ANTIBODIES TARGETING FC RECEPTOR-LIKE 5 AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Patent Application Serial No. 62/263,586, filed December 4, 2015, the contents of which are incorporated by reference in their entirety, and to which priority is claimed.

FIELD OF THE SUBJECT MATTER

The presently disclosed subject matter relates to fully human antibodies that bind to Fc Receptor-like 5 (FcRL5), and methods of using the same. The presently disclosed subject matter further relates to fully human antibodies that bind to domain 9 of FcRL5.

BACKGROUND OF THE SUBJECT MATTER

Fc receptor-like (FcRL) proteins are a family of cellular receptors homologous to FcγRI and are predominantly expressed by B cells. FcRL5 is expressed on both mature B cells and plasma cells, and is induced by Epstein-Barr virus (EBV) proteins (Polson et al., Int. Immunol. 18:1363-1373 (2006); Mohan et al., Blood. 107:4433-4439 (2006)). FcRL5 has been shown to inhibit B cell antigen receptor signaling and the co-stimulation of FcRL5 and the B cell antigen receptor promotes proliferation and differentiation of naive B cells (Dement-Brown et al., J. Leukoc. Biol. 91:59-67 (2012)). FcRL5 has been implicated in human diseases, including cancer and autoimmune conditions (Kochi et al. Nat. Genet. 37:478-485 (2005); Li et al. Blood. 112(1):179-87 (2008)). In particular, FcRL5 has been shown to be overexpressed on malignant B cells of hairy cell leukemia, chronic lymphocytic leukemia, mantle cell lymphoma and multiple myeloma patients (Polson et al., Int. Immunol. 18(9):1363-73 (2006); Li et al. (2008)). In addition, serum levels of soluble FcRL5 are elevated in patients with several types of B cell tumors (Ise et al., Leukemia. 21:169-174 (2007)). Given the significant association between FcRL5 and B cell cancers, therapeutics targeting FcRL5 are desired.

SUMMARY

In one aspect, the present invention refers to an isolated anti-FcRL5 antibody or an antigen-binding fragment thereof comprising: a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID

NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299 and SEQ ID NO:303; and a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300 and SEQ ID NO:304, wherein the antibody or antigen-binding portion thereof binds to an FcRL5 polypeptide.

In another aspect, the present invention refers to an isolated anti-FcRL5 antibody or an antigen-binding fragment thereof comprising: a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ

ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299, SEQ ID NO:303, and conservative modifications thereof; and a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300, SEQ ID NO:304, and conservative modifications thereof, wherein the antibody or antigen-binding portion thereof binds to an FcRL5 polypeptide.

In yet another example, the present invention refers to an isolated anti-FcRL5 antibody or an antigen-binding fragment thereof comprising: a light chain variable region comprising an amino acid sequence that is at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299 and SEQ ID NO:303; and a heavy chain variable region comprising an amino acid sequence that is at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID

NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300 and SEQ ID NO:304, wherein the antibody or antigen-binding portion thereof binds to an FcRL5 polypeptide.

In yet another example, the present invention refers to an isolated anti-FcRL5 antibody or an antigen-binding fragment thereof comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region and the light chain variable region are selected from the group consisting of:

i. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:3, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:4;

ii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:7, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:8;

iii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:11, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:12;

iv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:15, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:16;

v. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:19, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:20;

vi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:23, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:24;

vii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:27, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:28;

viii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:31, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:32;

ix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:35, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:36;

x. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:39, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:40;

xi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:43, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:44;

xii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:47, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:48;

xiii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:51, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:52;

xiv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:55, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:56;

xv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:59, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:60;

xvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:63, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:64;

xvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:67, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:68;

xviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:71, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:72;

xix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:75, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:76;

xx. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:79, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:80;

xxi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:83, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:84;

xxii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:87, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:88;

xxiii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:91, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:92;

xxiv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:95, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:96;

xxv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:99, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:100;

xxvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:103, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:104;

xxvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:107, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:108;

xxviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:111, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:112;

xxix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:115, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:116;

xxx. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:119, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:120;

xxxi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:123, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:124;

xxxii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:127, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:128;

xxxiii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:131, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:132;

xxxiv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:135, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:136;

xxxv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:139, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:140;

xxxvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:143, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:144;

xxxvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:147, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:148;

xxxviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:151, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:152;

xxxix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:155, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:156;

xl. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:159, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:160;

xli. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:163, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:164;

xlii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:167, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:168;

xliii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:171, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:172;

xliv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:175, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:176;

xlv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:179, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:180;

xlvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:183, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:184;

xlvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:187, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:188;

xlviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:191, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:192;

xlix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:195, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:196;

l. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:199, and (b) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:200.

li. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:203, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:204;

lii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:207, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:208;

liii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:211, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:212;

liv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:215, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:216;

lv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:219, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:220;

lvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:223, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:224;

lvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:227, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:228;

lviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:231, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:232;

lix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:235, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:236;

lx. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:239, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:240;

lxi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:243, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:244;

lxii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:247, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:248;

lxiii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:251, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:252;

lxiv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:255, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:256;

lxv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:259, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:260;

lxvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:263, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:264;

lxvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:267, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:268;

lxviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:271, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:272;

lxix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:275, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:276;

lxx. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:279, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:280;

lxxi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:283, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:284;

lxxii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:287, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:288;

lxxiii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:291, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:292;

lxxiv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:279, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:280;

lxxv. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:283, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:284;

lxxvi. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:287, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:288;

lxxvii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:291, and (b) a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:292;

lxxviii. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:295, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:296;

lxxix. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:299, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:300; and

lxxx. a light chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:303, and a heavy chain variable region comprising amino acids having a sequence set forth in SEQ ID NO:304.

In yet another example, the present invention refers to an antibody or antigen-binding fragment thereof comprising:

i. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539, 543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591; and

ii. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592;

wherein the antibody or antigen-binding fragment thereof specifically binds FcRL5.

In yet another example, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising:

i. a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 309, 315, 321, 326, 332, 335, 340, 346, 354, 360, 366, 372, 378, 387, 393, 403, 411, 420, 425, 436, 440, 444, 471, 480, 500, 510, 515, 520, 525, 537, 551, 559, 565, 582 and 589;

ii. a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 310, 316, 322, 327, 333, 336, 341, 355, 361, 367, 373, 379, 388, 404, 412, 421, 426, 431, 441, 445, 450, 466, 472, 475, 481, 496, 501, 506, 511, 516, 521, 526, 538, 552, 560, 566, 583 and 590;

iii. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539, 543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591;

iv. a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 312, 318, 324, 329, 338, 343, 348, 352, 357, 363, 369, 381, 390, 397, 401, 406, 416, 423, 428, 433, 447, 460, 468, 474, 477, 483, 490, 498, 503, 508, 518, 533, 540, 544, 547, 556, 562, 568, 571, 580, 585 and 588;

v. a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 313, 319, 330, 344, 349, 358, 364, 370, 382, 385, 391, 398, 409, 417, 429, 434, 438, 448, 454, 461, 469, 478, 484, 487, 504, 513, 523, 534, 429, 448, 548, 557, 563, 572, 575 and 586; and

vi. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592;

wherein the antibody or an antigen-binding fragment thereof specifically binds FcRL5.

In a further aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable

region CDR1 comprising the amino acid sequence of SEQ ID NO:411; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:412; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:463; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:318; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:319; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:419.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:515; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:516; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:517; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:318; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:319; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:531.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:403; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:404; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:532; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:533; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:534; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:535.

