

CLAIMS

1. A protein comprising a first antigen binding unit specifically binding to DLL3 and a second antigen binding unit specifically binding to CD3, wherein said first antigen binding unit specifically binding to DLL3 is selected from the group consisting of i) to xviii):
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- i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3);
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- ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3);
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- iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3);
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- iv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3);
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- v) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3);
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- vi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ

ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3);

5 vii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3);

10 viii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3);

15 ix) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:145 (CDR1), SEQ ID NO:146 (CDR2) and SEQ ID NO:147 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:148 (CDR1), SEQ ID NO:149 (CDR2) and SEQ ID NO:150 (CDR3);

20 x) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:151 (CDR1), SEQ ID NO:152 (CDR2) and SEQ ID NO:153 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:154 (CDR1), SEQ ID NO:155 (CDR2) and SEQ ID NO:156 (CDR3);

25 xi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:157 (CDR1), SEQ ID NO:158 (CDR2) and SEQ ID NO:159 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:160 (CDR1), SEQ ID NO:161 (CDR2) and SEQ ID NO:162 (CDR3);

30 xii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:163 (CDR1), SEQ ID NO:164 (CDR2) and SEQ ID NO:165 (CDR3) and heavy chain CDRs comprising the amino acid

sequences of SEQ ID NO:166 (CDR1), SEQ ID NO:167 (CDR2) and SEQ ID NO:168 (CDR3);

xiii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:169 (CDR1), SEQ ID NO:170 (CDR2) and
5 SEQ ID NO:171 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:172 (CDR1), SEQ ID NO:173 (CDR2) and SEQ ID NO:174 (CDR3);

xiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:175 (CDR1), SEQ ID NO:176 (CDR2) and
10 SEQ ID NO:177 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:178 (CDR1), SEQ ID NO:179 (CDR2) and SEQ ID NO:180 (CDR3);

xv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:181 (CDR1), SEQ ID NO:182 (CDR2) and
15 SEQ ID NO:183 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:184 (CDR1), SEQ ID NO:185 (CDR2) and SEQ ID NO:186 (CDR3);

xvi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:187 (CDR1), SEQ ID NO:188 (CDR2) and
20 SEQ ID NO:189 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:190 (CDR1), SEQ ID NO:191 (CDR2) and SEQ ID NO:192 (CDR3);

xvii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:193 (CDR1), SEQ ID NO:194(CDR2) and
25 SEQ ID NO:195 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:196 (CDR1), SEQ ID NO:197 (CDR2) and SEQ ID NO:198 (CDR3); and

xviii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:199 (CDR1), SEQ ID NO:200 (CDR2) and
30 SEQ ID NO:201 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:202 (CDR1), SEQ ID NO:203 (CDR2) and SEQ ID NO:204 (CDR3)..

2. The protein of claim 1, wherein said first antigen binding unit specifically binding to DLL3 comprises a first light chain variable domain and a first heavy chain variable domain and is selected from the group consisting of i) to xviii):

- 5 i) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:37 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:38;
- ii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequences of SEQ ID NO:39 and heavy chain variable domain
10 comprising the amino acid sequences of SEQ ID NO:40;
- iii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:41 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:42;
- iv) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:43 and heavy chain variable domain
15 comprising the amino acid sequence of SEQ ID NO:44;
- v) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:45 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:46;
- 20 vi) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:47 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:48;
- vii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:205 and heavy chain variable domain
25 comprising the amino acid sequence of SEQ ID NO:206;
- viii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:207 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:208;
- ix) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:209 and heavy chain variable domain
30 comprising the amino acid sequence of SEQ ID NO:210;

- x) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:211 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:212;
- xi) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:213 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:214;
- xii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:215 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:216;
- xiii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:217 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:218;
- xiv) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:219 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:220;
- xv) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:221 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:222;
- xvi) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:223 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:224;
- xvii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:225 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:226; and
- xviii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:227 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:228.
3. The protein of claims 1 or 2, wherein said second antigen binding unit specifically binding to CD3 is selected from the group consisting of i)-iii):

