

CLAIMS

1. An antibody or an antigen-binding fragment thereof specifically binding to TRPV6, wherein the antibody or the antigen-binding fragment thereof comprises three heavy chain complementarity determining regions HCDR1, HCDR2 and HCDR3 and three light chain complementarity determining regions LCDR1, LCDR2 and LCDR3, and wherein

the three heavy chain complementarity determining regions HCDR1, HCDR2 and HCDR3 are included in the following heavy chain variable region:

- (a) a heavy chain variable region shown in SEQ ID NO: 25;
- (b) a heavy chain variable region shown in SEQ ID NO: 27; or
- (c) a heavy chain variable region shown in SEQ ID NO: 29,

and the three light chain complementarity determining regions LCDR1, LCDR2 and LCDR3 are included in the following light chain variable region:

- (d) a light chain variable region shown in SEQ ID NO: 26;
- (e) a light chain variable region shown in SEQ ID NO: 28; or
- (f) a light chain variable region shown in SEQ ID NO: 30.

2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody or the antigen-binding fragment thereof comprises three heavy chain complementarity determining regions HCDR1, HCDR2 and HCDR3 and three light chain complementarity determining regions LCDR1, LCDR2 and LCDR3 selected from the group consisting of:

(a) HCDR1 shown in SEQ ID NO: 7, HCDR2 shown in SEQ ID NO: 8, HCDR3 shown in SEQ ID NO: 9, LCDR1 shown in SEQ ID NO: 10, LCDR2 shown in SEQ ID NO: 11 and LCDR3 shown in SEQ ID NO: 12;

(b) HCDR1 shown in SEQ ID NO: 13, HCDR2 shown in SEQ ID NO: 14, HCDR3 shown in SEQ ID NO: 15, LCDR1 shown in SEQ ID NO: 16, LCDR2 shown in SEQ ID NO: 17 and LCDR3 shown in SEQ ID NO: 18; and

(c) HCDR1 shown in SEQ ID NO: 19, HCDR2 shown in SEQ ID NO: 20, HCDR3 shown in SEQ ID NO: 21, LCDR1 shown in SEQ ID NO: 22, LCDR2 shown in SEQ ID NO: 23 and LCDR3 shown in SEQ ID NO: 24.

3. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain variable region V_H selected from the group consisting of:

- (a) a heavy chain variable region shown in SEQ ID NO: 25;
- (b) a heavy chain variable region shown in SEQ ID NO: 27; and
- (c) a heavy chain variable region shown in SEQ ID NO: 29.

4. The antibody or the antigen-binding fragment thereof according to claim 3, wherein the antibody or the antigen-binding fragment thereof further comprises a light chain variable region V_L selected from the group consisting of:

- (a) a light chain variable region shown in SEQ ID NO: 26;
- (b) a light chain variable region shown in SEQ ID NO: 28; and
- (c) a light chain variable region shown in SEQ ID NO: 30.

5. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain variable region V_H and a light chain variable region V_L selected from the group consisting of:

- (a) a heavy chain variable region shown in SEQ ID NO: 25 and a light chain variable region shown in SEQ ID NO: 26;
- (b) a heavy chain variable region shown in SEQ ID NO: 27 and a light chain variable region shown in SEQ ID NO: 28; and
- (c) a heavy chain variable region shown in SEQ ID NO: 29 and a light chain variable region shown in SEQ ID NO: 30.

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 5, wherein the antigen-binding fragment is selected from $F(ab')_2$, Fab' , Fab , Fv , $scFv$, $dsFv$ or dAb .

7. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 6, wherein the antibody or the antigen-binding fragment thereof further has a conjugated moiety.

8. The antibody or the antigen-binding fragment thereof according to claim 7, wherein the conjugated moiety is a therapeutic agent, a radioactive isotope, a detectable tag, a pharmacokinetically modified moiety or a purified moiety.