In a further aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:411; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:412; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:543; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:544; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:448; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:545.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:372; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:475; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:570; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:571; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:572; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:573.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:440; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:441; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:442; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:329; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:330; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:443.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:309; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:310; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:489; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:490; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:313; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:491.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 scFv antibody comprising a light chain variable region, a heavy chain variable region and a peptide linker, wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 594, 596, 598, 600, 602, 604, 606, 608, 610, 612, 614, 616, 618, 620, 622, 624, 626, 628, 630, 632, 634, 636, 638, 640, 642, 644, 646, 648, 650, 652, 654, 656, 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686,

688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 714, 716, 718, 720, 722, 724, 726, 728, 730, 732, 734, 736, 738, 740, 742 and 744.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 scFv antibody comprising a light chain variable region, a heavy chain variable region and a peptide linker, wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 650, 664, 678, 700, 702, 710 and 726.

In a further aspect, the present invention refers to an isolated anti-FcRL5 scFv antibody comprising a light chain variable region, a heavy chain variable region, a peptide linker and a His-tag and HA-tag, wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 802, 816, 830, 852, 854, 862 and 878.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof that cross-competes for binding to FcRL5 with an isolated anti-FcRL5 antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention refers to an isolated anti-FcRL5 antibody or antigen-binding fragment thereof that cross-competes for binding to domain 9 of FcRL5 with an isolated anti-FcRL5 antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention refers to an isolated antibody or antigen-binding portion thereof which cross-competes for binding to human FcRL5 with a reference antibody or reference antigen-binding portion thereof, wherein the reference antibody or reference antigen-binding portion thereof comprises:

i. a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID

NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299, SEQ ID NO:303, and conservative modifications thereof; and

a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300, SEQ ID NO:304, and conservative modifications thereof.

In yet another aspect, the present invention refers to an isolated antibody or antigen-binding portion thereof which cross-competes for binding to human FcRL5 with a reference antibody or reference antigen-binding portion thereof, wherein the reference antibody or reference antigen-binding portion thereof comprises:

i. a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 309, 315, 321, 326, 332, 335, 340, 346, 354, 360, 366, 372, 378, 387, 393, 403, 411, 420, 425, 436, 440, 444, 471, 480, 500, 510, 515, 520, 525, 537, 551, 559, 565, 582 and 589;

ii. a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 310, 316, 322, 327, 333, 336, 341, 355, 361, 367, 373, 379, 388, 404, 412, 421, 426, 431, 441, 445, 450, 466, 472, 475, 481,

496, 501, 506, 511, 516, 521, 526, 538, 552, 560, 566, 583 and 590;

iii. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539, 543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591;

iv. a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 312, 318, 324, 329, 338, 343, 348, 352, 357, 363, 369, 381, 390, 397, 401, 406, 416, 423, 428, 433, 447, 460, 468, 474, 477, 483, 490, 498, 503, 508, 518, 533, 540, 544, 547, 556, 562, 568, 571, 580, 585 and 588;

v. a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 313, 319, 330, 344, 349, 358, 364, 370, 382, 385, 391, 398, 409, 417, 429, 434, 438, 448, 454, 461, 469, 478, 484, 487, 504, 513, 523, 534, 429, 448, 548, 557, 563, 572, 575 and 586; and

vi. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592.

In yet another aspect, the present invention refers to an isolated antibody or antigen-binding portion thereof which cross-competes for binding to domain 9 of human FcRL5 with a reference antibody or reference antigen-binding portion thereof, wherein the reference antibody or reference antigen-binding portion thereof comprises:

i. a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID

NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299, SEQ ID NO:303, and conservative modifications thereof; and

ii. a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300, SEQ ID NO:304, and conservative modifications thereof.

In yet another aspect, the present invention refers to an isolated antibody or an antigen-binding portion thereof which cross-competes for binding to domain 8 or domain 9 of FcRL5 with a reference antibody or reference antigen-binding portion thereof, wherein the reference antibody or reference antigen-binding portion thereof comprises:

i. a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 309, 315, 321, 326, 332, 335, 340, 346, 354, 360, 366, 372, 378, 387, 393, 403, 411, 420, 425, 436, 440, 444, 471, 480, 500, 510, 515, 520, 525, 537, 551, 559, 565, 582 and 589;

