

Claims

1. An antigen-binding protein comprising an antibody light chain variable region (VL) and an antibody heavy chain variable region (VH),
wherein the VL comprises amino acid mutations D30bE and V104L, and further comprises one or more of amino acid mutations E55Q and E93N compared with an amino acid sequence as shown in SEQ ID NO: 22; and/or
wherein the VH comprises amino acid mutations I37V, A49S, S50V, D54A or D54G, and further comprises amino acid mutation N60A compared with the amino acid sequence as shown in SEQ ID NO: 50.
2. The antigen-binding protein of claim 1, wherein the VL further comprises amino acid mutations D94Y, and optionally comprises one or more of the following amino acid mutations: V29L, anyone of Y30aA, Y30aS and Y30aD, any one of G30cA, G30cY and G30cW, any one of D30Y, D30A, D30E, D30F, D30G and D30N; and/or
wherein the VH further comprises amino acid mutations P61D, I67F, D73N or F78L, and optionally comprises one or more of the following amino acid mutations: T30R, S31Q, S96T or H97N.
3. The antigen-binding protein of claim 1 or 2, wherein the VL and the VH comprise the following amino acid mutations:

VL amino acid mutations	VH amino acid mutations
D30bE, E55Q, V104L	I37V,A49S,S50V,D54A,N60A,P61D,I67F
D30bE,E55Q,D94Y,V104L	I37V,A49S,S50V,D54G,N60A,P61D,I67F
D30bE, E93N, V104L	I37V,A49S,S50V,D54A,N60A,P61D,I67F,D73N,F78L
D30bE, E93N, V104L	I37V,A49S,S50V,D54G,N60A,P61D,I67F,D73N,F78L
D30bE, E55Q, V104L	I37V,A49S,S50V,D54A,N60A,I67F,F78L
D30bE, E93N, V104L	I37V,A49S,S50V,D54A,N60A,I67F,F78L
D30bE,E55Q,E93N,V104L	I37V,A49S,S50V,D54A,N60A,I67F,F78L
D30bE,E55Q,D94Y,V104L	I37V,A49S,S50V,D54A,N60A,I67F,F78L
D30bE, E55Q, V104L	I37V,A49S,S50V,D54G,N60A,I67F,F78L
D30bE, E93N, V104L	I37V,A49S,S50V,D54G,N60A,I67F,F78L
D30bE,E55Q,E93N,V104L	I37V,A49S,S50V,D54G,N60A,I67F,F78L

D30bE,E55Q,D94Y,V104L	I37V,A49S,S50V,D54G,N60A,I67F,F78L
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4. The antigen-binding protein of anyone of claims 1 to 3, wherein the VL further comprises amino acid mutations selected from
- (i) V29L, D30Y, Y30aD;
 - (ii) D30A, Y30aD, G30cW;
 - (iii) Y30aA;
 - (iv) Y30aD;
 - (v) Y30aD, G30cY;
 - (vi) Y30aS
 - (vii) D30E, Y30aD, G30cW;
 - (viii) D30F, Y30aD;
 - (ix) D30G, Y30aD, G30cA;
 - (x) D30N, Y30aD, G30cA;
 - (x) D30N, Y30aD, G30cW;
- and/or
- wherein the VH further comprises amino acid mutations mutations selected from:
- (i) S96T, H97T;
 - (ii) T30R;
 - (iii) S96T;
 - (iv) H97N; or
 - (v) S31Q.
5. An antigen-binding protein comprising an antibody light chain variable region (VL) and an antibody heavy chain variable region (VH), wherein the VL comprises LCDR1, LCDR2, LCDR3, and the VH comprises HCDR1, HCDR2 and HCDR3, wherein
- (1) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 45, 3, 17 and 19;
 - (2) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 46, 4, 17 and

19;

(3) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 37, 42, 45, 5, 17 and 19;

(4) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 47, 6, 17 and 19;

(5) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 45, 7, 17 and 19;

(6) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 45, 8, 17 and 19;

(7) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 48, 9, 17 and 19;

(8) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 45, 10, 17 and 19;

(9) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 48, 11, 17 and 19;

(10) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 45, 12, 17 and 19;

(11) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 47, 12, 17 and 19;

(12) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively

comprise the amino acid sequences as shown in SEQ ID NO: 36, 42, 47, 13, 17 and 19; or

(13) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 respectively comprise the amino acid sequences as shown in SEQ ID NO: 38, 42, 45, 14, 17 and 19.

