CLAIMS

1. An antibody, or a functional fragment thereof, that specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1) but does not compete with binding of E-cadherin, N-cadherin, or R-cadherin to the extracellular domain of KLRG1, for use in therapy,

which comprises a heavy chain variable region comprising three heavy chain complementarity determining regions (CDR-H1, CDR-H2 and CDR-H3), and a light chain variable region comprising three light chain complementary determining regions (CDR-L1, CDR-L2 and CDR-L3), wherein said antibody, or fragment thereof comprises:

i) SEQ ID NO: 16 (CDR-H1), SEQ ID NO: 17 (CDR-H2), SEQ ID NO: 18 (CDR-H3), SEQ ID NO: 19 (CDR-L1), SEQ ID NO:20 (CDR-L2), and SEQ ID NO:21 (CDR-L3);

ii) SEQ ID NO:22 (CDR-H1), SEQ ID NO:23 (CDR-H2), SEQ ID NO:24 (CDR-H3), SEQ ID NO:25 (CDR-L1), SEQ ID NO:26 (CDR-L2), and SEQ ID NO:27 (CDR-L3);

iii) SEQ ID NO:28 (CDR-H1), SEQ ID NO:29 (CDR-H2), SEQ ID NO:30 (CDR-H3), SEQ ID NO:31 (CDR-L1), SEQ ID NO:32 (CDR-L2), and SEQ ID NO:33 (CDR-L3);

iv) SEQ ID NO:34 (CDR-H1), SEQ ID NO:35 (CDR-H2), SEQ ID NO:36 (CDR-H3), SEQ ID NO:37 (CDR-L1), SEQ ID NO:38 (CDR-L2), and SEQ ID NO:39 (CDR-L3);

v) SEQ ID NO:40 (CDR-H1), SEQ ID NO:41 (CDR-H2), SEQ ID NO:42 (CDR-H3), SEQ ID NO:43 (CDR-L1), SEQ ID NO:44 (CDR-L2), and SEQ ID NO:45 (CDR-L3); or

vi) SEQ ID NO:46 (CDR-H1), SEQ ID NO:47 (CDR-H2), SEQ ID NO:48 (CDR-H3), SEQ ID NO:49 (CDR-L1), SEQ ID NO:50 (CDR-L2), and SEQ ID NO:51 (CDR-L3); wherein said functional fragment comprises a peptide binding Fc-effector molecule.

2. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of i); wherein the heavy chain variable region comprises SEQ ID NO 4, or a sequence at least 90% identical to SEQ ID NO:4;

and the light chain variable region comprises SEQ ID NO: 5, or a sequence at least 90% identical to SEQ ID NO:5.

3. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of ii); wherein the heavy chain variable region comprises SEQ ID NO:6, or a sequence at least 90% identical to SEQ ID NO:6; and the light chain variable region comprises SEQ ID NO:7, or a sequence at least 90% identical to SEQ ID NO:7.

4. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of iii); wherein the heavy chain variable region comprises SEQ ID NO:8, or a sequence at least 90% identical to SEQ ID NO:8; and the light chain variable region comprises SEQ ID NO:9, or a sequence at least 90% identical to SEQ ID NO:9.

5. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of iv); wherein the heavy chain variable region comprises SEQ ID NO: 10, or a sequence at least 90% identical to SEQ ID NO:10; and the light chain variable region comprises SEQ ID NO: 11, or a sequence at least 90% identical to SEQ ID NO:11.

6. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of v); wherein the heavy chain variable region comprises SEQ ID NO: 12, or a sequence at least 90% identical to SEQ ID NO:12; and the light chain variable region comprises SEQ ID NO: 13, or a sequence at least 90% identical to SEQ ID NO:13.

7. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of vi); wherein the heavy chain variable region comprises SEQ ID NO: 14, or a sequence at least 90% identical to SEQ ID NO:14; and the light chain variable region comprises SEQ ID NO: 15, or a sequence at least 90% identical to SEQ ID NO:15.

8. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of ii); wherein the heavy chain variable region comprises SEQ ID NO: 52, or a sequence at least 90% identical to SEQ ID NO:52; and the light chain variable region comprises SEQ ID NO: 53, or a sequence at least 90% identical to SEQ ID NO:53.

9. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises

the three heavy chain CDRs and the three light chain CDRs of iii); wherein the heavy chain variable region comprises SEQ ID NO: 54, or a sequence at least 90% identical to SEQ ID NO:54; and the light chain variable region comprises SEQ ID NO: 55, or a sequence at least 90% identical to SEQ ID NO:55.

10. The antibody, or the functional fragment thereof, of claim 1, wherein the antibody, or fragment thereof, comprises a chimeric antibody, or a fragment thereof.

11. The antibody of claim 1, wherein the antibody, or the functional fragment thereof, comprises a humanized antibody or a functional fragment thereof.

12. Use of an antibody, or a functional fragment thereof, that comprises:

i) SEQ ID NO: 16 (CDR-H1), SEQ ID NO: 17 (CDR-H2), SEQ ID NO: 18 (CDR-H3), SEQ ID NO: 19 (CDR-L1), SEQ ID NO:20 (CDR-L2), and SEQ ID NO:21 (CDR-L3);

ii) SEQ ID NO:22 (CDR-H1), SEQ ID NO:23 (CDR-H2), SEQ ID NO:24 (CDR-H3), SEQ ID NO:25 (CDR-L1), SEQ ID NO:26 (CDR-L2), and SEQ ID NO:27 (CDR-L3);

iii) SEQ ID NO:28 (CDR-H1), SEQ ID NO:29 (CDR-H2), SEQ ID NO:30 (CDR-H3), SEQ ID NO:31 (CDR-L1), SEQ ID NO:32 (CDR-L2), and SEQ ID NO:33 (CDR-L3);

iv) SEQ ID NO:34 (CDR-H1), SEQ ID NO:35 (CDR-H2), SEQ ID NO:36 (CDR-H3), SEQ ID NO:37 (CDR-L1), SEQ ID NO:38 (CDR-L2), and SEQ ID NO:39 (CDR-L3);

v) SEQ ID NO:40 (CDR-H1), SEQ ID NO:41 (CDR-H2), SEQ ID NO:42 (CDR-H3), SEQ ID NO:43 (CDR-L1), SEQ ID NO:44 (CDR-L2), and SEQ ID NO:45 (CDR-L3); or

vi) SEQ ID NO:46 (CDR-H1), SEQ ID NO:47 (CDR-H2), SEQ ID NO:48 (CDR-H3), SEQ ID NO:49 (CDR-L1), SEQ ID NO:50 (CDR-L2), and SEQ ID NO:51 (CDR-L3); wherein the functional fragment comprises a peptide binding Fc-effector molecule,

and that specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1) for the manufacture of a medicament for the treatment of a disorder associated with excess KLRG1 expressing T cells in a subject in need thereof, wherein the antibody or functional antibody fragment depletes excess KLRG1 expressing T cells, without releasing checkpoint inhibition, and without subsequently activating pathogenic CD8+ cytotoxic T and/or NK cells directed to self-tissues.

13. The use of claim 12, wherein the medicament is manufactured for treatment of a transplant disorder.

14. The use of claim 12, wherein the medicament is manufactured for treatment of an autoimmune disease.

15. Use of an antibody, or a functional fragment thereof, that comprises:

a) a heavy chain variable region comprising SEQ ID NO:4 or a sequence at least 90% identical to SEQ ID NO:4; and a light chain variable region comprising SEQ ID NO:5 or a sequence at least 90% identical to SEQ ID NO:5, wherein no changes are made to the CDRs;