- i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3);
- 5 ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3); and
- 10 iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:96 (CDR1), SEQ ID NO:97 (CDR2) and SEQ ID NO:98 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:99 (CDR1), SEQ ID NO:100 (CDR2) and SEQ ID NO:101 (CDR3).
- 15 4. The protein of any one of claims 1 to 3, wherein said second antigen binding unit specifically binding to CD3 comprises a second light chain variable domain and a second heavy chain variable domain selected from the group consisting of i) to iii):
- i) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:67 and a heavy chain variable domain
- 20 comprising the amino acid sequence of SEQ ID NO:68;
- ii) an antigen binding unit comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:69 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:70; and
- iii) an antigen binding unit comprising a light chain variable domain comprising the
- 25 amino acid sequence of SEQ ID NO:102 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:103.
5. The protein of any one of claims 1 to 4, wherein
- i) said first antigen binding unit specifically binding to DLL3 comprises from its N-
- 30 to C-terminus a first light chain variable domain, a first light chain constant domain, a first peptide linker, a first heavy chain variable domain and a first heavy chain constant CH1 domain; and

- ii) said second antigen binding unit specifically binding to CD3 comprises from its N- to C-terminus a second light chain variable domain, a second light chain constant domain, a second peptide linker, a second heavy chain variable domain and a second heavy chain constant CH1 domain.

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6. The protein of claim 5, wherein said first and/or second peptide linker comprises 26 to 42 amino acids, preferably any one of 30 to 40 amino acids, 34 to 40 amino acids, or 36 to 39 amino acids, more preferably 38 amino acids.
- 10 7. The protein of claims 5 or 6, wherein said first linker and/or second linker is a Gly-Ser linker, preferably comprising the amino acid sequence of SEQ ID NO:89, more preferably said first and second peptide linker comprise the same sequence.
8. The protein of any one of claims 5 to 7 further comprising a first and a second Fc domain, said first Fc domain covalently linked to said first antigen binding unit, and a
15 said second Fc domain covalently linked to said second antigen binding unit.
9. The protein of claim 8, wherein
- i) said first Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and said
20 second Fc domain comprises a threonine (T) at position 407 [Y407T], or
- ii) said first Fc domain comprises a tryptophan (W) at position 366 [T366W], and said second Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], or
- iii) said second Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and
25 said first Fc domain comprises a threonine (T) at position 407 [Y407T], or
- iv) said second Fc domain comprises a tryptophan (W) at position 366 [T366W], and said first Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V],
- preferably wherein said first or said second Fc domain further comprises an arginine at
30 position 435 [H435R] and a phenylalanine at position 436 [Y436F].

10. The protein of claim 9, wherein said first and/or said second Fc domain further comprises an alanine at position 234[L234A] and at position 235 [L235A].
11. The protein of any one of claims 5 to 10, wherein the first light chain constant domain and the second light chain constant domain comprise a human kappa or lambda domain.
12. A protein comprising a first polypeptide chain specifically binding to DLL3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:241, SEQ ID NO: 242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO: 245, SEQ ID NO: 246, SEQ ID NO: 247, SEQ ID NO: 248, SEQ ID NO: 249, SEQ ID NO: 250, SEQ ID NO: 251, and SEQ ID NO: 252 and a second polypeptide chain specifically binding to CD3 comprising the amino acid sequence of SEQ ID NO:79, SEQ ID NO:80 or SEQ ID NO:105.
13. An isolated nucleic acid molecule encoding the first antigen binding unit and/or the second antigen binding unit of a protein of any one of claims 1 to 5, optionally further encoding a first and/or a second Fc domain.
14. An isolated nucleic acid molecule encoding the first and/or the second polypeptide chain of claim 12.
15. An expression vector comprising the nucleic acid molecule of claim 13 or 14.
16. A host cell transfected with the expression vector of claim 15.
17. A method of manufacturing a protein of any one of claims 1 to 12 comprising
- i) cultivating the host cell of claim 16 under conditions allowing expression of the protein of any one of claims 1 to 12; and,
 - ii) recovering the protein; and optionally
 - iii) further purifying and/or modifying and/or formulating the protein.

