SUMMARY

[0008] In one aspect, the present disclosure refers to a an antibody that binds human and/or mouse TSG-6, wherein the antibody comprises 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 one example, the present disclosure relates to novel anti-TSG-6 antibodies. In some examples, the anti-TSG-6 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-TSG-6 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-TSG-6 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-TSG-6 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-TSG-6 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-TSG-6 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:11 and a lightchain variable region comprising an amino acid sequence of SEQ ID NO:12. In some examples, the anti-TSG-6 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 aminoacid sequence of SEQ ID NO:14. In some examples, the anti-TSG-6 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:15 and a lightchain variable region comprising an amino acid sequence of SEQ ID NO:16. In some examples, the anti-TSG-6 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 aminoacid sequence of SEQ ID NO:18. In some examples, the anti-TSG-6 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:19 and a lightchain variable region comprising an amino acid sequence of SEQ **ID** NO:20. In some examples, the anti-TSG-6 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 aminoacid sequence of SEQ **ID** NO:22. In some examples, the anti-TSG-6 antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ **ID** NO:23 and a lightchain variable region comprising an amino acid sequence of SEQ **ID** NO:24. In some examples, the anti-TSG-6 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 aminoacid sequence of SEQ **ID** NO:26.

[0009] In another aspect, the present disclosure refers to a an antibody that binds human and/or mouse TSG-6, the antibody comprising: a vhCDRl comprising SEQ ID NO:75, a vhCDR2 comprising SEQ ID NO:76, a vhCDR3 comprising SEQ ID NO:77, a vlCDRl comprising SEQ ID NO:78, a vlCDR2 comprising SEQ ID NO:79, and a vlCDR3 comprising SEQ ID NO:80. In some examples, the anti-TSG-6 antibodies include a vhCDRl comprising SEQ ID NO:27, a vhCDR2 comprising SEQ ID NO:28, a vhCDR3 comprising SEQ ID NO:29, a vlCDRl comprising SEQ ID

one of the anti-TSG-6 antibodies described herein. In some examples, the nucleic acid composition includes a first nucleic acid comprising the heavy chain, and a second nucleic acidcomprising the light chain.

[0013] In another aspect, the present disclosure refers to an expression vector composition comprising the nucleic acid composition as disclosed herein, wherein: (i) the first nucleic acid is contained in a first expression vector and the second nucleic acid is contained in a second expression vector; or (ii) the first nucleic acid and the second nucleic acid are contained in a single expression vector. Another example of the present disclosure relates to an expression vector compositionthat includes any one of the nucleic acid compositions encoding any one of the anti-TSG-6 antibodies described herein. In some examples, the first nucleic acid is contained in a firstexpression 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.

[0014] Another aspect of the present disclosure relates to a host cell that includes any one of the expression vectors described herein. Also presented is a method of making anti-TSG-6 antibodies, and the method includes culturing the host cell under conditions wherein the antibodies expressed, and recovering the antibodies.

[0015] In another example, the present disclosure relates to a composition that includes any one of the anti-TSG-6 antibodies described herein, and a pharmaceutical acceptable carrier or diluent.

[0015a] In another aspect, the present disclosure refers 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.

[0015b] In another aspect, the present disclosure refers to a composition comprising the antibody as disclosed herein, and a pharmaceutical acceptable carrier or diluent.

[0016] In another aspect, the present disclosure refers to the use of an antibody as disclosed herein or a composition as disclosed herein in the manufacture of a medicament for treating cancer in a subject. 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-TSG-6 antibodies described herein, or any one of the compositions described herein. In some examples, the method stimulates an immune response in the subject and the method includes administering to the subject an effective amount of an anti-TSG-6 antibody, or a composition thereof, that acts as a TSG-6 antagonist. In some examples, the method suppresses an immune response in the subject and the method includes administering to the subject an effective amount of an anti-TSG-6 antibody, or a composition thereof, that acts as a TSG-6 agonist.

[0017] In another aspect, the present disclosure refers to the use of an antibody as disclosed herein or a composition as disclosed herein in the manufacture of a medicament for treating cancer in a subject, wherein the antibody serves as a TSG-6 antagonist, wherein optionally the cancer has high expression of TSG-6 and/or HC-HA, further optionally the subject to be treated has high expression of TSG-6 and/or HC-HA, optionally wherein the cancer is: (i) a solid tumor; and/or (ii) melanoma. In further examples and in accordance with any of the above, the present disclosure describes a method

of treating cancer in a subject comprising administering to the subject an effective amount of an antibody where the antibody serves as a TSG-6 antagonist. In some examples, the cancer being treated has high expression of TSG-6 and/or HC-HA. In further examples, the subject to be treated has high expression of TSG-6 and/or HC-HA. Insome examples, the cancer is a solid tumor. In further examples, the cancer is melanoma. In some examples, the antibody is combined with one or more additional therapeutic agents to treat cancer. In further examples, the additional therapeutic agents are other immune checkpoint inhibitors. In some examples, the immune checkpoint inhibitors are selected from the group consisting of a PD-1 inhibitor, a PD-Ll inhibitor, a CTLA-4 inhibitor, a TIM-3 inhibitor, and a LAG-3 inhibitor.