b) a heavy chain variable region comprising SEQ ID NO:6 or a sequence at least 90% identical to SEQ ID NO:6; and a light chain variable region comprising SEQ ID NO:7 or a sequence at least 90% identical to SEQ ID NO:7, wherein no changes are made to the CDRs;

c) a heavy chain variable region comprising SEQ ID NO:8 or a sequence at least 90% identical to SEQ ID NO:8; and a light chain variable region comprising SEQ ID NO:9 or a sequence at least 90% identical to SEQ ID NO:9, wherein no changes are made to the CDRs;

d) a heavy chain variable region comprising SEQ ID NO:10 or a sequence at least 90% identical to SEQ ID NO:10; and a light chain variable region comprising SEQ ID NO:11 or a sequence at least 90% identical to SEQ ID NO:11, wherein no changes are made to the CDRs;

e) a heavy chain variable region comprising SEQ ID NO:12 or a sequence at least 90% identical to SEQ ID NO:12; and a light chain variable region comprising SEQ ID NO:13 or a sequence at least 90% identical to SEQ ID NO:13, wherein no changes are made to the CDRs;

f) a heavy chain variable region comprising SEQ ID NO:14 or a sequence at least 90% identical to SEQ ID NO:14; and a light chain variable region comprising SEQ ID NO:15 or a sequence at least 90% identical to SEQ ID NO:15, wherein no changes are made to the CDRs;

g) a heavy chain variable region comprising SEQ ID NO:52 or a sequence at least 90% identical to SEQ ID NO:52; and a light chain variable region comprising SEQ ID NO:53 or a sequence at least 90% identical to SEQ ID NO:53, wherein no changes are made to the CDRs; or

h) a heavy chain variable region comprising SEQ ID NO:54 or a sequence at least 90% identical to SEQ ID NO:54; and a light chain variable region comprising SEQ ID NO:55 or a sequence at least 90% identical to SEQ ID NO:55, wherein no changes are made to the CDRs;

wherein the functional fragment comprises a peptide binding Fc-effector molecule; and wherein said antibody or functional fragment thereof

specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1) for the manufacture of a medicament for the treatment of cancer in a subject, wherein the cancer comprises cancer cells that express KLRG1 in the subject in need thereof, and wherein the medicament depletes the cancer cells expressing KLRG1 without releasing checkpoint inhibition

and without subsequently activating pathogenic CD8+ cytotoxic T and/or NK cells directed to self-tissues.

16. Use of an antibody, or a functional fragment thereof, that comprises

a) a heavy chain variable region comprising SEQ ID NO:4 or a sequence at least 90% identical to SEQ ID NO:4; and a light chain variable region comprising SEQ ID NO:5 or a sequence at least 90% identical to SEQ ID NO:5, wherein no changes are made to the CDRs;

b) a heavy chain variable region comprising SEQ ID NO:6 or a sequence at least 90% identical to SEQ ID NO:6; and a light chain variable region comprising SEQ ID NO:7 or a sequence at least 90% identical to SEQ ID NO:7, wherein no changes are made to the CDRs;

c) a heavy chain variable region comprising SEQ ID NO:8 or a sequence at least 90% identical to SEQ ID NO:8; and a light chain variable region comprising SEQ ID NO:9 or a sequence at least 90% identical to SEQ ID NO:9, wherein no changes are made to the CDRs;

d) a heavy chain variable region comprising SEQ ID NO:10 or a sequence at least 90% identical to SEQ ID NO:10; and a light chain variable region comprising SEQ ID NO:11 or a sequence at least 90% identical to SEQ ID NO:11, wherein no changes are made to the CDRs;

e) a heavy chain variable region comprising SEQ ID NO:12 or a sequence at least 90% identical to SEQ ID NO:12; and a light chain variable region comprising SEQ ID NO:13 or a sequence at least 90% identical to SEQ ID NO:13, wherein no changes are made to the CDRs;

