

Claims

What Is Claimed Is:

1. An antibody that binds human LILRB1 or LILRB2, the antibody comprising:

a) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:5;

b) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:9 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:13;

c) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:17 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:21;

d) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:25 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:29;

e) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:33 a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:37;

f) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:41 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:45;

g) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:49 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:53;

h) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:57 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:61;

i) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:65 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:69;

j) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:73 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:77;

k) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:81 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:85;

l) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:89 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:93;

m) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:97 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:101;

n) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:105 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:109;

o) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:113 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:117;

x) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:185 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:189;

y) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:193 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:197;

z) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:201 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:204; or

aa) a heavy chain variable region comprising a vhCDR1, a vhCDR2 and a vhCDR3 from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:208 and a light chain variable region comprising a vlCDR1, a vlCDR2, and a vlCDR3 from a light chain variable region comprising an amino acid sequence of SEQ ID NO:212.

2. An antibody that binds human LILRB1 or LILRB2, the antibody comprising:

a) a vhCDR1 comprising SEQ ID NO:2, a vhCDR2 comprising SEQ ID NO:3, a vhCDR3 comprising SEQ ID NO:4, a vlCDR1 comprising SEQ ID NO:6, a vlCDR2 comprising SEQ ID NO:7, and a vlCDR3 comprising SEQ ID NO:8;

b) a vhCDR1 comprising SEQ ID NO:10, a vhCDR2 comprising SEQ ID NO:11, a vhCDR3 comprising SEQ ID NO:12, a vlCDR1 comprising SEQ ID NO:14, a vlCDR2 comprising SEQ ID NO:15, and a vlCDR3 comprising SEQ ID NO:16;

c) a vhCDR1 comprising SEQ ID NO:18, a vhCDR2 comprising SEQ ID NO:19, a vhCDR3 comprising SEQ ID NO:20, a vlCDR1 comprising SEQ ID NO:22, a vlCDR2 comprising SEQ ID NO:23, and a vlCDR3 comprising SEQ ID NO:24;

d) a vhCDR1 comprising SEQ ID NO:26, a vhCDR2 comprising SEQ ID NO:27, a vhCDR3 comprising SEQ ID NO:28, a vlCDR1 comprising SEQ ID NO:30, a vlCDR2 comprising SEQ ID NO:31, and a vlCDR3 comprising SEQ ID NO:32;

e) a vhCDR1 comprising SEQ ID NO:34, a vhCDR2 comprising SEQ ID NO:35, a vhCDR3 comprising SEQ ID NO:36, a vlCDR1 comprising SEQ ID NO:38, a vlCDR2 comprising SEQ ID NO:39, and a vlCDR3 comprising SEQ ID NO:40;

