

## 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 at one or more positions selected from the group consisting of amino acid mutations E55Q and V104-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 ~~at one or more positions selected from the group consisting of D30b, V29, D30, Y30a and G30e.~~
3. ~~The antigen-binding protein of any one of claims 1-2, wherein the VL comprises amino acid mutations at positions of the following group: D30b, E55 and V104.~~
4. ~~The antigen-binding protein of any one of claims 1-3, wherein the VL comprises amino acid mutations at the positions selected from any group consisting of:~~
  - ~~(1) D30b, E55, V104, V29, D30 and Y30a;~~
  - ~~(2) D30b, E55, V104, D30, Y30a and G30e;~~
  - ~~(3) D30b, E55, V104 and Y30a;~~
  - ~~(4) D30b, E55, V104, Y30a and G30e;~~
  - ~~(5) D30b, E55, V104, D30, Y30a and G30e; and~~
  - ~~(6) D30b, E55, V104, D30 and Y30a.~~
5. ~~The antigen-binding protein of any one of claims 1-4, wherein the amino acid mutation~~

- at position E55 comprises E55Q.
6. ~~The antigen-binding protein of any one of claims 1-5, wherein the amino acid mutation at position V104 comprises V104L.~~
  7. ~~The antigen-binding protein of any one of claims 2-6, wherein the amino acid mutation at position D30b comprises D30bE.~~
  8. ~~The antigen-binding protein of any one of claims 2-7, wherein the amino acid mutation at position V29 comprises V29 L.~~
  9. ~~The antigen-binding protein of any one of claims 2-8, wherein the amino acid mutation at position Y30a comprises any one selected from the group consisting of Y30A, Y30aS and Y30aD.~~
  10. ~~The antigen-binding protein of any one of claims 2-9, wherein the amino acid mutation at position D30 comprises any one selected from the group consisting of D30Y, D30A, D30E, D30F, D30G and D30N.~~
  11. ~~The antigen-binding protein of any one of claims 2-10, wherein the amino acid mutation at position G30c comprises any one selected from the group consisting of G30cA, G30cY and G30cW.~~
  12. ~~The antigen-binding protein of any one of claims 2-11, wherein the VL comprises amino acid mutations of the following group: D30bE, E55Q and V104L.~~
  13. ~~The antigen-binding protein of any one of claims 1-12, wherein the VL comprises an amino acid sequence as shown in SEQ ID NO: 57.~~
  14. ~~The antigen-binding protein of any one of claims 1-13, wherein the VL comprises any one of amino acid sequences as shown in SEQ ID NOs: 23-34.~~
  15. ~~The antigen-binding protein of claims 1-14, comprising an antibody heavy chain variable region (VH), wherein the VH comprises amino acid mutations at one or more positions selected from the group consisting of I37, A49, S50 and D54 compared with the amino acid sequence as shown in SEQ ID NO: 50.~~
  16. ~~The antigen-binding protein of claim 15, wherein the VH comprises amino acid mutations at one or more positions selected from the group consisting of N60, P61, I67, T30, S31, S96 and H97.~~

- ~~17. The antigen-binding protein of any one of claims 15-16, wherein the VH comprises amino acid mutations at positions of the following group: N60, P61, I67, I37, A49, S50 and D54.~~
- ~~18. The antigen-binding protein of any one of claims 15-17, wherein the VH comprises amino acid mutations at positions selected from any group consisting of:
  - ~~— (1) — N60, P61, I67, I37, A49, S50, D54, S96 and H97;~~
  - ~~— (2) — N60, P61, I67, I37, A49, S50, D54 and T30;~~
  - ~~— (3) — N60, P61, I67, I37, A49, S50, D54 and S96;~~
  - ~~— (4) — N60, P61, I67, I37, A49, S50, D54 and S31; and~~
  - ~~— (5) — N60, P61, I67, I37, A49, S50, D54 and H97.~~~~
- ~~19. The antigen-binding protein of any one of claims 15-18, wherein the amino acid mutation at position I37 comprises I37V.~~
- ~~20. The antigen-binding protein of any one of claims 15-19, wherein the amino acid mutation at position A49 comprises A49S.~~
- ~~21. The antigen-binding protein of any one of claims 15-20, wherein the amino acid mutation at the position S50 comprises S50V.~~
- ~~22. The antigen-binding protein of any one of claims 15-21, wherein the amino acid mutation at position D54 comprises D54A.~~
- ~~23. The antigen-binding protein of any one of claims 16-22, wherein the amino acid mutation at the position N60 comprises N60A.~~
- ~~24. The antigen-binding protein of any one of claims 16-23, wherein the amino acid mutation at position P61 comprises P61D.~~
- ~~25. The antigen-binding protein of any one of claims 16-24, wherein the amino acid mutation at position I67 comprises I67F.~~
- ~~26. The antigen-binding protein of claims 16-25, wherein the amino acid mutation at the position T30 comprises T30R.~~
- ~~27. The antigen-binding protein of any one of claims 16-26, wherein the amino acid mutation at position S31 comprises S31Q.~~
- ~~28. The antigen-binding protein of any one of claims 16-27, wherein the amino acid~~

