WHAT IS CLAIMED IS:

1. A protein comprising:

(a) a first antigen-binding site comprising an Fab fragment that binds NKG2D;

(b) a second antigen-binding site comprising a single-chain variable fragment (scFv) that binds CD33 comprising a heavy chain variable domain and a light chain variable domain; and

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16, wherein the scFv is linked to the antibody Fc domain or a portion thereof sufficient to bind CD16, or the third antigen-binding site that binds CD16, via a hinge comprising Ala-Ser or Gly-Ala-Ser.

2. The protein of claim 1, wherein the scFv is linked to the antibody Fc domain.

3. The protein of claim 1 or 2, wherein the heavy chain variable domain of the scFv forms a disulfide bridge with the light chain variable domain of the scFv.

4. The protein of claim 3, wherein the disulfide bridge is formed between C44 from the heavy chain variable domain and C100 from the light chain variable domain.

5. The protein of any one of claims 1-4, wherein the scFv is linked to the antibody Fc domain, wherein the light chain variable domain of the scFv is positioned at the N-terminus of the heavy chain variable domain of the scFv, and is linked to the heavy chain variable domain of the scFv via a flexible linker, and wherein the flexible linker amino acid sequence is the amino acid sequence of SEQ ID NO:186.

6. The protein according to any one of claims 2-4, wherein the heavy chain variable domain of the scFv is linked to the light chain variable domain of the scFv via a flexible linker.

7. The protein of claim 6, wherein the flexible linker comprises the amino acid sequence of SEQ ID NO:186.

8. The protein according to any one of claims 2-4 and 6-7, wherein the heavy chain variable domain of the scFv is positioned at the N-terminus or the C-terminus of the light chain variable domain of the scFv.

9. The protein of claim 8, wherein the light chain variable domain of the scFv is positioned at the N-terminus of the heavy chain variable domain of the scFv.

10. The protein according to any one of claims 1-9, wherein the Fab fragment is linked to the antibody Fc domain or a portion thereof sufficient to bind CD16 or the third antigen-binding site that binds CD16.

11. The protein of claim 10, wherein the heavy chain portion of the Fab fragment comprises a heavy chain variable domain and a CH1 domain, and wherein the heavy chain variable domain is linked to the CH1 domain.

12. The protein according to claim 10 or 11, wherein the Fab fragment is linked to the antibody Fc domain.

13. A protein comprising:
(a) a first antigen-binding site that binds NKG2D;
(b) a second antigen-binding site that binds CD33; and
(c) an antibody Fc domain or a portion thereof sufficient to bind CD16, or a third antigen-binding site that binds CD16,
and wherein the second antigen-binding site that binds CD33 comprises:
(i) a heavy chain complementarity-determining region 1 (CDR1) sequence comprising the amino acid sequence of SEQ ID NO:45 or SEQ ID NO:181, a heavy chain complementarity-determining region 2 (CDR2) sequence comprising the amino acid sequence of SEQ ID NO:46, and a heavy chain complementarity-determining region 3 (CDR3) sequence comprising the amino acid sequence of SEQ ID NO:47 or SEQ ID NO:182; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:48, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:49, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:50;
(ii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:21 or SEQ ID NO:434, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:22, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:23 or SEQ ID NO:435; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:24, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:25, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:26;

(iii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:27 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:28, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:29 or SEQ ID NO:436; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:30, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:31, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:32;

(iv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:33 or SEQ ID NO:183, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:34, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:35 or SEQ ID NO:184; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:36, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:185 or SEQ ID NO:37, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:38;

(v) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:39 or SEQ ID NO:437, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:40, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:41 or SEQ ID NO:438; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:42, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:43, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:44;

(vi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:51 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:52, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:53 or SEQ ID NO:439; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:54, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:55, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:56;

(vii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:57 or SEQ ID NO:440, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:58, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:59 or SEQ ID NO:441; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:60, a light chain CDR2 sequence comprising the amino acid

sequence of SEQ ID NO:61, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:62;

(viii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:63 or SEQ ID NO:442, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:64, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:65 or SEQ ID NO:443; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:66, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:67, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:68;

(ix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:69 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:70, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71 or SEQ ID NO:444; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:72, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:73, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:74;

