[0005] Human LILRB3 (also called CD85A, ILT5, LIR3 or HL9) contains 4 extracellular immunoglobulin domains, a transmembrane domain and 4 cytoplasmic immunoreceptor tyrosine-based inhibition motifs (ITIMs). Expression of LILRB3 has been reported on monocytes, monocyte-derived osteoclasts, granulocytes, dendritic cells, osteoclasts and progenitor mast cells. The ligand for LILRB3 has not been identified, and little is known about the function of LILRB3. Collectively, these findings suggest that the development of agents useful in modulating signaling from LILRB3 would be of great benefit in diseases involving dysregulation of the immune system, including inflammatory diseases, autoimmune diseases and cancer.

SUMMARY

[0006] In one example, the present disclosure relates to novel anti-LILRB3 antibodies. In one aspect, the present disclosure refers to an antibody that binds human LILRB3, 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:2; b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:3 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:4; c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:5 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:6; d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:8; e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:9 a light chain variable region comprising an amino acid sequence of SEQ ID NO:10; f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:11 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:12; g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:13 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:14; h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:15 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:16; i) 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:18; j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:19 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:20; k) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:21 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:22; l) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:23 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:24; or m) 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:26. In some examples, the anti-LILRB3 antibodies include 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:2. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:3 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:4. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:5 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:6. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:8. In some examples, the anti-LILRB3 antibodies include 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:10. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:11 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:12. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of

SEQ ID NO:13 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:14. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:15 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:16. In some examples, the anti-LILRB3 antibodies include 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:18. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:19 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:20. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:21 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:22. In some examples, the anti-LILRB3 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:23 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:24. In some examples, the anti-LILRB3 antibodies include 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:26.

[0007] In another aspect, the present disclosure refers to an antibody that binds human LILRB3, the antibody comprising: a) a vhCDR1 comprising SEQ ID NO:27, a vhCDR2 comprising SEQ ID NO:28, a vhCDR3 comprising SEQ ID NO:29, a vlCDR1 comprising SEQ ID NO:30, a vlCDR2 comprising SEQ ID NO:31, and a vlCDR3 comprising SEQ ID NO:32; b) a vhCDR1 comprising SEQ ID NO:33, a vhCDR2 comprising SEQ ID NO:34, a vhCDR3 comprising SEQ ID NO:35, a vlCDR1 comprising SEQ ID NO:36, a vlCDR2 comprising SEQ ID NO:37, and a vlCDR3 comprising SEQ ID NO:38; c) a vhCDR1 comprising SEQ ID NO:39, a vhCDR2 comprising SEQ ID NO:40, a vhCDR3 comprising SEQ ID NO:41, a vlCDR1 comprising SEQ ID NO:42, a vlCDR2 comprising SEQ ID NO:43, and a vlCDR3 comprising SEQ ID NO:44; d) a vhCDR1 comprising SEQ ID NO:45, a vhCDR2 comprising SEQ ID NO:46, a vhCDR3 comprising SEQ ID NO:47, a vlCDR1 comprising SEQ ID NO:48, a vlCDR2 comprising SEQ ID NO:49, and a vlCDR3 comprising SEQ ID NO:50; e) a vhCDR1 comprising SEQ ID NO:51, a vhCDR2 comprising SEQ ID NO:52, a vhCDR3 comprising SEQ ID NO:53, a vlCDR1 comprising SEQ ID NO:54, a vlCDR2 comprising SEQ ID NO:55, and a vlCDR3 comprising SEQ ID NO:56; f) a vhCDR1 comprising SEQ ID NO:57, a vhCDR2 comprising SEQ ID NO:58, a vhCDR3 comprising SEQ ID NO:59, a vlCDR1 comprising SEQ ID NO:60, a vlCDR2 comprising SEQ ID NO:61, and a vlCDR3 comprising SEQ ID NO:62; g) a vhCDR1 comprising SEQ ID NO:63, a vhCDR2 comprising SEQ ID NO:64, a vhCDR3 comprising SEQ ID NO:65, a vlCDR1 comprising SEQ ID NO:66, a vlCDR2 comprising SEQ ID NO:67, and a vlCDR3 comprising SEQ ID NO:68; h) a vhCDR1 comprising SEQ ID NO:69, a vhCDR2 comprising SEQ ID NO:70, a vhCDR3 comprising SEQ ID NO:71, a vlCDR1 comprising SEQ ID NO:72, a vlCDR2 comprising SEQ ID NO:73, and a vlCDR3 comprising SEQ ID NO:74; i) a vhCDR1 comprising SEQ ID NO:75, a vhCDR2 comprising SEQ ID NO:76, a vhCDR3 comprising SEQ ID NO:77, a vlCDR1 comprising SEQ ID NO:78, a vlCDR2 comprising SEQ ID NO:79, and a vlCDR3 comprising SEQ ID NO:80; j) a vhCDR1 comprising SEQ ID NO:81, a vhCDR2 comprising SEQ ID NO:82, a vhCDR3 comprising SEQ ID NO:83, a vlCDR1 comprising SEQ ID NO:84, a vlCDR2 comprising SEQ ID NO:85, and a vlCDR3 comprising SEQ ID NO:86; k) a vhCDR1 comprising SEQ ID NO:87, a vhCDR2 comprising SEQ ID NO:88, a vhCDR3 comprising SEQ ID NO:89, a vlCDR1 comprising SEQ ID NO:~~80~~90, a vlCDR2 comprising SEQ ID NO:~~81~~91, and a vlCDR3 comprising SEQ ID NO:~~82~~92; l) a vhCDR1 comprising SEQ ID NO:93, a vhCDR2 comprising SEQ ID NO:94, a vhCDR3 comprising SEQ ID NO:95, a vlCDR1 comprising SEQ ID NO:96, a vlCDR2 comprising SEQ ID NO:97, and a vlCDR3 comprising SEQ ID NO:98; ~~and~~ or m) a vhCDR1 comprising SEQ ID NO:99, a vhCDR2 comprising SEQ ID NO:100, a vhCDR3 comprising SEQ ID NO:101, a vlCDR1 comprising SEQ ID NO:102, a