- mutation at position S96 comprises ~~S96T~~.
29. ~~The antigen-binding protein of any one of claims 16-28, wherein the amino acid mutation at position H97 comprises H97N.~~
30. ~~The antigen-binding protein of any one of claims 15-29, wherein the VH comprises amino acid mutations of the following group: N60A, P61D, I67F, I37V, A49S, S50V and D54A.~~
31. ~~The antigen-binding protein of any one of claims 15-20, wherein the VH comprises amino acid sequence as shown in SEQ ID NO: 58.~~
32. ~~The antigen-binding protein of any one of claims 15-31, wherein the VH comprises any one of amino acid sequence as shown in SEQ ID NOs: 51-56.~~
- 33.3. The antigen-binding protein of any one of claims 15-321 or 2, wherein the VL and the VH comprise the following amino acid mutations mutations at positions selected from any group consisting of:
- ~~(1) the VL including amino acid mutations at the following positions: D30b, E55, V104, V29, D30 and Y30a; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54, S96 and H97;~~
  - ~~(2) the VL including amino acid mutations at the following positions: D30b, E55, V104, D30, Y30a and G30c; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54 and T30;~~
  - ~~(3) the VL including amino acid mutations at the following positions: D30b, E55, V104 and Y30a; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54 and S96;~~
  - ~~(4) the VL including amino acid mutations at the following positions: D30b, E55, V104 and Y30a; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50 and D54;~~
  - ~~(5) the VL including amino acid mutations at the following positions: D30b, E55, V104, Y30a and G30c; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50 and D54;~~
  - ~~(6) the VL including amino acid mutations at the following positions: D30b, E55,~~

V104 and Y30a; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54 and H97;

~~(7) the VL including amino acid mutations at the following positions: D30b, E55, V104, D30, Y30a and G30c; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50 and D54;~~

~~(8) the VL including amino acid mutations at the following positions: D30b, E55, V104, D30 and Y30a; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54 and H97;~~

~~(9) the VL including amino acid mutations at the following positions: D30b, E55, V104, D30, Y30a, and G30c; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54, and S96; and~~

~~(10) the VL including amino acid mutations at the following positions: D30b, E55, V104, D30, Y30a and G30c; the VH including amino acid mutations at the following positions: N60, P61, I67, I37, A49, S50, D54 and S31.~~

| <u>VL amino acid mutations</u> | <u>VH amino acid mutations</u>                      |
|--------------------------------|-----------------------------------------------------|
| <u>D30bE, E55Q, V104L</u>      | <u>I37V,A49S,S50V,D54A,N60A,P61D,I67F</u>           |
| <u>D30bE,E55Q,D94Y,V104L</u>   | <u>I37V,A49S,S50V,D54G,N60A,P61D,I67F</u>           |
| <u>D30bE, E93N, V104L</u>      | <u>I37V,A49S,S50V,D54A,N60A,P61D,I67F,D73N,F78L</u> |
| <u>D30bE, E93N, V104L</u>      | <u>I37V,A49S,S50V,D54G,N60A,P61D,I67F,D73N,F78L</u> |
| <u>D30bE, E55Q, V104L</u>      | <u>I37V,A49S,S50V,D54A,N60A,I67F,F78L</u>           |
| <u>D30bE, E93N, V104L</u>      | <u>I37V,A49S,S50V,D54A,N60A,I67F,F78L</u>           |
| <u>D30bE,E55Q,E93N,V104L</u>   | <u>I37V,A49S,S50V,D54A,N60A,I67F,F78L</u>           |
| <u>D30bE,E55Q,D94Y,V104L</u>   | <u>I37V,A49S,S50V,D54A,N60A,I67F,F78L</u>           |
| <u>D30bE, E55Q, V104L</u>      | <u>I37V,A49S,S50V,D54G,N60A,I67F,F78L</u>           |
| <u>D30bE, E93N, V104L</u>      | <u>I37V,A49S,S50V,D54G,N60A,I67F,F78L</u>           |
| <u>D30bE,E55Q,E93N,V104L</u>   | <u>I37V,A49S,S50V,D54G,N60A,I67F,F78L</u>           |
| <u>D30bE,E55Q,D94Y,V104L</u>   | <u>I37V,A49S,S50V,D54G,N60A,I67F,F78L</u>           |