6. The antigen-binding protein of any one of claims 1 to 5, wherein the VL further comprises amino acid mutation V104L compared with an amino acid sequence as shown in SEQ ID NO: 22; and wherein the VH further comprises amino acid mutations I37V, A49S, S50V, D54A or D54G, N60A, P61D and/or I67F compared with the amino acid sequence as shown in SEQ ID NO: 50.
7. The antigen-binding protein of claim 6, wherein the VL comprises framework regions LFR1, LFR2, LFR3 and LFR4, and the VH comprises framework regions HFR1, HFR2, HFR3 and HFR4, wherein HFR1, HFR2, HFR3, HFR4, LFR1, LFR2, LFR3 and LFR4 respectively comprise amino acid sequences as shown in SEQ ID NO: 35, 40, 44, 49, 1, 15, 18 and 21.
8. The antigen-binding protein of claim 6 or 7, wherein
 - 1) the VL comprises amino acid sequence as shown in SEQ ID NO: 23, and the VH comprises amino acid sequence as shown in SEQ ID NO: 51;
 - 2) the VL comprises amino acid sequence as shown in SEQ ID NO: 24, and the VH comprises amino acid sequence as shown in SEQ ID NO: 52;
 - 3) the VL comprises amino acid sequence as shown in SEQ ID NO: 25, and the VH comprises amino acid sequence as shown in SEQ ID NO: 53;
 - 4) the VL comprises amino acid sequence as shown in SEQ ID NO: 26, and the VH comprises amino acid sequence as shown in SEQ ID NO: 54;
 - 5) the VL comprises amino acid sequence as shown in SEQ ID NO: 27, and the VH comprises amino acid sequence as shown in SEQ ID NO: 51;
 - 6) the VL comprises amino acid sequence as shown in SEQ ID NO: 28, and the VH comprises amino acid sequence as shown in SEQ ID NO: 51;

- 7) the VL comprises amino acid sequence as shown in SEQ ID NO: 29, and the VH comprises amino acid sequence as shown in SEQ ID NO: 55;
- 8) the VL comprises amino acid sequence as shown in SEQ ID NO: 30, and the VH comprises amino acid sequence as shown in SEQ ID NO: 51;
- 9) the VL comprises amino acid sequence as shown in SEQ ID NO: 31, and the VH comprises amino acid sequence as shown in SEQ ID NO: 55;
- 10) the VL comprises amino acid sequence as shown in SEQ ID NO: 32, and the VH comprises amino acid sequence as shown in SEQ ID NO: 51;
- 11) the VL comprises amino acid sequence as shown in SEQ ID NO: 32, and the VH comprises amino acid sequence as shown in SEQ ID NO: 54;
- 12) the VL comprises amino acid sequence as shown in SEQ ID NO: 33, and the VH comprises amino acid sequence as shown in SEQ ID NO: 54; or
- 13) the VL comprises amino acid sequence as shown in SEQ ID NO: 34, and the VH comprises amino acid sequence as shown in SEQ ID NO: 56.
9. The antigen-binding protein of any one of claims 1 to 8, comprising an antibody heavy chain constant region and/or an antibody light chain constant region.
10. The antigen-binding protein of claim 9, wherein heavy chain constant region is a human IgG1 constant region.
11. The antigen-binding protein of claim 10, wherein the human IgG1 constant region comprises one or more of amino acid mutations M252Y, S254T and T256E.
12. The antigen-binding protein of claim 11, wherein the human IgG1 constant region comprises any one of amino acid sequences as shown in SEQ ID NOs: 60-61.
13. The antigen-binding protein of any one of claims 1 to 12, wherein the antibody light chain constant region comprises an amino acid sequence as shown in SEQ ID NO: 59.
14. One or more isolated nucleic acid molecules encoding the antigen-binding protein of any one of claims 1 to 13.
15. A vector comprising the nucleic acid molecules of claim 14.
16. A cell comprising the nucleic acid molecule of claim 14 or the vector of claim 15.
17. A method for preparing the antigen-binding protein of claim 5, comprising culturing the cell comprising one or more isolated nucleic acid molecules of claim 14, or the vector of claim 15.

18. An immunoconjugate comprising the antigen-binding protein of any one of claims 1 to 13.
19. A pharmaceutical composition comprising the antigen-binding protein of any one of claims 1 to 13, one or more isolated nucleic acid molecules of claim 14, the vector of claim 15, the cell of claim 16, or the immunoconjugate of claim 18 and optionally a pharmaceutically acceptable carrier.
20. The antigen-binding protein of any one of claims 1 to 13, one or more isolated nucleic acid molecules of claim 14, the vector of claim 15, the cell of claim 16, the immunoconjugate of claim 18 or the pharmaceutical composition of claim 19, for use as a medicament.
21. The antigen-binding protein of any one of claims 1 to 13, one or more isolated nucleic acid molecules of claim 14, the vector of claim 15, the cell of claim 16, the immunoconjugate of claim 18 or the pharmaceutical composition of claim 19 for use in the method for alleviating or treating a disease associated with abnormal level of IgE.
22. Use of the antigen-binding protein of any one of claims 1 to 13, one or more isolated nucleic acid molecules of claim 14, the vector of claim 15, the cell of claim 16, the immunoconjugate of claim 18 or the pharmaceutical composition of claim 19 in the manufacture of a medicament for alleviating or treating a disease associated with abnormal level of IgE.