9. An isolated nucleic acid encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8.

10. The nucleic acid according to claim 9, wherein the nucleic acid comprises:

(a) a nucleic acid sequence shown in SEQ ID NO: 31 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 31, and a nucleic acid sequence shown in SEQ ID NO: 32 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 32;

(b) a nucleic acid sequence shown in SEQ ID NO: 33 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 33, and a nucleic acid sequence shown in SEQ ID NO: 34 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 34; or

(c) a nucleic acid sequence shown in SEQ ID NO: 35 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 35, and a nucleic acid sequence shown in SEQ ID NO: 6 or a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO: 6.

11. A vector comprising the nucleic acid sequence according to claim 9 or 10.

12. A host cell comprising the vector according to claim 11.

13. A multispecific antibody comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8, and one or more antibodies or antigen-binding portions thereof specifically binding to other antigens.

14. An antibody conjugate comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8 or the multispecific antibody according to claim 13.

15. A hybridoma cell strain secreting an anti-TRPV6 monoclonal antibody, wherein the hybridoma cell strain is 12CT9.5.1, 16CT4.1.1.2 or 16CT18.1.1.2 and deposited in China Center for Type Culture Collection, and the deposit number of the 12CT9.5.1 is CCTCC NO: C202119, the deposit number of the 16CT4.1.1.2 is CCTCC NO: C202124, and the deposit number of the 16CT18.1.1.2 is CCTCC NO: C202125.

16. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8, the isolated nucleic acid according to any one of claims 9-10, the vector according to claim 11, the host cell according to claim 12, the multispecific antibody according to claim 13 or the antibody conjugate according to claim 14, and a pharmaceutically acceptable carrier.

17. A reagent for analyzing and detecting TRPV6 in a sample from a subject, wherein the reagent comprises one or more of the antibodies or antigen-binding fragments thereof according to any one of claims 1 to 8.

18. A method for detecting TRPV6 in a sample from a subject, comprising:

- (1) contacting the sample with the antibody or the antigen-binding fragment according to any one of claims 1-18;
- (2) optionally, removing unbound antibodies or antibody fragments;
- (3) detecting the antibody or antibody fragment binding to TRPV6 in the sample.

19. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-8, or the pharmaceutical composition of claim 16 in the manufacture of an agent for determining disease formation or the risk of forming a disease in a subject, assessing the progression or prognosis of a disease in a subject,

or predicting or monitoring the response of a subject being receiving a treatment for a disease to the treatment in the subject.

20. The use according to claim 19, wherein the disease is cancer.

21. The use according to claim 20, wherein the cancer is breast cancer, ovarian cancer, endometrial cancer, bile duct cancer, gastric cancer, esophageal cancer, lung cancer, intestinal cancer, or pancreatic cancer; and preferably, the cancer is HER2⁺ breast cancer, triple negative breast cancer, or colorectal cancer.

22. A kit comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8, and optionally, further comprising a reagent for detecting the binding of the antibody or the antigen-binding fragment thereof to TRPV6.

23. A method for preparing an antibody specifically binding to TRPV6, comprising:

- (1) coupling the amino acid sequence shown in SEQ ID NO: 3 with a carrier protein to obtain TRPV6 antigen peptide;
- (2) immunizing a mouse with the TRPV6 antigen peptide obtained by step (1) as an immunogen;
- (3) performing cell fusion, and screening and cloning of an immunopeptide to obtain a positive hybridoma cell line that efficiently secretes an antibody specifically binding to TRPV6; and
- (4) obtaining the antibody specifically binding to TRPV6.

24. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-8, the isolated nucleic acid according to any one of claims 9-10, the vector according to claim 11, the host cell according to claim 12, the multispecific antibody according to claim 13, the antibody conjugate according to claim 14 and the pharmaceutical composition according to claim 16 in the

manufacture of a drug for treating and/or preventing and/or diagnosing diseases related to TRPV6.