CLAIMS

1. An isolated ST2 antibody or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment thereof comprises:

(i) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3, wherein

(1) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 15 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 20 or an amino acid sequence having at least 80% identity thereto;

(2) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 16 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 21 or an amino acid sequence having at least 80% identity thereto;

(3) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 12 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 17 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 22 or an amino acid sequence having at least 80% identity thereto;

(4) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 13 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 18 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 23 or an amino acid sequence having at least 80% identity thereto;

(5) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 14 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 19 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 22 or an amino acid sequence having at least 80% identity thereto; or

(6) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 18 or an amino acid sequence having at least 80% identity thereto, and heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 24 or an amino acid sequence having at least 80% identity thereto;

(ii) light chain CDR1, light chain CDR2 and light chain CDR3, wherein

(1) light chain CDR1 comprises a sequence set forth in SEQ ID NO: 25 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 29 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 32 or an amino acid sequence having at least 80% identity thereto;

(2) light chain CDR1 comprises a sequence set forth in SEQ ID NO: 26 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto;

(3) light chain CDR1 comprises a sequence set forth in SEQ ID NO: 27 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto; or

(4) light chain CDR1 comprises a sequence set forth in SEQ ID NO: 28 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 31 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 33 or an amino acid sequence having at least 80% identity thereto; or

(iii) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 set forth in (i), and light chain CDR1, light chain CDR2 and light chain CDR3 set forth in (ii), wherein

the amino acid sequence of SEQ ID NO: 17 is AIDPETGDTVYX$_1$X$_2$KFX$_3$G, wherein X$_1$ = N or A, X$_2$ = Q, E or K, and X$_3$ = K or Q;

the amino acid sequence of SEQ ID NO: 30 is QX$_4$SNLAS, wherein X$_4$ = M or L.

2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein

the amino acid sequence of SEQ ID NO: 17 is AIDPETGDTVYX$_1$X$_2$KFX$_3$G, wherein

(i) X$_1$ = N or A, X$_2$ = Q, and X$_3$ = K or Q;

(ii) X$_1$ = N or A, X$_2$ = E, and X$_3$ = K or Q; or

(iii) X$_1$ = N or A, X$_2$ = K, X$_3$ = K or Q.

3. The antibody or the antigen-binding fragment thereof according to claim 1 or 2, wherein the antibody or the antigen-binding fragment thereof comprises heavy chain CDR1, heavy chain CDR2, heavy chain CDR3, light chain CDR1, light chain CDR2, and light chain CDR3, wherein

(1) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 15 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 20 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 25 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 29 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 32 or an amino acid sequence having at least 80% identity thereto;

(2) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 16 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 21 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 26 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto;

(3) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 12 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 17 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 22 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 27 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto,

and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto;

(4) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 13 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 18 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 23 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 27 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto;

(5) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 14 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 19 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 22 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 27 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 30 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 34 or an amino acid sequence having at least 80% identity thereto; or

(6) heavy chain CDR1 comprises a sequence set forth in SEQ ID NO: 11 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR2 comprises a sequence set forth in SEQ ID NO: 18 or an amino acid sequence having at least 80% identity thereto, heavy chain CDR3 comprises a sequence set forth in SEQ ID NO: 24 or an amino acid sequence having at least 80% identity thereto, light chain CDR1 comprises a sequence set forth in SEQ ID NO: 28 or an amino acid sequence having at least 80% identity thereto, light chain CDR2 comprises a sequence set forth in SEQ ID NO: 31 or an amino acid sequence having at least 80% identity thereto, and light chain CDR3 comprises a sequence set forth in SEQ ID NO: 33 or an amino acid sequence having at least 80% identity thereto; wherein

the amino acid sequence of SEQ ID NO: 17 is AIDPETGDTVYX$_1$X$_2$KFX$_3$G, wherein

(i) X_1 = N or A, X_2 = Q, and X_3 = K or Q;

(ii) X_1 = N or A, X_2 = E, and X_3 = K or Q; or

(iii) X_1 = N or A, X_2 = K, X_3 = K or Q;

in addition, the amino acid sequence of SEQ ID NO: 30 is QX$_4$SNLAS, wherein X_4 = M or L.

4. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 3, wherein the antibody or the antigen-binding fragment thereof is chimeric or humanized.

5. An isolated ST2 antibody or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment thereof comprises:

(i) a heavy chain variable region, wherein the amino acid sequence of the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 35, 37, 39, 41, 43, 45, 71 or 73, or an amino acid sequence having at least 80% identity to the sequence set forth in SEQ ID NO: 35, 37, 39, 41, 43, 45, 71 or 73;

(i) a light chain variable region, wherein the amino acid sequence of the light chain variable region comprises a sequence set forth in SEQ ID NO: 36, 38, 40, 42, 44, 46 or 79, or an amino acid sequence having at least 80% identity to the sequence set forth in SEQ ID NO: 36, 38, 40, 42, 44, 46 or 79; or

(iii) a heavy chain variable region set forth in (i) and a light chain variable region set forth in (ii).