[0010] Another aspect of the present disclosure refers to an expression vector composition comprising the nucleic acid composition as disclosed herein, wherein ~~the~~ a first nucleic acid is contained in a first expression vector and ~~the~~ a second nucleic acid is contained in a second expression vector. In another aspect, the present disclosure refers to an expression vector composition comprising the nucleic acid composition as disclosed herein, wherein ~~the~~ a first nucleic acid and ~~the~~ a second nucleic acid are contained in a single expression vector. In one example, the present disclosure relates to an expression vector composition that includes any one of the nucleic acid compositions described herein. In some examples, the first nucleic acid is contained in a first expression vector and the second nucleic acid is contained in a second expression vector. In some other examples, the first nucleic acid and the second nucleic acid are contained in a single expression vector.

[0011] Another aspect of the present disclosure relates to a host cell that includes any one of the expression vectors described herein. Another aspect of the present disclosure refes to a method of making an antibody comprising culturing said host cell as disclosed herein under conditions wherein the antibody is expressed, and recovering the antibody. Also presented is a method of making anti-LILRB3 antibodies, and the method includes culturing the host cell under conditions wherein the antibodies expressed, and recovering the antibodies.

[0012] In another aspect, the present disclosure refers to a composition comprising the antibody as disclosed herein, and a pharmaceutical acceptable carrier or diluent. For example, the present disclosure relates to a composition that includes any one of the anti-LILRB3 antibodies described herein, and a pharmaceutical acceptable carrier or diluent.

[0013] Also described is a method of modulating an immune response in a subject, and the method includes administering to the subject an effective amount of any one of the anti-LILRB3 antibodies described herein, or any one of the compositions described herein. In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for ~~modulating~~ treating an ~~immune response in~~inflammatory disease in a subject. In some examples, the method includes administering to the subject an effective amount of an anti-LILRB3 antibody that serves as a LILRB3 antagonist, or a pharmaceutical composition thereof. In some examples, the method includes administering to the subject an effective amount of an anti-LILRB3 antibody that serves as a LILRB3 agonist, or a pharmaceutical composition thereof.

[0014] In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating cancer in a subject. In another example, the present disclosure relates to a method of treating cancer in a subject, and the method includes administering to the subject an effective amount of an anti-LILRB3 antibody described herein or any one of the compositions described herein. In some examples, the cancer to be treated upregulates LILRB3 compared to the corresponding non-cancerous tissue. In some examples, the subject to be treated expresses a high level of LILRB3 on hematopoeitic cells. The cancer to be treated can be any cancer. In some examples, an anti-LILRB3 antibody is used in combination with one or more additional therapeutic agents to treat cancer. In some examples, such anti-cancer therapeutic agents are other immune checkpoint inhibitors, such as Ipilimumab, Nivolumab, Pembrolizumab, Avelumab, Durvalumab, and Atezolizumab.