(x) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:75 or SEQ ID NO:445, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:76, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:77 or SEQ ID NO:446; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:78, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:79, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:80;

(xi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:528 or SEQ ID NO:304, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:305, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:529 or SEQ ID NO:306; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:307, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:308, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:309;

(xii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:530 or SEQ ID NO:310, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:311, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:531 or SEQ ID NO:312; and a light chain CDR1 sequence comprising the amino acid

sequence of SEQ ID NO:313, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:314, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:315;

(xiii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:532 or SEQ ID NO:316, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:317, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:533 or SEQ ID NO:318; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:319, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:320, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:321;

(xiv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:534 or SEQ ID NO:322, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:323, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:535 or SEQ ID NO:324; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:325, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:326, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:327;

(xv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:536 or SEQ ID NO:328, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:329, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:537 or SEQ ID NO:330; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:331, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:332, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:333;

(xvi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:538 or SEQ ID NO:334, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:335, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:539 or SEQ ID NO:336; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:337, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:338, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:339;

(xvii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:540 or SEQ ID NO:340, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:341, a heavy chain CDR3 sequence comprising the amino acid

sequence of SEQ ID NO:541 or SEQ ID NO:342; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:343, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:344, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:345;

(xviii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:542 or SEQ ID NO:346, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:347, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:543 or SEQ ID NO:348; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:349, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:350, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:351;

(xix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:544 or SEQ ID NO:352, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:353, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:545 or SEQ ID NO:354; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:355, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:356, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:357;

(xx) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:546 or SEQ ID NO:358, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:359, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:547 or SEQ ID NO:360; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:361, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:362, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:363;

(xxi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:548 or SEQ ID NO:364, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:365, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:549 or SEQ ID NO:366; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:367, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:368, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:369;

(xxii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:550 or SEQ ID NO:370, a heavy chain CDR2 sequence comprising the amino acid sequence of

SEQ ID NO:371, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:551 or SEQ ID NO:372; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:373, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:374, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:375;

(xxiii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:552 or SEQ ID NO:376, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:377, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:553 or SEQ ID NO:378; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:379, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:380, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:381;

(xxiv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:554 or SEQ ID NO:382, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:383, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:555 or SEQ ID NO:384; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:385, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:386, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:387;

(xxv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:556 or SEQ ID NO:388, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:389, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:557 or SEQ ID NO:390; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:391, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:392, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:393;

(xxvi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:558 or SEQ ID NO:394, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:395, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:559 or SEQ ID NO:396; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:397, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:398, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:399;

(xxvii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:560 or SEQ ID NO:400, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:401, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:561 or SEQ ID NO:402; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:403, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:404, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:405;
(xxviii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:562 or SEQ ID NO:406, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:407, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:563 or SEQ ID NO:408; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:409, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:410, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:411; or
(xxix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:564 or SEQ ID NO:412, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:413, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:565 or SEQ ID NO:414; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:415, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:416, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:417.

14. The protein according to claim 13, wherein the heavy chain variable domain and the light chain variable domain of the second antigen-binding site are present on the same polypeptide.

15. The protein according to any one of claims 1-14, wherein the first antigen-binding site comprises:
(1) a heavy chain complementarity-determining region 1 (CDR1) sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain complementarity-determining region 2 (CDR2) sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain complementarity-determining region 3 (CDR3) sequence comprising the amino acid sequence of SEQ ID NO:193; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid

sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;

(2) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:93, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:94, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:95; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:96, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:97, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:98;

(3) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:99, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:100, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:101; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:102, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:103, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:104;

(4) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:105, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:106, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:107; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:108, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:109, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:110;

(5) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:195; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;

(6) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:117, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:118, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:119; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:120, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:121, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:122;

(7) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a

heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:588; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;
(8) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:591; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;
(9) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:594; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;
(10) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:597; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116; or
(11) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:192, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:123; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116.

16. The protein according to claim 15, wherein the first antigen-binding site comprises:
(1) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:87 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88;
(2) a heavy chain variable domain comprising an amino acid sequence at least 95% identical

to the amino acid sequences of SEQ ID NO:81 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:82;
(3) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:83 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:84;
(4) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:85 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:86;
(5) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:191 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88;
(6) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:89 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:90;
(7) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:586 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88;
(8) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:589 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88;
(9) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:592 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88;
(10) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:595 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88; or
(11) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:91 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:88.