f) a heavy chain variable region comprising SEQ ID NO:14 or a sequence at least 90% identical to SEQ ID NO:14; and a light chain variable region comprising SEQ ID NO:15 or a sequence at least 90% identical to SEQ ID NO:15, wherein no changes are made to the CDRs;

g) a heavy chain variable region comprising SEQ ID NO:52 or a sequence at least 90% identical to SEQ ID NO:52; and a light chain variable region comprising SEQ ID NO:53 or a sequence at least 90% identical to SEQ ID NO:53, wherein no changes are made to the CDRs; or

h) a heavy chain variable region comprising SEQ ID NO:54 or a sequence at least 90% identical to SEQ ID NO:54; and a light chain variable region comprising SEQ ID NO:55 or a sequence at least 90% identical to SEQ ID NO:55, wherein no changes are made to the CDRs;

wherein the functional fragment comprises a peptide binding Fc-effector molecule; and wherein said antibody or fragment thereof

specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1), for the manufacture of a medicament for use in the treatment of cancer in a subject undergoing checkpoint therapy, wherein the cancer comprises cancer cells that express KLRG1 in the subject in need thereof and the medicament depletes the cancer cells expressing KLRG1.

17. Use of an antibody, or a functional fragment thereof, that comprises

a) a heavy chain variable region comprising SEQ ID NO:4 or a sequence at least 90% identical to SEQ ID NO:4; and a light chain variable region comprises SEQ ID NO:5 or a sequence at least 90% identical to SEQ ID NO:5, wherein no changes are made to the CDRs;

b) a heavy chain variable region comprising SEQ ID NO:6 or a sequence at least 90% identical to SEQ ID NO:6; and a light chain variable region comprising SEQ ID NO:7 or a sequence at least 90% identical to SEQ ID NO:7, wherein no changes are made to the CDRs;

c) a heavy chain variable region comprising SEQ ID NO:8 or a sequence at least 90% identical to SEQ ID NO:8; and a light chain variable region comprising SEQ ID NO:9 or a sequence at least 90% identical to SEQ ID NO:9, wherein no changes are made to the CDRs;

d) a heavy chain variable region comprising SEQ ID NO:10 or a sequence at least 90% identical to SEQ ID NO:10; and a light chain variable region comprising SEQ ID NO:11 or a sequence at least 90% identical to SEQ ID NO:11, wherein no changes are made to the CDRs;

e) a heavy chain variable region comprising SEQ ID NO:12 or a sequence at least 90% identical to SEQ ID NO:12; and a light chain variable region comprising SEQ ID NO:13 or a sequence at least 90% identical to SEQ ID NO:13, wherein no changes are made to the CDRs;

f) a heavy chain variable region comprising SEQ ID NO:14 or a sequence at least 90% identical to SEQ ID NO:14; and a light chain variable region comprising SEQ ID NO:15 or a sequence at least 90% identical to SEQ ID NO:15, wherein no changes are made to the CDRs;

g) a heavy chain variable region comprising SEQ ID NO:52 or a sequence at least 90% identical to SEQ ID NO:52; and a light chain variable region comprising SEQ ID NO:53 or a sequence at least 90% identical to SEQ ID NO:53, wherein no changes are made to the CDRs; or

h) a heavy chain variable region comprising SEQ ID NO:54 or a sequence at least 90% identical to SEQ ID NO:54; and a light chain variable region comprising SEQ ID NO:55 or a sequence at least 90% identical to SEQ ID NO:55, wherein no changes are made to the CDRs;

wherein the functional fragment comprises a peptide binding Fc-effector molecule,

for use in the manufacture of a medicament for the treatment of a cancer associated with excess killer cell lectin-like receptor G1 (KLRG1) expressing T cell and/or excess KLRG1 expressing NK cells and/or KLRG1 expressing cancer cells in a mixed population of cells, in a subject in need thereof, wherein the antibody or functional fragment thereof specifically binds to KLRG1 and depletes KLRG1 expressing T cells and/or KLRG1 expressing NK cells and/or KLRG1 expressing cancer cells.

