

f) antagonizes CXCR5-CXCL13 signaling in a cAMP reporter assay with an EC50 of about 961 pM;

g) exhibits ADCC activity against human B cells expressing hCXCR5 with an EC50 of about 2.01 pM with a standard deviation of about plus or minus 2.28 pM;

h) exhibits ADCC activity against human Tfh-like cells expressing hCXCR5 with an EC50 of about 4.28 pM with a standard deviation of about plus or minus 2.88 pM;

i) exhibits ADCC activity against human Tfh cells expressing hCXCR5 with an EC50 of about 0.11 pM;

j) exhibits ADCC activity against cynomolgus monkey B cells expressing cynoCXCR5 with an EC50 of about 15.3 pM with a standard deviation of about plus or minus 11.7 pM;

k) binds hCXCR5 but does not detectably bind human chemokine receptors CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CMKLR1, CXCR3R1, CXCR1, CXCR2, CXCR3, CXCR4, CXCR6, CXCR7, and XCR1;

l) inhibits binding of CXCR5 to CXCL13;

m) binds CXCR5+ human B cells with an apparent affinity of an EC50 of less than about 26 pM, but does not bind cells expressing CXCR5 mouse, rat or rabbit orthologs;

n) antagonizes CXCL13 inhibition of cAMP release triggered by forskolin;

o) triggers ADCC of CXCR5-expressing cells in human donor and cynomolgus PBMCs and human donor TMCs;

p) binds human CXCR5 but does not bind human chemokine receptors CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CMKLR1, CXCR3R1, CXCR1, CXCR2, CXCR3, CXCR4, CXCR6, CXCR7, or XCR1;

q) depletes B cells in the peripheral blood;

r) depletes Tfh-like cells in the peripheral blood;

s) depletes bona fide Tfh cells in the spleen; and

t) impairs humoral immune memory response.