

WHAT IS CLAIMED IS:

1. An 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, a V_H-CDR2 sequence, and a V_H-CDR3 sequence selected from the group consisting of

- (i) SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, respectively;
- (ii) SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, respectively;
- (iii) SEQ ID NO: 23, SEQ ID NO: 24, and SEQ ID NO: 25, respectively; and
- (iv) SEQ ID NO: 33, SEQ ID NO: 34, and SEQ ID NO: 35, respectively;

and/or

(b) the V_L comprises a V_L-CDR1 sequence, a V_L-CDR2 sequence, and a V_L-CDR3 sequence selected from the group consisting of

- (i) SEQ ID NO: 8, SEQ ID NO: 9, and SEQ ID NO: 10, respectively;
- (ii) SEQ ID NO: 18, SEQ ID NO: 19, and SEQ ID NO: 20, respectively;
- (iii) SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30, respectively; and
- (iv) SEQ ID NO: 38, SEQ ID NO: 39, and SEQ ID NO: 40, respectively.

2. An 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 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 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. An antibody or antigen binding fragment thereof comprising:

(a) a light chain immunoglobulin variable domain sequence that is at least 95% identical to the light chain immunoglobulin variable domain sequence of any one of SEQ ID NOs: 7, 17, 27, or 37; and/or

(b) 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, 12, 22, or 32.

5. The 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 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', scF_v, and F_v.

7. The 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 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 antibody or antigen binding fragment of claim 8, wherein the epitope is a conformational epitope or a non-conformational epitope.
10. The 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 antibody or antigen binding fragment of any one of claims 1-10 and a pharmaceutically-acceptable carrier, wherein the 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 sequence encoding the antibody or antigen binding fragment of any one of claims 1-10.
13. A recombinant nucleic acid sequence selected from the group consisting of: SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31, and 36.
14. A host cell or a vector comprising the recombinant nucleic acid sequence of claim 12 or claim 13.

15. A kit comprising the antibody or antigen binding fragment of any one of claims 1-10 and instructions for use.
16. The kit of claim 15, wherein the 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. A method for treating a DLL3-associated cancer in a subject in need thereof, comprising: administering to the subject a therapeutically effective amount of the antibody or antigen binding fragment of any one of claims 1-10, wherein the antibody or antigen binding fragment is conjugated to at least one additional therapeutic agent.
18. The method 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 method of claim 17 or 18, wherein the DLL3-associated 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 antibody or antigen binding fragment of any one of claims 1-10, wherein the antibody or antigen binding fragment is conjugated to a detectable label; and
 detecting the signal generated by the detectable label in the biological sample.