18. An antibody, or a functional fragment thereof, that specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1), and which comprises a heavy chain variable region comprising three heavy chain complementarity determining regions (CDR-H1, CDR-H2 and CDR-H3), and a light chain variable region comprising three light chain complementary determining regions (CDR-L1, CDR-L2 and CDR-L3), wherein said antibody, or fragment thereof comprises:

i) SEQ ID NO: 16 (CDR-H1), SEQ ID NO: 17 (CDR-H2), SEQ ID NO: 18 (CDR-H3), SEQ ID NO: 19 (CDR-L1), SEQ ID NO:20 (CDR-L2), and SEQ ID NO:21 (CDR-L3);

ii) SEQ ID NO:22 (CDR-H1), SEQ ID NO:23 (CDR-H2), SEQ ID NO:24 (CDR-H3), SEQ ID NO:25 (CDR-L1), SEQ ID NO:26 (CDR-L2), and SEQ ID NO:27 (CDR-L3);

iii) SEQ ID NO:28 (CDR-H1), SEQ ID NO:29 (CDR-H2), SEQ ID NO:30 (CDR-H3), SEQ ID NO:31 (CDR-L1), SEQ ID NO:32 (CDR-L2), and SEQ ID NO:33 (CDR-L3);

iv) SEQ ID NO:34 (CDR-H1), SEQ ID NO:35 (CDR-H2), SEQ ID NO:36 (CDR-H3), SEQ ID NO:37 (CDR-L1), SEQ ID NO:38 (CDR-L2), and SEQ ID NO:39 (CDR-L3);

v) SEQ ID NO:40 (CDR-H1), SEQ ID NO:41 (CDR-H2), SEQ ID NO:42 (CDR-H3), SEQ ID NO:43 (CDR-L1), SEQ ID NO:44 (CDR-L2), and SEQ ID NO:45 (CDR-L3); or

vi) SEQ ID NO:46 (CDR-H1), SEQ ID NO:47 (CDR-H2), SEQ ID NO:48 (CDR-H3), SEQ ID NO:49 (CDR-L1), SEQ ID NO:50 (CDR-L2), and SEQ ID NO:51 (CDR-L3).

19. An antibody, or a functional fragment thereof, that specifically binds to an extracellular domain of killer cell lectin-like receptor G1 (KLRG1) and which comprises:

a) a heavy chain variable region comprising SEQ ID NO:4 or a sequence at least 90% identical to SEQ ID NO:4; and a light chain variable region comprising SEQ ID NO:5 or a sequence at least 90% identical to SEQ ID NO:5, wherein no changes are made to the CDRs;

b) a heavy chain variable region comprising SEQ ID NO:6 or a sequence at least 90% identical to SEQ ID NO:6; and a light chain variable region comprising SEQ ID NO:7 or a sequence at least 90% identical to SEQ ID NO:7, wherein no changes are made to the CDRs;

c) a heavy chain variable region comprising SEQ ID NO:8 or a sequence at least 90% identical to SEQ ID NO:8; and a light chain variable region comprising SEQ ID NO:9 or a sequence at least 90% identical to SEQ ID NO:9, wherein no changes are made to the CDRs;

d) a heavy chain variable region comprising SEQ ID NO:10 or a sequence at least 90% identical to SEQ ID NO:10; and a light chain variable region comprising SEQ ID NO:11 or a sequence at least 90% identical to SEQ ID NO:11, wherein no changes are made to the CDRs;

e) a heavy chain variable region comprising SEQ ID NO:12 or a sequence at least 90% identical to SEQ ID NO:12; and a light chain variable region comprising SEQ ID NO:13 or a sequence at least 90% identical to SEQ ID NO:13, wherein no changes are made to the CDRs;