ii. a heavy chain variable region CDR2 comprising an amino acid sequence

selected from the group consisting of SEQ ID NOs: 310, 316, 322, 327, 333, 336, 341, 355, 361, 367, 373, 379, 388, 404, 412, 421, 426, 431, 441, 445, 450, 466, 472, 475, 481, 496, 501, 506, 511, 516, 521, 526, 538, 552, 560, 566, 583 and 590;

iii. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539, 543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591;

iv. a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 312, 318, 324, 329, 338, 343, 348, 352, 357, 363, 369, 381, 390, 397, 401, 406, 416, 423, 428, 433, 447, 460, 468, 474, 477, 483, 490, 498, 503, 508, 518, 533, 540, 544, 547, 556, 562, 568, 571, 580, 585 and 588;

v. a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 313, 319, 330, 344, 349, 358, 364, 370, 382, 385, 391, 398, 409, 417, 429, 434, 438, 448, 454, 461, 469, 478, 484, 487, 504, 513, 523, 534, 429, 448, 548, 557, 563, 572, 575 and 586; and

vi. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592.

In yet another aspect, the present invention refers to a composition comprising the antibody or antigen-binding fragment thereof of the present disclosure, and a pharmaceutically acceptable carrier.

In yet another aspect, the present invention refers to an immunoconjugate comprising the antibody or antigen-binding fragment thereof as disclosed herein, linked to a therapeutic agent.

In yet another aspect, the present invention refers to a composition comprising the immunoconjugateas disclosed herein and a pharmaceutically acceptable carrier.

In yet another aspect, the present invention refers to a bispecific molecule comprising the antibody or antigen-binding fragment thereof as disclosed herein, linked to a second functional moiety.

In yet another aspect, the present invention refers to a composition comprising the bispecific molecule as disclosed herein and a pharmaceutically acceptable carrier.

In yet another aspect, the present invention refers to an isolated nucleic acid that encodes an antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention refers to an expression vector comprising the nucleic acid molecule as disclosed herein.

In yet another aspect, the present invention refers to a host cell comprising the expression vector as disclosed herein.

In yet another aspect, the present invention refers to a method for detecting FcRL5 in a whole cell or tissue, comprising:

i. contacting a cell or tissue with the antibody or antigen-binding fragment thereof of any one of claims 1-34, wherein said antibody or antigen-binding fragment thereof comprises a detectable label; and

ii. determining the amount of the labeled antibody or antigen-binding fragment thereof bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of FcRL5 in said cell or tissue.

In yet another aspect, the present invention refers to the use of the antibody or antigen-binding fragment thereof as disclosed herein in the manufacture of a medicament for treating cancer in a subject.

In yet another aspect, the present invention refers to a kit for treating cancer, comprising the antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention refers to an immunoconjugate comprising an antibody or antigen-binding fragment thereof linked to a therapeutic agent, wherein the antibody or antigen-binding fragment thereof comprises:

i. a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 309, 315, 321, 326, 332, 335, 340, 346, 354, 360, 366, 372, 378, 387, 393, 403, 411, 420, 425, 436, 440, 444, 471, 480, 500, 510, 515, 520, 525, 537, 551, 559, 565, 582 and 589;

ii. a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 310, 316, 322, 327, 333, 336, 341, 355, 361, 367, 373, 379, 388, 404, 412, 421, 426, 431, 441, 445, 450, 466, 472, 475, 481, 496, 501, 506, 511, 516, 521, 526, 538, 552, 560, 566, 583 and 590;

iii. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539, 543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591;

iv. a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 312, 318, 324, 329, 338, 343, 348, 352, 357, 363, 369, 381, 390, 397, 401, 406, 416, 423, 428, 433, 447, 460, 468, 474, 477, 483, 490, 498, 503, 508, 518, 533, 540, 544, 547, 556, 562, 568, 571, 580, 585 and 588;

v. a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 313, 319, 330, 344, 349, 358, 364, 370, 382, 385, 391, 398, 409, 417, 429, 434, 438, 448, 454, 461, 469, 478, 484, 487, 504, 513, 523, 534, 429, 448, 548, 557, 563, 572, 575 and 586; and

vi. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592;

wherein the antibody or an antigen-binding fragment thereof specifically binds FcRL5.