18. A protein comprising a first polypeptide chain specifically binding to DLL3 and a second polypeptide chain specifically binding to CD3, wherein said first polypeptide chain comprises a first light chain, a first linker, and a first heavy chain and said second polypeptide chain comprises a second light chain, a second linker, and a second heavy chain, preferably wherein the C-terminus of said first light chain is covalently linked to the N-terminus of said first heavy chain via said first peptide linker and wherein the C-terminus of said second light chain is covalently linked to the N-terminus of said second heavy chain via said second peptide linker.
19. The protein of claim 18, wherein said first polypeptide chain specifically binding to DLL3 comprises a light chain variable domain and heavy chain variable domain comprising CDR sequences selected from the group consisting of i) to xviii):
- i) light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and a heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3);
 - ii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3);
 - iii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3);
 - iv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3);
 - v) light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy

chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1),
SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3);

vi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:31
(CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1),
SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3)

vii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:133
(CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:136
(CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3);

viii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:139
(CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:142
(CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3);

ix) light chain CDRs comprising the amino acid sequences of SEQ ID NO:145
(CDR1), SEQ ID NO:146 (CDR2) and SEQ ID NO:147 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:148
(CDR1), SEQ ID NO:149 (CDR2) and SEQ ID NO:150 (CDR3);

x) light chain CDRs comprising the amino acid sequences of SEQ ID NO:151
(CDR1), SEQ ID NO:152 (CDR2) and SEQ ID NO:153 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:154
(CDR1), SEQ ID NO:155 (CDR2) and SEQ ID NO:156 (CDR3);

xi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:157
(CDR1), SEQ ID NO:158 (CDR2) and SEQ ID NO:159 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:160
(CDR1), SEQ ID NO:161 (CDR2) and SEQ ID NO:162 (CDR3);

xii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:163
(CDR1), SEQ ID NO:164 (CDR2) and SEQ ID NO:165 (CDR3) and heavy
chain CDRs comprising the amino acid sequences of SEQ ID NO:166
(CDR1), SEQ ID NO:167 (CDR2) and SEQ ID NO:168 (CDR3);

- xiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:169 (CDR1), SEQ ID NO:170 (CDR2) and SEQ ID NO:171 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:172 (CDR1), SEQ ID NO:173 (CDR2) and SEQ ID NO:174 (CDR3);
- 5 light chain CDRs comprising the amino acid sequences of SEQ ID NO:175 (CDR1), SEQ ID NO:176 (CDR2) and SEQ ID NO:177 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:178 (CDR1), SEQ ID NO:179 (CDR2) and SEQ ID NO:180 (CDR3);
- xiv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:181 (CDR1), SEQ ID NO:182 (CDR2) and SEQ ID NO:183 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:184 (CDR1), SEQ ID NO:185 (CDR2) and SEQ ID NO:186 (CDR3);
- 10 light chain CDRs comprising the amino acid sequences of SEQ ID NO:187 (CDR1), SEQ ID NO:188 (CDR2) and SEQ ID NO:189 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:190 (CDR1), SEQ ID NO:191 (CDR2) and SEQ ID NO:192 (CDR3);
- xv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:193 (CDR1), SEQ ID NO:194 (CDR2) and SEQ ID NO:195 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:196 (CDR1), SEQ ID NO:197 (CDR2) and SEQ ID NO:198 (CDR3); and
- 20 light chain CDRs comprising the amino acid sequences of SEQ ID NO:199 (CDR1), SEQ ID NO:200 (CDR2) and SEQ ID NO:201 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:202 (CDR1), SEQ ID NO:203 (CDR2) and SEQ ID NO:204 (CDR3).
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20. The protein of claim 18 or 19, wherein said second polypeptide chain specifically binding to CD3 comprises a light chain variable domain and heavy chain variable domain comprising CDR sequences selected from the group consisting of i) to iii):
- i) light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3);
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- ii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3); and
- 5 iii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:96 (CDR1), SEQ ID NO:97 (CDR2) and SEQ ID NO:98 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:99 (CDR1), SEQ ID NO:100 (CDR2) and SEQ ID NO:101 (CDR3).
- 10 21. The protein of any one of claims 18 to 20, wherein said first polypeptide chain specifically binding to DLL3 comprises a light chain variable domain and a heavy chain variable domain selected from the group consisting of i) to xviii):
- 15 i) a light chain variable domain comprising the amino acid sequences of SEQ ID NO:37 and heavy chain variable domain comprising the amino acid sequences of SEQ ID NO:38;
- 20 ii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:39 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:40;
- 20 iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:41 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:42;
- 25 iv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:43 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:44;
- 25 v) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:45 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:46;
- 30 vi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:47 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:48;