[0015] In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating an autoimmune disease in a subject. In another example, the present disclosure relates to a method

of treating an autoimmune disease in a subject, and the method includes administering to the subject an effective amount of any one of the anti-LILRB3 antibodies described herein, or any one of the compositions described herein.

[0016] In another aspect, the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating allergic inflammation in a subject. In another example, the present disclosure relates to a method of treating an autoimmune disease in a subject, and the method includes administering to the subject an effective amount of an anti-LILRB3 antibody described herein, or any one of the compositions described herein.

[0017] In a further example, the present disclosure relates to a method of treating allergic inflammation in a subject, and the method includes administering to the subject an effective amount of any one of the anti-LILRB3 antibodies described herein, or any one of the compositions described herein.

[0018] In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for modulating differentiation of osteoclasts to treat bone loss or bone resorption in a subject suffering or susceptible of suffering from a condition selected from the group consisting of osteoporosis, osteodystrophy, osteopenia, osteomalacia, hyperparathyroidism, hyperthyroidism, hypogonadism, thyrotoxicosis, systemic mastocytosis, adult hypophosphatasia, hyperadrenocorticism, osteogenesis imperfecta, Paget's disease, Cushing's disease/syndrome, Tumer syndrome, Gaucher disease, Ehlers-Danlos syndrome, Marfan's syndrome, Menkes' syndrome, Fanconi's syndrome, multiple myeloma, hypercalcemia, hypocalcemia, arthritides, periodontal disease, rickets (including vitamin D dependent, type I and II, and x-linked hypophosphatemic rickets) or other form of vitamin D deficiency such as vitamin D deficiency associated with chronic kidney disease or kidney failure, fibrogenesis imperfecta ossium, osteosclerotic disorders such as pycnodysostosis and damage caused by macrophage-mediated inflammatory processes~~in a subject~~. In a further example, the present disclosure relates to a method of modulating osteoclast differentiation, and the method includes administering to the subject an effective amount of any one of the anti-LILRB3 antibodies described herein, or any one of the compositions described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The invention may be best understood from the following detailed description when read in conjunction with the accompanying drawings. Included in the drawings are the following figures:

[0020] **FIGURE 1A and FIGURE 1B** show LILBR3 surface expression on various hematopoietic subsets using flow cytometry.

[0021] **FIGURE 2** shows the effect of LILRB3 antibodies or LILRB3-Fc protein on responsiveness of T cells in primary mixed lymphocyte reactions (MLR).

[0022] **FIGURE 3** shows the ability of PBMCs to regulate surface expression of activation markers in response to T cell stimulation after incubation with the LILRB3 7C5 antibody.

[0023] **FIGURE 4** shows the effect of the LILRB3 7C5 antibody on cytokine production by PBMCs in response to T cell stimulation.

[0024] **FIGURE 5** shows cytokine release of unstimulated blood when incubated with the LILRB3 7C5 antibody.

Claims

What Is Claimed Is:

1. An antibody that binds human LILRB3, 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:2;

b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:3 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:4;

c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:5 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:6;

d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:8;

e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:9 a light chain variable region comprising an amino acid sequence of SEQ ID NO:10;

f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:11 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:12;

g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:13 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:14;

h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:15 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:16;

i) 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:18;

j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:19 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:20;

k) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:21 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:22;

l) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:23 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:24; ~~and~~or

m) 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:26.

2. An antibody that binds human LILRB3, the antibody comprising:

a) a vhCDR1 comprising SEQ ID NO:27, a vhCDR2 comprising SEQ ID NO:28, a vhCDR3 comprising SEQ ID NO:29, a vlCDR1 comprising SEQ ID NO:30, a vlCDR2 comprising SEQ ID NO:31, and a vlCDR3 comprising SEQ ID NO:32;

b) a vhCDR1 comprising SEQ ID NO:33, a vhCDR2 comprising SEQ ID NO:34, a vhCDR3 comprising SEQ ID NO:35, a vlCDR1 comprising SEQ ID NO:36, a vlCDR2 comprising SEQ ID NO:37, and a vlCDR3 comprising SEQ ID NO:38;

c) a vhCDR1 comprising SEQ ID NO:39, a vhCDR2 comprising SEQ ID NO:40, a vhCDR3 comprising SEQ ID NO:41, a vlCDR1 comprising SEQ ID NO:42, a vlCDR2 comprising SEQ ID NO:43, and a vlCDR3 comprising SEQ ID NO:44;