- f) a vhCDR1 comprising SEQ ID NO:42, a vhCDR2 comprising SEQ ID NO:43, a vhCDR3 comprising SEQ ID NO:44, a vlCDR1 comprising SEQ ID NO:46, a vlCDR2 comprising SEQ ID NO:47, and a vlCDR3 comprising SEQ ID NO:48;
- g) a vhCDR1 comprising SEQ ID NO:50, a vhCDR2 comprising SEQ ID NO:51, a vhCDR3 comprising SEQ ID NO:52, a vlCDR1 comprising SEQ ID NO:54, a vlCDR2 comprising SEQ ID NO:55, and a vlCDR3 comprising SEQ ID NO:56;
- h) a vhCDR1 comprising SEQ ID NO:58, a vhCDR2 comprising SEQ ID NO:59, a vhCDR3 comprising SEQ ID NO:60, a vlCDR1 comprising SEQ ID NO:62, a vlCDR2 comprising SEQ ID NO:63, and a vlCDR3 comprising SEQ ID NO:64;
- i) a vhCDR1 comprising SEQ ID NO:66, a vhCDR2 comprising SEQ ID NO:67, a vhCDR3 comprising SEQ ID NO:68, a vlCDR1 comprising SEQ ID NO:70, a vlCDR2 comprising SEQ ID NO:71, and a vlCDR3 comprising SEQ ID NO:72;
- j) a vhCDR1 comprising SEQ ID NO:74, a vhCDR2 comprising SEQ ID NO:75, a vhCDR3 comprising SEQ ID NO:76, a vlCDR1 comprising SEQ ID NO:78, a vlCDR2 comprising SEQ ID NO:79, and a vlCDR3 comprising SEQ ID NO:80;
- k) a vhCDR1 comprising SEQ ID NO:82, a vhCDR2 comprising SEQ ID NO:83, a vhCDR3 comprising SEQ ID NO:84, a vlCDR1 comprising SEQ ID NO:86, a vlCDR2 comprising SEQ ID NO:87, and a vlCDR3 comprising SEQ ID NO:88;
- l) a vhCDR1 comprising SEQ ID NO:90, a vhCDR2 comprising SEQ ID NO:91, a vhCDR3 comprising SEQ ID NO:92, a vlCDR1 comprising SEQ ID NO:94, a vlCDR2 comprising SEQ ID NO:95, and a vlCDR3 comprising SEQ ID NO:96;
- m) a vhCDR1 comprising SEQ ID NO:98, a vhCDR2 comprising SEQ ID NO:99, a vhCDR3 comprising SEQ ID NO:100, a vlCDR1 comprising SEQ ID NO:102, a vlCDR2 comprising SEQ ID NO:103, and a vlCDR3 comprising SEQ ID NO:104;
- n) a vhCDR1 comprising SEQ ID NO:106, a vhCDR2 comprising SEQ ID NO:107, a vhCDR3 comprising SEQ ID NO:108, a vlCDR1 comprising SEQ ID NO:110, a vlCDR2 comprising SEQ ID NO:111, and a vlCDR3 comprising SEQ ID NO:112;
- o) a vhCDR1 comprising SEQ ID NO:114, a vhCDR2 comprising SEQ ID NO:115, a vhCDR3 comprising SEQ ID NO:116, a vlCDR1 comprising SEQ ID NO:118, a vlCDR2 comprising SEQ ID NO:119, and a vlCDR3 comprising SEQ ID NO:120;
- p) a vhCDR1 comprising SEQ ID NO:122, a vhCDR2 comprising SEQ ID NO:123, a vhCDR3 comprising SEQ ID NO:124, a vlCDR1 comprising SEQ ID NO:126, a vlCDR2 comprising SEQ ID NO:127, and a vlCDR3 comprising SEQ ID NO:128;

q) a vhCDR1 comprising SEQ ID NO:130, a vhCDR2 comprising SEQ ID NO:131, a vhCDR3 comprising SEQ ID NO:132, a vlCDR1 comprising SEQ ID NO:134, a vlCDR2 comprising SEQ ID NO:135, and a vlCDR3 comprising SEQ ID NO:136;

r) a vhCDR1 comprising SEQ ID NO:138, a vhCDR2 comprising SEQ ID NO:139, a vhCDR3 comprising SEQ ID NO:140, a vlCDR1 comprising SEQ ID NO:142, a vlCDR2 comprising SEQ ID NO:143, and a vlCDR3 comprising SEQ ID NO:144;

s) a vhCDR1 comprising SEQ ID NO:146, a vhCDR2 comprising SEQ ID NO:147, a vhCDR3 comprising SEQ ID NO:148, a vlCDR1 comprising SEQ ID NO:150, a vlCDR2 comprising SEQ ID NO:151, and a vlCDR3 comprising SEQ ID NO:152;

t) a vhCDR1 comprising SEQ ID NO:154, a vhCDR2 comprising SEQ ID NO:155, a vhCDR3 comprising SEQ ID NO:156, a vlCDR1 comprising SEQ ID NO:158, a vlCDR2 comprising SEQ ID NO:159, and a vlCDR3 comprising SEQ ID NO:160;

u) a vhCDR1 comprising SEQ ID NO:162, a vhCDR2 comprising SEQ ID NO:163, a vhCDR3 comprising SEQ ID NO:164, a vlCDR1 comprising SEQ ID NO:166, a vlCDR2 comprising SEQ ID NO:167, and a vlCDR3 comprising SEQ ID NO:168;

v) a vhCDR1 comprising SEQ ID NO:170, a vhCDR2 comprising SEQ ID NO:171, a vhCDR3 comprising SEQ ID NO:172, a vlCDR1 comprising SEQ ID NO:174, a vlCDR2 comprising SEQ ID NO:175, and a vlCDR3 comprising SEQ ID NO:176;

w) a vhCDR1 comprising SEQ ID NO:178, a vhCDR2 comprising SEQ ID NO:179, a vhCDR3 comprising SEQ ID NO:180, a vlCDR1 comprising SEQ ID NO:182, a vlCDR2 comprising SEQ ID NO:183, and a vlCDR3 comprising SEQ ID NO:184;