- vii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:205 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:206;
- 5 viii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:207 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:208 ;
- ix) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:209 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:210;
- 10 x) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:211 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:212;
- xi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:213 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:214 ;
- 15 xii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:215 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:216;
- xiii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:217 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:218;
- 20 xiv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:219 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:220;
- 25 xv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:221 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:222 ;
- xvi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:223 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:224;
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xvii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:225 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:226; and

xviii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:227 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:228.

22. The protein of any one of claims 19 to 22, wherein said second polypeptide chain specifically binding to CD3 comprises a light chain variable domain and a heavy chain variable domain selected from the group consisting of i)-iii):

i) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:67 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:68;

ii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:69 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:70; and

iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:102 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:103.

23. The protein of any one of claims 18 to 22, wherein said first and/or second peptide linker comprises 26 to 42 amino acids, preferably any one of 30 to 40 amino acids, 34 to 40 amino acids, or 36 to 39 amino acids, more preferably 38 amino acids.

24. The protein of claim 23, wherein said first linker and/or second linker is a Gly-Ser linker, preferably comprising the amino acid sequence of SEQ ID NO:89, more preferably said first and second peptide linker comprise the same sequence.

25. The protein of any one of claims 18 to 24, wherein

i) said first heavy chain comprises a tyrosine (Y) at position 366 [T366Y], and said second heavy chain comprises a threonine (T) at position 407 [Y407T], or

- ii) said first heavy chain comprises a tryptophan (W) at position 366 [T366W], and said second heavy chain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], or
- iii) said second heavy chain comprises a tyrosine (Y) at position 366 [T366Y], and said first heavy chain comprises a threonine (T) at position 407 [Y407T], or
- iv) said second heavy chain comprises a tryptophan (W) at position 366 [T366W], and said first heavy chain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], preferably wherein said first or said second heavy chain further comprises an arginine at position 435 [H435R] and a phenylalanine at position 436 [Y436F].
26. The protein of claim 25, wherein said first and/or said second heavy chain further comprises an alanine at position 234[L234A] and at position 235 [L235A].
27. The protein of any one of claims 18 to 26, wherein said first light chain and said second light chain comprise a human kappa or lambda domain.
28. The protein of any one of claims 1 to 12 or 18 to 27 for use in medicine.
29. A pharmaceutical composition comprising the protein of any one of claims 1 to 12 or 18 to 27 and a pharmaceutically acceptable carrier.
30. A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of the protein of any one of claims 1 to 12 or 18 to 27.
31. Use of the protein of any one of claims 1 to 12 or 18 to 27 for preparing a pharmaceutical composition for treating cancer.
32. The protein of any one of claims 1 to 12 or 18 to 27 for use in a method of treating cancer.

33. The method of claim 30, the use of claim 31 or the protein for use of claim 32, wherein the cancer is a DLL3 expressing tumor, preferably wherein the cancer is SCLC, glioblastoma or a DLL3 expressing neuroendocrine tumor.
- 5 34. The method of claim 30 or 33, the use of claim 31 or 33, or the protein for use of claim 32 or 33, wherein said protein is used in combination with a chemotherapeutic agent, a therapeutically active compound that inhibits angiogenesis, a signal transduction pathway inhibitor, an EGFR inhibitor, an immune modulator, an immune checkpoint inhibitor, or a hormonal therapy agent.
- 10 35. The method, use or protein for use of claim 34, wherein said protein is in combination with an immune checkpoint inhibitor, preferably an anti-PD-1 antibody or an anti-PD-L1 antibody.
- 15 36. The method, use or protein for use of claim 35, wherein the anti-PD-1 antibody is selected from the group consisting of PD1-1, PD1-2, PD1-3, PD1-4, and PD1-5.
37. An anti-DLL3 antibody molecule comprising
- 20 i) light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3); or
- 25 ii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3); or
- 30 iii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3); or
- iv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain

CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3); or

v) light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3); or

vi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3); or

vii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3); or

viii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3); or

ix) light chain CDRs comprising the amino acid sequences of SEQ ID NO:145 (CDR1), SEQ ID NO:146 (CDR2) and SEQ ID NO:147 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:148 (CDR1), SEQ ID NO:149 (CDR2) and SEQ ID NO:150 (CDR3); or

x) light chain CDRs comprising the amino acid sequences of SEQ ID NO:151 (CDR1), SEQ ID NO:152 (CDR2) and SEQ ID NO:153 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:154 (CDR1), SEQ ID NO:155 (CDR2) and SEQ ID NO:156 (CDR3); or

xi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:157 (CDR1), SEQ ID NO:158 (CDR2) and SEQ ID NO:159 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:160 (CDR1), SEQ ID NO:161 (CDR2) and SEQ ID NO:162 (CDR3); or

xii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:163 (CDR1), SEQ ID NO:164 (CDR2) and SEQ ID NO:165 (CDR3) and heavy chain

- CDRs comprising the amino acid sequences of SEQ ID NO:166 (CDR1), SEQ ID NO:167 (CDR2) and SEQ ID NO:168 (CDR3); or
- xiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:169 (CDR1), SEQ ID NO:170 (CDR2) and SEQ ID NO:171 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:172 (CDR1), SEQ ID NO:173 (CDR2) and SEQ ID NO:174 (CDR3); or
- xiv) comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:175 (CDR1), SEQ ID NO:176 (CDR2) and SEQ ID NO:177 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:178 (CDR1), SEQ ID NO:179 (CDR2) and SEQ ID NO:180 (CDR3); or
- xv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:181 (CDR1), SEQ ID NO:182 (CDR2) and SEQ ID NO:183 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:184 (CDR1), SEQ ID NO:185 (CDR2) and SEQ ID NO:186 (CDR3); or
- xvi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:187 (CDR1), SEQ ID NO:188 (CDR2) and SEQ ID NO:189 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:190 (CDR1), SEQ ID NO:191 (CDR2) and SEQ ID NO:192 (CDR3); or
- xvii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:193 (CDR1), SEQ ID NO:194 (CDR2) and SEQ ID NO:195 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:196 (CDR1), SEQ ID NO:197 (CDR2) and SEQ ID NO:198 (CDR3); or
- xviii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:199 (CDR1), SEQ ID NO:200 (CDR2) and SEQ ID NO:201 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:202 (CDR1), SEQ ID NO:203 (CDR2) and SEQ ID NO:204 (CDR3).
38. The anti-DLL3 antibody molecule of claim 37 wherein said antibody molecule is a monoclonal, a chimeric, a humanized or a human antibody molecule.
39. The anti-DLL3 antibody molecule of claim 37 or 38 wherein said antibody molecule is a Fab, F(ab')₂, Fab', Fv or scFv.

40. The anti-DLL3 antibody molecule of any one of claims 37 to 39, wherein the heavy chain constant region is selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.
- 5 41. The anti-DLL3 antibody molecule of any one of claims 37 to 40, wherein the light chain constant region is kappa or lambda.
42. A method of detecting DLL3 in a biological sample comprising
(a) contacting the sample with an anti-DLL3 antibody of any one of claims 37 to
10 41;
(b) permitting formation of antibody-antigen complexes in the sample; and
(c) detecting the anti-DLL3 antibody.
43. The method of claim 42, wherein the anti-DLL3 antibody is detected by a
15 detectable signal, preferably said signal is detected by immunocytochemistry (ICC), immunohistochemistry (IHC), Western Blotting, Flow cytometry and/or ELISA.
44. The method of any of claims 42 or 43, wherein the biological sample is a tissue
20 sample, preferably a fixed tissue sample, more preferably a formalin-fixed and paraffin-embedded tissue sample.
45. The method of claim 44, wherein the anti-DLL3 antibody is detected by IHC.
- 25 46. The method of any one of claims 42 to 45, wherein the tissue sample is a tumor tissue sample, more preferably a tumor tissue sample isolated from a tumor selected from the group consisting of SCLC, LCNEC, glioma, glioblastoma, melanoma, or other neuroendocrine tumors.
- 30 47. A kit for detecting DLL3 comprising an antibody of any of claims 37 to 41, and instructions for use.