d) a vhCDR1 comprising SEQ ID NO:45, a vhCDR2 comprising SEQ ID NO:46, a vhCDR3 comprising SEQ ID NO:47, a vlCDR1 comprising SEQ ID NO:48, a vlCDR2 comprising SEQ ID NO:49, and a vlCDR3 comprising SEQ ID NO:50;

e) a vhCDR1 comprising SEQ ID NO:51, a vhCDR2 comprising SEQ ID NO:52, a vhCDR3 comprising SEQ ID NO:53, a vlCDR1 comprising SEQ ID NO:54, a vlCDR2 comprising SEQ ID NO:55, and a vlCDR3 comprising SEQ ID NO:56;

f) a vhCDR1 comprising SEQ ID NO:57, a vhCDR2 comprising SEQ ID NO:58, a vhCDR3 comprising SEQ ID NO:59, a vlCDR1 comprising SEQ ID NO:60, a vlCDR2 comprising SEQ ID NO:61, and a vlCDR3 comprising SEQ ID NO:62;

g) a vhCDR1 comprising SEQ ID NO:63, a vhCDR2 comprising SEQ ID NO:64, a vhCDR3 comprising SEQ ID NO:65, a vlCDR1 comprising SEQ ID NO:66, a vlCDR2 comprising SEQ ID NO:67, and a vlCDR3 comprising SEQ ID NO:68;

h) a vhCDR1 comprising SEQ ID NO:69, a vhCDR2 comprising SEQ ID NO:70, a vhCDR3 comprising SEQ ID NO:71, a vlCDR1 comprising SEQ ID NO:72, a vlCDR2 comprising SEQ ID NO:73, and a vlCDR3 comprising SEQ ID NO:74;

i) a vhCDR1 comprising SEQ ID NO:75, a vhCDR2 comprising SEQ ID NO:76, a vhCDR3 comprising SEQ ID NO:77, a vlCDR1 comprising SEQ ID NO:78, a vlCDR2 comprising SEQ ID NO:79, and a vlCDR3 comprising SEQ ID NO:80;

j) a vhCDR1 comprising SEQ ID NO:81, a vhCDR2 comprising SEQ ID NO:82, a vhCDR3 comprising SEQ ID NO:83, a vlCDR1 comprising SEQ ID NO:84, a vlCDR2 comprising SEQ ID NO:85, and a vlCDR3 comprising SEQ ID NO:86;

k) a vhCDR1 comprising SEQ ID NO:87, a vhCDR2 comprising SEQ ID NO:88, a vhCDR3 comprising SEQ ID NO:89, a vlCDR1 comprising SEQ ID NO:~~80~~90, a vlCDR2 comprising SEQ ID NO:~~81~~91, and a vlCDR3 comprising SEQ ID NO:~~82~~92;

l) a vhCDR1 comprising SEQ ID NO:93, a vhCDR2 comprising SEQ ID NO:94, a vhCDR3 comprising SEQ ID NO:95, a vlCDR1 comprising SEQ ID NO:96, a vlCDR2 comprising SEQ ID NO:97, and a vlCDR3 comprising SEQ ID NO:98; ~~and~~ or

m) a vhCDR1 comprising SEQ ID NO:99, a vhCDR2 comprising SEQ ID NO:100, a vhCDR3 comprising SEQ ID NO:101, a vlCDR1 comprising SEQ ID NO:102, a vlCDR2 comprising SEQ ID NO:103, and a vlCDR3 comprising SEQ ID NO:104.

~~3. The antibody according to any of the previous claims, wherein the antibody binds human LILRB3.~~

~~4~~3. The antibody according to ~~any one of the previous~~ claim~~s~~ 1 or 2, wherein the antibody comprises a constant region with an amino acid sequence at least 90% identical to a human IgG.

~~5~~4. The antibody according to claim ~~4~~3, wherein the human IgG is selected from a group consisting of IgG1, IgG2, IgG3 and IgG4.

~~6~~5. The antibody according to claim ~~5~~4, wherein the IgG is an IgG1.

~~7~~6. The antibody according to claim ~~5~~4, wherein the IgG is an IgG2.

~~8~~7. A nucleic acid composition encoding the antibody according to any one of the previous claims.