In yet another aspect, the present invention refers to an immunoconjugate comprising an antibody or antigen-binding fragment thereof linked to a therapeutic agent, wherein the antibody or antigen-binding fragment thereof comprises:

i. a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID

NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223, SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299, SEQ ID NO:303, and conservative modifications thereof; and

ii. a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300, SEQ ID NO:304, and conservative modifications thereof,

wherein the antibody or antigen-binding portion thereof binds to an FcRL5 polypeptide.

The presently disclosed subject matter provides fully human antibodies that bind to Fc Receptor-like 5 (FcRL5), and methods of using the same. The presently disclosed subject matter further provides fully human antibodies that specifically bind domain 7, 8 or 9 of FcRL5. It is based, at least in part, on the discovery of 76 clones from a human phage display library that specifically bind to FcRL5.

In various non-limiting examples, the presently disclosed subject matter provides for antibodies, and particularly variable regions of antibodies, that bind specifically to human FcRL5, as well as nucleic acids encoding said antibodies and variable regions, vectors comprising said nucleic acids and methods of producing said antibodies. The presently disclosed subject matter further provides pharmaceutical compositions comprising the disclosed anti-FcRL5 antibodies and methods of treatment. 76 species of antibodies, as well as competitively binding antibodies, are provided.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 depicts the FcRL5 expression in various normal tissues and human cancer cell lines.

Figure 2 depicts the screening of anti-FcRL5 scFvs using 3T3 cells expressing FcRL5 or FcRL1, 2, 3, 4 or 6.

Figure 3A-D. (A) A representation of the domains of FcRL5 and the soluble, glycosylphosphatidylinositol (GPI)-anchored and transmembrane forms of FcRL5. (B) A representation of the vector used to express a mutated form of FcRL5 that lacks domain 9 (also referred to herein as FcRL5Δdom9). (C) The nucleotide sequences of full length FcRL5 and the form of FcRL5 that lacks domain 9. (D) A representation of the differences in the nucleotide sequences of full length FcRL5 and the mutated form of FcRL5 in which domain 9 is deleted (referred to herein as "FcRL5Δdom9").

Figure 4 depicts the screening of anti-FcRL5 scFv ET200-39 on 3T3 cells expressing FcRL5Δdom9.

Figure 5 depicts the screening of anti-FcRL5 scFv ET200-104 on 3T3 cells expressing FcRL5Δdom9.

Figure 6 depicts the screening of anti-FcRL5 scFv ET200-105 on 3T3 cells expressing FcRL5Δdom9.

Figure 7 depicts the screening of anti-FcRL5 scFv ET200-109 on 3T3 cells expressing FcRL5Δdom9.

Figure 8 depicts the screening of anti-FcRL5 scFv ET200-117 on 3T3 cells expressing FcRL5Δdom9.

Figure 9A-B depicts the FACS analysis of anti-FcRL5/CD3 bispecific antibodies.

Figure 10 illustrates the CLIPS technology. The CLIPS reaction takes place between bromo groups of the CLIPS scaffold and thiol sidechains of cysteines. The reaction is fast and specific under mild conditions. Using this elegant chemistry, native

39. A bispecific molecule comprising the antibody or antigen-binding fragment thereof of any one of claims 1-34, linked to a second functional moiety.

40. The bispecific molecule of claim 39, wherein the second functional moiety has a different binding specificity than said antibody or antigen binding fragment thereof.

41. The bispecific molecule of claim 39, wherein the second functional moiety has a binding specificity for an immune cell.

42. The bispecific molecule of claim 39, wherein the second functional moiety has a binding specificity for CD3.

43. A composition comprising the bispecific molecule of any one of claims 39-42 and a pharmaceutically acceptable carrier.