17. The protein according to any one of claims 1-12, wherein the second antigen-binding site comprises:

(i) a heavy chain complementarity-determining region 1 (CDR1) sequence comprising the amino acid sequence of SEQ ID NO:45 or SEQ ID NO:181, a heavy chain complementarity-determining region 2 (CDR2) sequence comprising the amino acid sequence of SEQ ID NO:46, and a heavy chain complementarity-determining region 3 (CDR3) sequence comprising the amino acid sequence of SEQ ID NO:47 or SEQ ID NO:182; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:48, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:49, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:50;

(ii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:21 or SEQ ID NO:434, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:22, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:23 or SEQ ID NO:435; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:24, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:25, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:26;

(iii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:27 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:28, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:29 or SEQ ID NO:436; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:30, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:31, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:32;

(iv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:33 or SEQ ID NO:183, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:34, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:35 or SEQ ID NO:184; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:36, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:185 or SEQ ID NO:37, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:38;

(v) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:39 or SEQ ID NO:437, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:40, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID

NO:41 or SEQ ID NO:438; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:42, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:43, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:44;

(vi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:51 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:52, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:53 or SEQ ID NO:439; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:54, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:55, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:56;

(vii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:57 or SEQ ID NO:440, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:58, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:59 or SEQ ID NO:441; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:60, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:61, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:62;

(viii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:63 or SEQ ID NO:442, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:64, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:65 or SEQ ID NO:443; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:66, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:67, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:68;

(ix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:69 or SEQ ID NO:181, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:70, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71 or SEQ ID NO:444; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:72, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:73, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:74;

(x) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:75 or SEQ ID NO:445, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ

ID NO:76, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:77 or SEQ ID NO:446; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:78, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:79, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:80;

(xi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:528 or SEQ ID NO:304, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:305, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:529 or SEQ ID NO:306; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:307, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:308, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:309;

(xii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:530 or SEQ ID NO:310, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:311, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:531 or SEQ ID NO:312; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:313, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:314, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:315;

(xiii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:532 or SEQ ID NO:316, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:317, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:533 or SEQ ID NO:318; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:319, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:320, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:321;

(xiv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:534 or SEQ ID NO:322, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:323, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:535 or SEQ ID NO:324; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:325, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:326, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:327;

(xv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:536 or SEQ ID NO:328, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:329, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:537 or SEQ ID NO:330; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:331, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:332, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:333;

(xvi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:538 or SEQ ID NO:334, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:335, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:539 or SEQ ID NO:336; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:337, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:338, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:339;

(xvii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:540 or SEQ ID NO:340, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:341, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:541 or SEQ ID NO:342; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:343, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:344, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:345;

(xviii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:542 or SEQ ID NO:346, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:347, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:543 or SEQ ID NO:348; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:349, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:350, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:351;

(xix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:544 or SEQ ID NO:352, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:353, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:545 or SEQ ID NO:354; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:355, a light chain CDR2 sequence comprising the amino acid

sequence of SEQ ID NO:356, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:357;

(xx) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:546 or SEQ ID NO:358, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:359, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:547 or SEQ ID NO:360; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:361, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:362, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:363;

(xxi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:548 or SEQ ID NO:364, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:365, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:549 or SEQ ID NO:366; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:367, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:368, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:369;

(xxii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:550 or SEQ ID NO:370, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:371, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:551 or SEQ ID NO:372; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:373, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:374, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:375;

(xxiii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:552 or SEQ ID NO:376, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:377, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:553 or SEQ ID NO:378; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:379, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:380, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:381;

(xxiv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:554 or SEQ ID NO:382, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:383, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:555 or SEQ ID NO:384; and a light chain CDR1 sequence

comprising the amino acid sequence of SEQ ID NO:385, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:386, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:387;

(xxv) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:556 or SEQ ID NO:388, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:389, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:557 or SEQ ID NO:390; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:391, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:392, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:393;

(xxvi) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:558 or SEQ ID NO:394, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:395, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:559 or SEQ ID NO:396; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:397, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:398, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:399;

(xxvii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:560 or SEQ ID NO:400, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:401, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:561 or SEQ ID NO:402; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:403, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:404, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:405;

(xxviii) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:562 or SEQ ID NO:406, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:407, a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:563 or SEQ ID NO:408; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:409, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:410, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:411; or

(xxix) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:564 or SEQ ID NO:412, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:413, a heavy chain CDR3 sequence comprising the amino acid

sequence of SEQ ID NO:565 or SEQ ID NO:414; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:415, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:416, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:417.