·

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.
- ~~34.9.~~ The antigen-binding protein of any one of claims 1-~~33~~ to 8, comprising an antibody heavy chain constant region and/or an antibody light chain constant region.
- ~~35.~~ The antigen-binding protein of claim 34, wherein the antibody heavy chain constant region is derived from a human IgG constant region.
- ~~36.10.~~ The antigen-binding protein of claim ~~35~~9, wherein heavy chain constant region is the a human IgG1 constant region comprises a human IgG1 constant region.
- ~~37.11.~~ The antigen-binding protein of claim ~~36~~10, wherein the human IgG1 constant region comprises one or more of amino acid mutations selected from the group consisting of M252Y, S254T and T256E.
- ~~38.12.~~ The antigen-binding protein of claim ~~37~~11, wherein the human IgG1 constant region comprises any one of amino acid sequences as shown in SEQ ID NOs: 60-61.
- ~~39.~~ The antigen-binding protein of any one of claims 1-~~38~~, comprising an antibody light chain constant region.
- ~~40.13.~~ The antigen-binding protein of ~~claim 39~~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.
- ~~41.14.~~ One or more isolated nucleic acid molecules encoding the antigen-binding protein of any one of claims 1-~~40~~to 13.
- ~~42.15.~~ A vector comprising the nucleic acid molecules of claim ~~41~~14.
- ~~43.16.~~ A cell comprising the nucleic acid molecules of claim ~~14~~41 or the vector of claim ~~42~~15.

- ~~17. A method for preparing the antigen-binding protein of any one of claims 1-40~~claim 5,  
comprising culturing the cell comprising one or more isolated nucleic acid molecules of  
claim 14, or the vector of claim 15, of claim 43 under a condition allowing expression of  
the antigen-binding protein of any one of claims 1-40.
- ~~44.~~18. An immunoconjugate comprising the antigen-binding protein of any one of claims 1 to  
13.
- ~~45.~~19. A pharmaceutical composition comprising the antigen-binding protein of any one of  
claims 1-40 to 13, one or more isolated nucleic acid molecules of claim 14,~~the nucleic acid~~  
~~molecules of claim 41,~~ the vector of claim 42-15 and/or, the cell of claim 43~~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.
- ~~46. Use of the antigen-binding protein of any one of claims 1-40, the nucleic acid molecules~~  
~~of claim 41, the vector of claim 42, the cell of claim 43 and/or the pharmaceutical~~  
~~composition of claim 45 in the preparation of a medicament for relieving or treating a~~  
~~disease associated with abnormal level of IgE.~~
- ~~47. A method for alleviating or treating a disease associated with abnormal level of IgE,~~  
~~comprising administering to a subject in need the antigen-binding protein of any one of~~  
~~claims 1-40, the nucleic acid molecules of claim 41, the vector of claim 42, the cell of~~

~~claim 43 and/or the pharmaceutical composition of claim 45.~~

~~48. A polypeptide comprising the antigen-binding protein of any one of claims 1-40.~~

~~49. An immunoconjugate comprising the antigen-binding protein of any one of claims 1-40.~~

~~50. A kit comprising the antigen-binding protein of any one of claims 1-40, the nucleic acid molecules of claim 41, the vector of claim 42, the cell of claim 43 and/ the pharmaceutical composition of claim 45.~~