44. An isolated nucleic acid that encodes an antibody or antigen-binding fragment thereof of any one of claims 1-34.

45. An expression vector comprising the nucleic acid molecule of claim 44.

46. A host cell comprising the expression vector of claim 46.

47. A method for detecting FcRL5 in a whole cell or tissue, comprising:

i. contacting a cell or tissue with the antibody or antigen-binding fragment thereof of any one of claims 1-34, wherein said antibody or antigen-binding fragment thereof comprises a detectable label; and

ii. determining the amount of the labeled antibody or antigen-binding fragment thereof bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of FcRL5 in said cell or tissue.

48. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-34 in the manufacture of a medicament for treating cancer in a subject.

49. The use of claim 48, wherein the use reduces the number of the cancerous cells.

50. The use of claim 48, wherein the use reduces the size of a tumor.

51. The use of claim 48, wherein the use eradicates the cancer in the subject.

52. The use of any one of claims 48-51, wherein the cancer is multiple myeloma or Waldenstrom's Macroglobulinemia.

53. The use of any one of claims 48-52, wherein the cancer is multiple myeloma.

54. The use of any one of claims 48-53, wherein the subject is a human.

55. The antibody or antigen-binding fragment thereof of any one of claims 1-34 for use in treating cancer in a subject.

56. The antibody or antigen-binding fragment thereof of claim 55, wherein the cancer is multiple myeloma or Waldenstrom's Macroglobulinemia.

57. The antibody or antigen-binding fragment thereof of claim 55 or 56, wherein the cancer is multiple myeloma.

58. A kit for treating cancer, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-34.

59. The kit of claim 58, wherein the kit further comprises written instructions for using the antibody or antigen-binding fragment thereof for treating a subject having cancer.

60. The kit of claim 58 or 59, wherein the cancer is multiple myeloma or Waldenstrom's Macroglobulinemia.

61. The kit of claim 60, wherein the cancer is multiple myeloma.

62. An immunoconjugate comprising an antibody or antigen-binding fragment thereof linked to a therapeutic agent, wherein the antibody or antigen-binding fragment thereof comprises:

i. a heavy chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 309, 315, 321, 326, 332, 335, 340, 346, 354, 360, 366, 372, 378, 387, 393, 403, 411, 420, 425, 436, 440, 444, 471, 480, 500, 510, 515, 520, 525, 537, 551, 559, 565, 582 and 589;

ii. a heavy chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 310, 316, 322, 327, 333, 336, 341, 355, 361, 367, 373, 379, 388, 404, 412, 421, 426, 431, 441, 445, 450, 466, 472, 475, 481, 496, 501, 506, 511, 516, 521, 526, 538, 552, 560, 566, 583 and 590;

iii. a heavy chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 311, 317, 323, 328, 334, 337, 342, 347, 351, 356, 362, 368, 374, 376, 380, 384, 389, 394, 396, 400, 405, 408, 412, 415, 422, 427, 432, 437, 442, 446, 451, 453, 456, 458, 459, 463, 464, 467, 473, 476, 482, 486, 489, 492, 494, 497, 502, 507, 512, 517, 522, 527, 529, 532, 536, 539,

543, 546, 550, 553, 555, 561, 567, 570, 574, 577, 578, 579, 584, 578, 587 and 591;

iv. a light chain variable region CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 312, 318, 324, 329, 338, 343, 348, 352, 357, 363, 369, 381, 390, 397, 401, 406, 416, 423, 428, 433, 447, 460, 468, 474, 477, 483, 490, 498, 503, 508, 518, 533, 540, 544, 547, 556, 562, 568, 571, 580, 585 and 588;

v. a light chain variable region CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 313, 319, 330, 344, 349, 358, 364, 370, 382, 385, 391, 398, 409, 417, 429, 434, 438, 448, 454, 461, 469, 478, 484, 487, 504, 513, 523, 534, 429, 448, 548, 557, 563, 572, 575 and 586; and

vi. a light chain variable region CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 314, 320, 325, 331, 339, 345, 350, 353, 359, 365, 371, 377, 383, 386, 392, 395, 399, 402, 407, 410, 414, 418, 419, 424, 430, 435, 439, 443, 449, 452, 455, 457, 462, 465, 470, 479, 485, 488, 491, 493, 495, 499, 505, 509, 514, 519, 524, 528, 530, 531, 535, 541, 542, 545, 549, 554, 558, 564, 569, 573, 576, 581 and 592;

wherein the antibody or an antigen-binding fragment thereof specifically binds FcRL5.