x) a vhCDR1 comprising SEQ ID NO:186, a vhCDR2 comprising SEQ ID NO:187, a vhCDR3 comprising SEQ ID NO:188, a vlCDR1 comprising SEQ ID NO:190, a vlCDR2 comprising SEQ ID NO:191, and a vlCDR3 comprising SEQ ID NO:192;

y) a vhCDR1 comprising SEQ ID NO:194, a vhCDR2 comprising SEQ ID NO:195, a vhCDR3 comprising SEQ ID NO:196, a vlCDR1 comprising SEQ ID NO:198, a vlCDR2 comprising SEQ ID NO:199, and a vlCDR3 comprising SEQ ID NO:200;

z) a vhCDR1 comprising SEQ ID NO:202, a vhCDR2 comprising SEQ ID NO:203, a vlCDR1 comprising SEQ ID NO:205, a vlCDR2 comprising SEQ ID NO:206, and a vlCDR3 comprising SEQ ID NO:207; or

aa) a vhCDR1 comprising SEQ ID NO:209, a vhCDR2 comprising SEQ ID NO:210, a vhCDR3 comprising SEQ ID NO:211, a vlCDR1 comprising SEQ ID NO:213, a vlCDR2 comprising SEQ ID NO:214, and a vlCDR3 comprising SEQ ID NO:215.

3. An antibody that binds human LILRB1 or LILRB2, the antibody comprising:
- a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:5;
 - b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:9 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:13;
 - c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:17 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:21;
 - d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:25 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:29;
 - e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:33 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:37;
 - f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:41 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:45;
 - g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:49 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:53;
 - h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:57 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:61;
 - i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:65 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:69;
 - j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:73 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:77;
 - k) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:81 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:85;
 - l) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:89 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:93;
 - m) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:97 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:101;
 - n) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:105 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:109;
 - o) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:113 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:117;
 - p) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:121 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:125;

q) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:129 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:133;

r) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:137 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:141;

s) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:145 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:149;

t) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:153 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:157;

u) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:161 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:165;

v) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:169 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:173;

w) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:177 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:181;

x) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:185 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:189;

y) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:193 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:197;

z) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:201 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:204; or

aa) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:208 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:212.

4. The antibody according to any one of the previous claims, wherein the antibody comprises a constant region with an amino acid sequence at least 90% identical to a human IgG.

5. The antibody according to claim 4, wherein the human IgG is selected from a group consisting of IgG1, IgG2, IgG3 and IgG4.

6. The antibody according to claim 5, wherein the IgG is an IgG1.

7. The antibody according to claim 5, wherein the IgG is an IgG2.

8. A nucleic acid composition encoding the antibody according to any of the previous claims.
9. An expression vector composition comprising the nucleic acid composition according to claim 8, wherein the first nucleic acid is contained in a first expression vector and the second nucleic acid is contained in a second expression vector.
10. An expression vector composition comprising the nucleic acid composition according to claim 8, wherein the first nucleic acid and the second nucleic acid are contained in a single expression vector.
11. A host cell comprising the expression vector composition of claim 9 or 10.
12. A method of making an antibody comprising culturing said host cell of claim 11 under conditions wherein the antibody is expressed, and recovering the antibody.
13. A composition comprising the antibody according to any one of claims 1-7, and a pharmaceutical acceptable carrier or diluent.
14. Use of the antibody according to any one of the claims 1-7 or the composition according to claim 13 in the manufacture of a medicament for modulating an immune response in a subject.
15. Use of the antibody according to any one of the claims 1-7 or the composition according to claim 13 in the manufacture of a medicament for treating cancer in a subject.
16. The use of claim 15, wherein the cancer upregulates LILRB1 or LILRB2.
17. The use according to any one of the claims 15-16, wherein the antibody is to be used in combination with one or more additional therapeutic agents.
18. The use of claim 17, wherein the additional therapeutic agents are other immune checkpoint inhibitors.

19. The use of claim 18, wherein the other immune checkpoint inhibitors are selected from the group consisting of Ipilimumab, Nivolumab, Pembrolizumab, Avelumab, Durvalumab, and Atezolizumab.

20. Use of the antibody according to any one of the claims 1-7 or the composition according to claim 13 in the manufacture of a medicament for treating an autoimmune disease in a subject.

21. The use according to claim 20, wherein the antibody is to be used in combination with one or more additional therapeutic agents.

22. Use of the antibody according to any one of the claims 1-7 or the composition according to claim 13 in the manufacture of a medicament for treating allergic inflammation in a subject.

23. The use according to claim 22, wherein the antibody is to be used in combination with one or more additional therapeutics.