f) a heavy chain variable region comprising SEQ ID NO:14 or a sequence at least 90% identical to SEQ ID NO:14; and a light chain variable region comprising SEQ ID NO:15 or a sequence at least 90% identical to SEQ ID NO:15, wherein no changes are made to the CDRs;

g) a heavy chain variable region comprising SEQ ID NO:52 or a sequence at least 90% identical to SEQ ID NO:52; and a light chain variable region comprising SEQ ID NO:53 or a sequence at least 90% identical to SEQ ID NO:53, wherein no changes are made to the CDRs; or

h) a heavy chain variable region comprising SEQ ID NO:54 or a sequence at least 90% identical to SEQ ID NO:54; and a light chain variable region comprising SEQ ID NO:55 or a sequence at least 90% identical to SEQ ID NO:55, wherein no changes are made to the CDRs.

20. The antibody, or the functional fragment thereof, of claim 18, wherein the antibody, or fragment thereof, comprises a monoclonal antibody, or a fragment or derivative thereof.

21. The antibody, or the functional fragment thereof, of claim 18, wherein the antibody, or fragment thereof, comprises a chimeric antibody, or a fragment thereof.

22. The antibody, or the functional fragment thereof, of claim 18, wherein the antibody, or fragment thereof, comprises a humanized antibody, or a fragment thereof.

23. A pharmaceutical composition, comprising the antibody, or the functional fragment thereof, of claim 18 and a pharmaceutically acceptable carrier.

24. A kit, comprising the antibody, or the functional fragment thereof, of claim 18 and instructions for use.

25. Use of an antibody, or a functional fragment thereof, that comprises:

i) SEQ ID NO: 16 (CDR-H1), SEQ ID NO: 17 (CDR-H2), SEQ ID NO: 18 (CDR-H3), SEQ ID NO: 19 (CDR-L1), SEQ ID NO:20 (CDR-L2), and SEQ ID NO:21 (CDR-L3);

ii) SEQ ID NO:22 (CDR-H1), SEQ ID NO:23 (CDR-H2), SEQ ID NO:24 (CDR-H3), SEQ ID NO:25 (CDR-L1), SEQ ID NO:26 (CDR-L2), and SEQ ID NO:27 (CDR-L3);

iii) SEQ ID NO:28 (CDR-H1), SEQ ID NO:29 (CDR-H2), SEQ ID NO:30 (CDR-H3), SEQ ID NO:31 (CDR-L1), SEQ ID NO:32 (CDR-L2), and SEQ ID NO:33 (CDR-L3);

iv) SEQ ID NO:34 (CDR-H1), SEQ ID NO:35 (CDR-H2), SEQ ID NO:36 (CDR-H3), SEQ ID NO:37 (CDR-L1), SEQ ID NO:38 (CDR-L2), and SEQ ID NO:39 (CDR-L3);

v) SEQ ID NO:40 (CDR-H1), SEQ ID NO:41 (CDR-H2), SEQ ID NO:42 (CDR-H3), SEQ ID NO:43 (CDR-L1), SEQ ID NO:44 (CDR-L2), and SEQ ID NO:45 (CDR-L3); or

vi) SEQ ID NO:46 (CDR-H1), SEQ ID NO:47 (CDR-H2), SEQ ID NO:48 (CDR-H3), SEQ ID NO:49 (CDR-L1), SEQ ID NO:50 (CDR-L2), and SEQ ID NO:51 (CDR-L3);

wherein the functional fragment comprises a peptide binding Fc-effector molecule,

in the manufacture of a medicament for use in the treatment of a disorder associated with excess killer cell lectin-like receptor G1 (KLRG1) expressing CD8 effector T cells in a subject in need thereof, wherein the antibody, or fragment thereof, specifically binds to the extracellular domain of KLRG1 but does not compete with binding of at least one of E-cadherin, N-cadherin, or R-cadherin to the extracellular domain of KLRG1, thereby selectively depleting the KLRG1 expressing CD8 effector T cells.