6. The antibody or the antigen-binding fragment thereof according to claim 5, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein

(1) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 35 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 36 or an amino acid sequence having at least 80% identity thereto;

(2) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 37 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 38 or an amino acid sequence having at least 80% identity thereto;

(3) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 39 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 40 or an amino acid sequence having at least 80% identity thereto;

(4) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 41 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 42 or an amino acid sequence having at least 80% identity thereto;

(5) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 43 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 44 or an amino acid sequence having at least 80% identity thereto;

(6) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 45 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 46 or an amino acid sequence having at least 80% identity thereto;

(7) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 71 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 79 or an amino acid sequence having at least 80% identity thereto; or

(8) the heavy chain variable region comprises a sequence set forth in SEQ ID NO: 73 or an amino acid sequence having at least 80% identity thereto, and the light chain variable region comprises a sequence set forth in SEQ ID NO: 79 or an amino acid sequence having at least 80% identity thereto.

7. An isolated ST2 antibody or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment thereof comprises:

(i) a heavy chain, wherein the amino acid sequence of the heavy chain comprises a sequence set forth in SEQ ID NO: 47, 51, 55, 59, 63, 67, 75 or 77, or an amino acid sequence having at least 80% identity to the sequence set forth in SEQ ID NO: 47, 51, 55, 59, 63, 67, 75 or 77;

(ii) a light chain, wherein the amino acid sequence of the light chain comprises a sequence set forth in SEQ ID NO: 49, 53, 57, 61, 65, 69 or 81, or an amino acid sequence having at least 80% identity to the sequence set forth in SEQ ID NO: 49, 53, 57, 61, 65, 69 or 81; or

(iii) a heavy chain set forth in (i) and a light chain set forth in (ii).

8. The antibody or the antigen-binding fragment thereof according to claim 7, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain and a light chain, wherein

(1) the heavy chain comprises a sequence set forth in SEQ ID NO: 47 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 49 or an amino acid sequence having at least 80% identity thereto;

(2) the heavy chain comprises a sequence set forth in SEQ ID NO: 51 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 53 or an amino acid sequence having at least 80% identity thereto;

(3) the heavy chain comprises a sequence set forth in SEQ ID NO: 55 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 57 or an amino acid sequence having at least 80% identity thereto;

(4) the heavy chain comprises a sequence set forth in SEQ ID NO: 59 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 61 or an amino acid sequence having at least 80% identity thereto;

(5) the heavy chain comprises a sequence set forth in SEQ ID NO: 63 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 65 or an amino acid sequence having at least 80% identity thereto;

(6) the heavy chain comprises a sequence set forth in SEQ ID NO: 67 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 69 or an amino acid sequence having at least 80% identity thereto;

(7) the heavy chain comprises a sequence set forth in SEQ ID NO: 75 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 81 or an amino acid sequence having at least 80% identity thereto; or

(8) the heavy chain comprises a sequence set forth in SEQ ID NO: 77 or an amino acid sequence having at least 80% identity thereto, and the light chain comprises a sequence set forth in SEQ ID NO: 81 or an amino acid sequence having at least 80% identity thereto.

9. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8, wherein the antibody or the antigen-binding fragment thereof is selected from a monoclonal antibody, an Fab fragment, an F(ab')2 fragment, an Fd fragment, an Fv fragment, a dAb, an isolated CDR region, a single-chain Fv molecule, or combinations thereof.

10. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 9, wherein the antibody or the antigen-binding fragment thereof specifically binds to human or monkey ST2 and blocks binding of IL33/ST2 and signaling thereof.

11. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 10, wherein the antibody or the antigen-binding fragment thereof does not substantially bind to IL1R1, IL1R2, IL1R3, IL1R7, IL1R8 and IL1R9.

12. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 11, wherein the antibody or the antigen-binding fragment thereof blocks IL5 secretion induced by IL33/ST2 on $CD4^+$ T cells.

13. An isolated nucleic acid molecule encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12.

14. An expression vector comprising the nucleic acid molecule according to claim 13.

15. A host cell comprising the nucleic acid molecule according to claim 13 or the expression vector according to claim 14.

16. A polypeptide fusion or multispecific molecule comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12.

17. A viral vector comprising a nucleic acid molecule encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12 or the nucleic acid molecule according to claim 13.

18. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12, and one or more pharmaceutically acceptable excipients, diluents or carriers.

19. A method for determining an ST2 expression level in a sample from a subject, wherein the method comprises contacting the sample with the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12 under such conditions that the antibody or the antigen-binding fragment thereof and ST2 form a complex.

20. Use of a therapeutically effective amount of the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 12 or the nucleic acid molecule according to claim 13 in the manufacture of a medicament for treating or ameliorating IL33/ST2-mediated related diseases and conditions in a subject in need.

21. The use according to claim 20, wherein the IL33/ST2-mediated related diseases and conditions include asthma, allergic rhinitis, chronic obstructive pulmonary disease, eosinophilic bronchitis, eosinophilic esophagitis, atopic dermatitis, psoriasis, systemic lupus erythematosus, pemphigoid, rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease, pulmonary fibrosis, hepatic fibrosis, systemic sclerosis, sarcoidosis, graft-versus-host disease (GVHD), diabetes, cardiovascular diseases, or combinations thereof.