18. The protein according to claim 13 or 14, wherein the heavy chain variable domain and the light chain variable domain of first antigen-binding site are present on the same polypeptide.

19. The protein according to any one of claims 13-18, wherein the second antigen-binding site comprises:

(a) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:9 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:10;

(b) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:1 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:2;

(c) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:3 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:4;

(d) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:5 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:6;

(e) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:7 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:8;

(f) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:11 and a light chain variable domain

comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:12;

(g) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:13 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:14;

(h) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:15 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:16;

(i) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:17 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:18;

(j) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:19 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:20;

(k) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:266 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:267;

(l) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:268 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:269;

(m) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:270 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:271;

(n) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:272 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:273;

(o) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:274 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:275;

(p) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:276 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:277;

(q) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:278 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:279;

(r) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:280 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:281;

(s) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:282 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:283;

(t) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:284 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:285;

(u) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:286 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:287;

(v) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:288 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:289;

(w) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:290 and a light chain variable domain

comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:291;

(x) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:292 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:293;

(y) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:294 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:295;

(z) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:296 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:297;

(aa) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:298 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:299;

(bb) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:300 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:301;

(cc) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:302 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:303;

(dd) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:418 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:419; or

(ee) a heavy chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:420 and a light chain variable domain comprising an amino acid sequence at least 95% identical to the amino acid sequences of SEQ ID NO:421.

20. The protein according to any one of claims 1-19 comprising an amino acid sequence selected from the amino acid sequences of SEQ ID NOs:188, 198, 206-223, and 447-488.

21. The protein according to any one of claims 1-12, wherein the scFv linked to the antibody Fc domain is the amino acid sequence of SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:243.

22. The protein according to any one of claims 1-19 comprising the amino acid sequence of SEQ ID NO:189, SEQ ID NO:196, SEQ ID NO:244, or SEQ ID NO:245.

23. The protein according to any one of claims 13-19 comprising an amino acid sequence at least 95% or at least 99% identical to an amino acid sequence selected from the amino acid sequences of SEQ ID NOs:188, 198, 206-223, or 447-488.

24. The protein according to any one of claims 13-19 comprising an amino acid sequence at least 95% or at least 99% identical to the amino acid sequence of SEQ ID NO:187, SEQ ID NO:197, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:243.

25. The protein according to any one of claims 13-19, wherein the protein comprises
(a) a first polypeptide comprising the amino acid sequence at least 95% or at least 99% identical to the amino acid sequence of SEQ ID NO:187;
(b) a second polypeptide comprising the amino acid sequence at least 95% or at least 99% identical to the amino acid sequence of SEQ ID NO:189; and
(c) a third polypeptide comprising the amino acid sequence at least 95% or at least 99% identical to the amino acid sequence of SEQ ID NO:190.

26. The protein of claim 25, wherein the first polypeptide is linked to the second polypeptide via heterodimerization and at least one disulfide bond, and wherein the second polypeptide is linked to the third polypeptide via a disulfide bond.

27. The protein according to any one of claims 1-26, wherein the protein binds to NKG2D with a K_D of 10 nM or weaker affinity, optionally wherein the K_D is measured by Biacore surface plasmon resonance (SPR) analysis.