63. An immunoconjugate comprising an antibody or antigen-binding fragment thereof linked to a therapeutic agent, wherein the antibody or antigen-binding fragment thereof comprises:

i. a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:39, SEQ ID NO:43, SEQ ID NO:47, SEQ ID NO:51, SEQ ID NO:55, SEQ ID NO:59, SEQ ID NO:63, SEQ ID NO:67, SEQ ID NO:71, SEQ ID NO:75, SEQ ID NO:79, SEQ ID NO:83, SEQ ID NO:87, SEQ ID NO:91, SEQ ID NO:95, SEQ ID NO:99, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:111, SEQ ID NO:115, SEQ ID NO:119, SEQ ID NO:123, SEQ ID NO:127, SEQ ID NO:131, SEQ ID NO:135, SEQ ID NO:139, SEQ ID NO:143, SEQ ID NO:147, SEQ ID NO:151, SEQ ID NO:155, SEQ ID NO:159, SEQ ID NO:163, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:175, SEQ ID NO:179, SEQ ID NO:183, SEQ ID NO:187, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:199, SEQ ID NO:203, SEQ ID NO:207, SEQ ID NO:211, SEQ ID NO:215, SEQ ID NO:219, SEQ ID NO:223,

SEQ ID NO:227, SEQ ID NO:231, SEQ ID NO:235, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:247, SEQ ID NO:251, SEQ ID NO:255, SEQ ID NO:259, SEQ ID NO:263, SEQ ID NO:267, SEQ ID NO:271, SEQ ID NO:275, SEQ ID NO:279, SEQ ID NO:283, SEQ ID NO:287, SEQ ID NO:291, SEQ ID NO:295, SEQ ID NO:299, SEQ ID NO:303, and conservative modifications thereof; and

ii. a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:20, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:32, SEQ ID NO:36, SEQ ID NO:40, SEQ ID NO:44, SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:60, SEQ ID NO:64, SEQ ID NO:68, SEQ ID NO:72, SEQ ID NO:76, SEQ ID NO:80, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:92, SEQ ID NO:96, SEQ ID NO:100, SEQ ID NO:104, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:116, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:132, SEQ ID NO:136, SEQ ID NO:140, SEQ ID NO:144, SEQ ID NO:148, SEQ ID NO:152, SEQ ID NO:156, SEQ ID NO:160, SEQ ID NO:164, SEQ ID NO:168, SEQ ID NO:172, SEQ ID NO:176, SEQ ID NO:180, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:192, SEQ ID NO:196, SEQ ID NO:200, SEQ ID NO:204, SEQ ID NO:208, SEQ ID NO:212, SEQ ID NO:216, SEQ ID NO:220, SEQ ID NO:224, SEQ ID NO:228, SEQ ID NO:232, SEQ ID NO:236, SEQ ID NO:240, SEQ ID NO:244, SEQ ID NO:248, SEQ ID NO:252, SEQ ID NO:256, SEQ ID NO:260, SEQ ID NO:264, SEQ ID NO:268, SEQ ID NO:272, SEQ ID NO:276, SEQ ID NO:280, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:292, SEQ ID NO:296, SEQ ID NO:300, SEQ ID NO:304, and conservative modifications thereof,

wherein the antibody or antigen-binding portion thereof binds to an FcRL5 polypeptide.

64. The immunoconjugate of claim 62 or 63, wherein said therapeutic agent is a drug, cytotoxin, or a radioactive isotope.