

Claims

1. An anti-DLL3 antibody or antigen binding fragment thereof comprising a heavy chain immunoglobulin variable domain (V_H) and a light chain immunoglobulin variable domain (V_L), wherein

(a) the V_H comprises a V_H-CDR1 sequence of SEQ ID NO: 3, a V_H-CDR2 sequence of SEQ ID NO: 4, and a V_H-CDR3 sequence of SEQ ID NO: 5 and the V_L comprises a V_L-CDR1 sequence of SEQ ID NO: 8, a V_L-CDR2 sequence of SEQ ID NO: 9, and a V_L-CDR3 sequence of SEQ ID NO: 10; or

(b) the V_H comprises a V_H-CDR1 sequence of SEQ ID NO: 13, a V_H-CDR2 sequence of SEQ ID NO: 14, and a V_H-CDR3 sequence of SEQ ID NO: 15 and the V_L comprises a V_L-CDR1 sequence of SEQ ID NO: 18, a V_L-CDR2 sequence of SEQ ID NO: 19, and a V_L-CDR3 sequence of SEQ ID NO: 20; or

(c) the V_H comprises a V_H-CDR1 sequence of SEQ ID NO: 23, a V_H-CDR2 sequence of SEQ ID NO: 24, and a V_H-CDR3 sequence of SEQ ID NO: 25 and the V_L comprises a V_L-CDR1 sequence of SEQ ID NO: 28, a V_L-CDR2 sequence of SEQ ID NO: 29, and a V_L-CDR3 sequence of SEQ ID NO: 30; or

(d) the V_H comprises a V_H-CDR1 sequence of SEQ ID NO: 33, a V_H-CDR2 sequence of SEQ ID NO: 34, and a V_H-CDR3 sequence of SEQ ID NO: 35 and the V_L comprises a V_L-CDR1 sequence of SEQ ID NO: 38, a V_L-CDR2 sequence of SEQ ID NO: 39, and a V_L-CDR3 sequence of SEQ ID NO: 40.

2. The anti-DLL3 antibody or antigen binding fragment of claim 1, wherein:

(a) the V_H comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 12, SEQ ID NO: 22, and SEQ ID NO: 32; and/or

(b) the V_L comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 7, SEQ ID NO: 17, SEQ ID NO: 27, and SEQ ID NO: 37.

3. The anti-DLL3 antibody or antigen binding fragment of claim 2, wherein the V_H amino acid sequence and the V_L amino acid sequence is selected from the group consisting of:

SEQ ID NO: 2 and SEQ ID NO: 7 (7-I1-B), respectively;

SEQ ID NO: 12 and SEQ ID NO: 17 (2-C8-A), respectively;

SEQ ID NO: 22 and SEQ ID NO: 27 (10-O18-A), respectively; and

SEQ ID NO: 32 and SEQ ID NO: 37 (6-G23-F), respectively.

4. The anti-DLL3 antibody or antigen binding fragment of claim 1 comprising:

(a) a light chain immunoglobulin variable domain sequence that is at least 95% identical to the light chain immunoglobulin variable domain sequence of SEQ ID NOs: 7 and a heavy chain immunoglobulin variable domain sequence that is at least 95% identical to the heavy chain immunoglobulin variable domain sequence present in any one of SEQ ID NOs: 2; or

(b) a light chain immunoglobulin variable domain sequence that is at least 95% identical to the light chain immunoglobulin variable domain sequence of SEQ ID NO: 17 and a heavy chain immunoglobulin variable domain sequence that is at least 95% identical to the heavy chain immunoglobulin variable domain sequence of SEQ ID NO: 12; or

(c) a light chain immunoglobulin variable domain sequence that is at least 95% identical to the light chain immunoglobulin variable domain sequence of SEQ ID NO: 27 and a heavy chain immunoglobulin variable domain sequence that is at least 95% identical to the heavy chain immunoglobulin variable domain sequence of SEQ ID NO: 22; or

(d) a light chain immunoglobulin variable domain sequence that is at least 95% identical to the light chain immunoglobulin variable domain sequence of SEQ ID NO: 37 and a heavy chain immunoglobulin variable domain sequence that is at least 95% identical to the heavy chain immunoglobulin variable domain sequence of SEQ ID NO: 32.

5. The anti-DLL3 antibody or antigen binding fragment of any one of claims 1-4, further comprising a Fc domain of an isotype selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgM, IgD, and IgE.

6. The anti-DLL3 antibody or antigen binding fragment of any one of claims 1-4, wherein the antigen binding fragment is selected from the group consisting of Fab, F(ab')₂, Fab', scFv, and Fv.
7. The anti-DLL3 antibody of any one of claims 1-5, wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, or a bispecific antibody.
8. The anti-DLL3 antibody or antigen binding fragment of any one of claims 1-7, wherein the antibody or antigen binding fragment binds to an epitope present in a mammalian DLL3 polypeptide.
9. The anti-DLL3 antibody or antigen binding fragment of claim 8, wherein the epitope is a conformational epitope or a non-conformational epitope.
10. The anti-DLL3 antibody or antigen binding fragment of claim 8 or 9, wherein the mammalian DLL3 polypeptide has an amino acid sequence comprising amino acid residues 27-492 of SEQ ID NO: 50 or SEQ ID NO: 51.
11. A composition comprising the anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10 and a pharmaceutically-acceptable carrier, wherein the anti-DLL3 antibody or antigen binding fragment is optionally conjugated to an agent selected from the group consisting of isotopes, dyes, chromagens, contrast agents, drugs, toxins, cytokines, enzymes, enzyme inhibitors, hormones, hormone antagonists, growth factors, radionuclides, metals, liposomes, nanoparticles, RNA, DNA or any combination thereof.
12. A recombinant nucleic acid encoding the anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10.
13. The recombinant nucleic acid of claim 12, comprising the sequences of
SEQ ID NO: 1 and SEQ ID NO: 6; or
SEQ ID NO: 11 and SEQ ID NO: 16; or
SEQ ID NO: 21 and SEQ ID NO: 26; or
SEQ ID NO: 31 and SEQ ID NO: 36.

14. A host cell or a vector comprising the recombinant nucleic acid of claim 12 or claim 13.
15. A kit comprising the anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10 and instructions for use.
16. The kit of claim 15, wherein the anti-DLL3 antibody or antigen binding fragment is coupled to at least one detectable label selected from the group consisting of a radioactive label, a fluorescent label, and a chromogenic label.
17. Use of a therapeutically effective amount of the anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10, in the manufacture of a medicament for treating a DLL3-positive cancer in a subject in need thereof, wherein the anti-DLL3 antibody or antigen binding fragment is conjugated to at least one additional therapeutic agent, and wherein said medicament is to be administered to the subject.
18. The use of claim 17, wherein the at least one additional therapeutic agent is selected from the group consisting of isotopes, drugs, toxins, cytokines, enzymes, enzyme inhibitors, hormones, hormone antagonists, growth factors, radionuclides, metals, liposomes, nanoparticles, RNA, DNA or any combination thereof.
19. The use of claim 17 or 18, wherein the DLL3-positive cancer is small-cell lung cancer, large cell neuroendocrine carcinoma, pulmonary neuroendocrine cancer, extrapulmonary neuroendocrine cancers, or melanoma.
20. A method for detecting DLL3 protein levels in a biological sample comprising:
 - contacting the biological sample with the anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10, wherein the anti-DLL3 antibody or antigen binding fragment is conjugated to a detectable label; and
 - detecting the signal generated by the detectable label in the biological sample.

21. The anti-DLL3 antibody or antigen binding fragment of any one of claims 1-10 for use as a medicament.