28. A protein comprising:

(a) a first antigen-binding site comprising a Fab fragment that binds NKG2D, wherein the Fab fragment comprises a heavy chain complementarity-determining region 1 (CDR1) sequence comprising the amino acid sequence of SEQ ID NO:111, a heavy chain complementarity-determining region 2 (CDR2) sequence comprising the amino acid sequence of SEQ ID NO:112, and a heavy chain complementarity-determining region 3 (CDR3) sequence comprising the amino acid sequence of SEQ ID NO:113; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:114, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:115, and a light chain CDR3 sequence comprising the amino acid sequences of SEQ ID NO:116;

(b) a second antigen-binding site comprising a single-chain variable fragment (scFv) that binds CD33, wherein the scFv comprises a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:45, a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:46, and a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:47; and a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:48, a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:49, and a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:50;

(c) an antibody Fc domain or a portion thereof sufficient to bind CD16.

29. The protein according to claim 28, wherein the protein comprises:

(a) a first polypeptide comprising the amino acid sequence of SEQ ID NO:189;

(b) a second polypeptide comprising the amino acid sequence of SEQ ID NO:187; and

(c) a third polypeptide comprising the amino acid sequence of SEQ ID NO:190,

wherein the first polypeptide is linked to the second polypeptide via heterodimerization and at least one disulfide bond, wherein the third polypeptide is linked to the first polypeptide via a disulfide bond.

30. A formulation comprising a protein of any one of claims 1-29, and a pharmaceutically acceptable carrier.

31. Use of the protein according to any one of claims 1-29 or the formulation according to claim 30 in the manufacture of a medicament for treating a CD33-expressing cancer.

32. The use of claim 31, wherein the cancer is selected from the group consisting of acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), chronic lymphocytic leukemia (CML), myeloid blast crisis of CML, acute lymphoblastic leukemia (ALL), acute lymphoblastic lymphoma, myeloproliferative neoplasms (MPNs), lymphoma, non-Hodgkin lymphomas, and classical Hodgkin lymphoma.

33. The use of claim 32, wherein the AML is selected from undifferentiated acute myeloblastic leukemia, acute myeloblastic leukemia with minimal maturation, acute myeloblastic leukemia with maturation, acute promyelocytic leukemia (APL), acute myelomonocytic leukemia, acute myelomonocytic leukemia with eosinophilia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia (AMKL), acute basophilic leukemia, acute panmyelosis with fibrosis, and blastic plasmacytoid dendritic cell neoplasm (BPDCN).

34. The use of claim 32 or 33, wherein the AML is characterized by expression of CLL-1 on the AML leukemia stem cells (LSCs).

35. The use of claim 34, wherein the LSCs further express a membrane marker selected from CD34, CD38, CD123, TIM3, CD25, CD32, and CD96.

36. The use of any one of claims 31-32, wherein the AML is a minimal residual disease (MRD).

37. The use of claim 36, wherein the MRD is characterized by the presence or absence of a mutation selected from *FLT3-ITD* ((Fms-like tyrosine kinase 3)-internal tandem duplications (ITD)), *NPM1* (Nucleophosmin 1), *DNMT3A* (DNA methyltransferase gene *DNMT3A)*, and *IDH* (Isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2)).

38. The use of claim 32, wherein the MDS is selected from MDS with multilineage dysplasia (MDS-MLD), MDS with single lineage dysplasia (MDS-SLD), MDS with ring sideroblasts (MDS-RS), MDS with excess blasts (MDS-EB), MDS with isolated del(5q), and MDS, unclassified (MDS-U).

39. The use of claim 32 or 38, wherein the MDS is a primary MDS or a secondary MDS.

40. The use of claim 32, wherein the ALL is selected from B-cell acute lymphoblastic leukemia (B-ALL) and T-cell acute lymphoblastic leukemia (T-ALL).

41. The use of claim 32, wherein the MPN is selected from polycythaemia vera, essential thrombocythemia (ET), and myelofibrosis.

42. The use of claim 32, wherein the non-Hodgkin lymphoma is selected from B-cell lymphoma and T-cell lymphoma.

43. The use of claim 32, wherein the lymphoma is selected from chronic lymphocytic leukemia (CLL), lymphoblastic lymphoma (LPL), diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), primary mediastinal large B-cell lymphoma (PMBL), follicular lymphoma, mantle cell lymphoma, hairy cell leukemia, plasma cell myeloma (PCM) or multiple myeloma (MM), mature T/NK neoplasms, and histiocytic neoplasms.

44. The protein according to any one of claims 1-29 or the formulation according to claim 30 for use in therapy.