~~9~~8. An expression vector composition comprising the nucleic acid composition according to claim ~~8~~7, wherein ~~the~~ a first nucleic acid is contained in a first expression vector and ~~the~~ a second nucleic acid is contained in a second expression vector.

~~10~~9. An expression vector composition comprising the nucleic acid composition according to claim ~~8~~7, wherein ~~the~~ a first nucleic acid and ~~the~~ a second nucleic acid are contained in a single expression vector.

1~~1~~0. A host cell comprising the expression vector composition of claim ~~9~~8 or ~~10~~9.

~~12~~11. A method of making an antibody comprising culturing said host cell of claim 1~~1~~0 under conditions wherein the antibody is expressed, and recovering the antibody.

~~13~~12. A composition comprising the antibody according to any one of claims 1-~~7~~6, and a pharmaceutical acceptable carrier or diluent.

13~~4~~. Use of the antibody according to any one of the claims 1-~~7~~ 6 or the composition according to claim ~~13~~ 12 in the manufacture of a medicament for ~~modulating an immune response~~treating an inflammatory disease in a subject.

~~15~~14. Use of the antibody according to any one of the claims 1-~~7~~ 6 or the composition according to claim ~~13~~ 12 in the manufacture of a medicament for treating cancer in a subject.

~~16~~15. The use of claim ~~15~~14, wherein the cancer upregulates LILRB3 compared to the corresponding non-cancerous tissue.

~~17. The use of claim 15 or 16, wherein the subject has a high level of LILRB3 on hematopoietic cancer cells.~~

~~18~~16. The use according to ~~any one of the~~ claim~~s~~ ~~15~~14 ~~-17~~or 15, wherein the cancer is leukemia.

~~19~~17. The use according to ~~any one of the~~ claim~~s~~ ~~15~~14~~-17~~ or 15, wherein the cancer is myeloma.

~~20~~18. The use according to any one of the claims ~~15~~14-~~19~~17, wherein the antibody or the composition is to be combined with one or more additional therapeutic agents to treat cancer.

19~~21~~. The use of claim ~~20~~18, wherein the additional therapeutic agents are other immune checkpoint inhibitors.

20~~2~~. The use of claim ~~21~~19, wherein the other immune checkpoint inhibitors are selected from the group consisting of Ipilimumab, Nivolumab, Pembrolizumab, Avelumab, Durvalumab, and Atezolizumab.

21~~3~~. Use of the antibody according to any one of the claims 1-~~7~~ 6 or the composition according to claim ~~13~~ 12 in the manufacture of a medicament for treating an autoimmune disease in a subject.

~~24~~22. The use according to claim ~~23~~21, wherein the antibody or the composition is to be combined with one or more additional therapeutic agents to treat autoimmune disease.

~~25~~23. Use of the antibody according to any one of the claims 1-~~7~~ 6 or the composition according to claim ~~13~~ 12 in the manufacture of a medicament for treating allergic inflammation in a subject.

~~26~~24. The use according to claim ~~25~~23, wherein the antibody or the composition is to be combined with one or more additional therapeutics to treat allergic inflammation.

~~27~~25. Use of the antibody according to any one of the claims 1-~~7~~ 6 or the composition according to claim ~~13~~ 12 in the manufacture of a medicament for modulating differentiation of osteoclasts ~~in a subject~~to treat bone loss or bone resorption in a subject suffering or susceptible of suffering from a condition selected from the group consisting of osteoporosis, osteodystrophy, osteopenia, osteomalacia, hyperparathyroidism, hyperthyroidism, hypogonadism, thyrotoxicosis, systemic mastocytosis, adult hypophosphatasia, hyperadrenocorticism, osteogenesis imperfecta, Paget's disease, Cushing's disease/syndrome, Tumer syndrome, Gaucher disease, Ehlers-Danlos syndrome, Marfan's syndrome, Menkes' syndrome, Fanconi's syndrome, multiple myeloma, hypercalcemia, hypocalcemia, arthritides, periodontal disease, rickets (including vitamin D

dependent, type I and II, and x-linked hypophosphatemic rickets) or other form of vitamin D deficiency such as vitamin D deficiency associated with chronic kidney disease or kidney failure, fibrogenesis imperfecta ossium, osteosclerotic disorders such as pycnodysostosis and damage caused by macrophage-mediated inflammatory processes.

~~28~~26. The use according to claim ~~27~~25, wherein the antibody or the composition is to be combined with one or more additional therapeutics to modulate differentiation of osteoclasts.