[0018] In another example, the present disclosure refers to the use of an antibody as disclosed herein or a composition as disclosed herein in the manufacture of a medicament for treating fibrosis in a subject, wherein the antibody serves as a TSG-6 antagonist, wherein optionally: (i) the fibrotic tissue has high expression of TSG-6 and/or HC-HA; (ii) the subject to be treated has high expression of TSG-6 and/or HC-HA; or (iii) the antibody is combined with one or more additional therapeutic agents to treat fibrosis. In another example, the present disclosure relates to a method of treating fibrosis in a subject comprising administering to the subject an effective amount of an antibody, wherein the antibody serves as a TSG-6 antagonist. In some examples, the fibrotic tissue has high expression of TSG-6 and/or HC-HA. In some examples the subject to be treated has high expression of TSG-6 and/or HC-HA. In some examples, the antibody is combined with one or more additional therapeutic agents to treat fibrosis.

[0019] In another example, the present disclosure refers to the use of an antibody as disclosed herein or a composition as disclosed herein in the manufacture of a medicament for treating an autoimmune or inflammatory disorder in a subject, wherein the antibody serves as a TSG-6 antagonist, wherein optionally: (i) the autoimmune or inflammatory disorder is idiopathic pulmonary artery hypertension; (ii) the subject to be treated has high expression of TSG-6 and/or HC-HA; (iii) the subject to be treated also has lung fibrosis; (iv) the antibody is combined with one or more additional therapeutic agents to treat pulmonary artery hypertension and/or lung fibrosis; or (v) the autoimmune or inflammatory disorder is asthma; optionally wherein the subject to be treated has: (a) high expression of TSG-6 and/or HC-HA; (b) high expression of TSG-6 and/or HC-HA in the lung; or (c) increased airway eosinophilia. In another example, the present disclosure relates to a method of treating an autoimmuneor inflammatory disorder in a subject comprising administering to the subject an effective amount of an antibody, wherein the antibody serves as a TSG-6 antagonist. In some examples, the autoimmune or inflammatory disorder is idiopathic pulmonary artery hypertension. In some examples, the subject has high expression of TSG-6 and/or HC-HA. In some examples, the subject also has lung fibrosis. In some examples, the antibody is combined with one or more additional therapeutic agents to treat pulmonary artery hypertension and/or lung fibrosis. In some examples, the autoimmune or inflammatory disorder is asthma.In some examples, the subject to be treated has high expression of TSG-6 and/or HC-HA. In some examples, the subject to be treated has high expression of TSG-6 and/or HC-HA in the lung. In some examples, the subject to be treated has increased airway eosinophilia.

[0020] In yet another example, the present disclosure refers to the use of an antibody as disclosed herein or a composition as disclosed herein in the manufacture of a medicament for treating an autoimmune or inflammatory disorder in a subject, wherein the antibody serves as a TSG-6 agonist, wherein optionally the autoimmune or inflammatory disorder is rheumatoid arthritis. In another

Claims

What Is Claimed Is:

1. An antibody that binds human and/or mouse TSG-6, wherein the antibody comprises

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.

2. An antibody that binds human and/or mouse TSG-6, the antibody comprising:
a vhCDRl comprising SEQ ID NO:75, a vhCDR2 comprising SEQ ID NO:76,
a vhCDR3 comprising SEQ ID NO:77, a vlCDRl comprising SEQ ID NO:78,
a vlCDR2 comprising SEQ ID NO:79, and a vlCDR3 comprising SEQ ID NO:80.

3. The antibody according to any of the previous claims, wherein:

the antibody comprises a constant region with an amino acid sequence at least 90% identical to a human IgGl.

4. A nucleic acid composition encoding the antibody according to any one of the previous claims.

5. An expression vector composition comprising the nucleic acid composition according to claim 4, wherein:

(i) the first nucleic acid is contained in a first expression vector and the second nucleic acid is contained in a second expression vector; or

(ii) the first nucleic acid and the second nucleic acid are contained in a single expression vector.

6. A host cell comprising the expression vector composition of claim 5.

7. A method of making an antibody comprising culturing said host cell of claim 6 under conditions wherein the antibody is expressed, and recovering the antibody.

8. A composition comprising the antibody according to any one of claims 1-3, and a pharmaceutical acceptable carrier or diluent.

9. Use of an antibody according to any one of the claims 1-3 or a composition according to

claim 8 in the manufacture of a medicament for treating cancer in a subject.

10. Use of an antibody according to any one of the claims 1-3 or a composition according to claim 8 in the manufacture of a medicament for treating cancer in a subject,

wherein the antibody serves as a TSG-6 antagonist,

wherein optionally the cancer has high expression of TSG-6 and/or HC-HA, further optionally the subject to be treated has high expression of TSG-6 and/or HC-HA,

optionally wherein the cancer is:

(i) a solid tumor; and/or
(ii) melanoma.

11. The use according to claim 9 or claim 10, wherein the antibody is combined with one or more additional therapeutic agents,

wherein optionally the additional therapeutic agents are other immunecheckpoint inhibitors,

further optionally the other immune checkpoint inhibitors are selected from the group consisting of a PD-1 inhibitor, a PD-Ll inhibitor, a CTLA-4 inhibitor, a TIM-3 inhibitor, and a LAG-3 inhibitor.

12. The use according to any one of claims 9 or 10, wherein the subject to be treated has low expression of TSG-6 and/or HC-HA.