need to develop novel antibodies against ERBB2 that address the disadvantages of the anti-ERBB2 antibodies that are currently available.

SUMMARY

[0007] In one example, there is provided an antigen-binding protein, or an antigen-binding fragment thereof, comprising (i) a heavy chain variable domain comprising a VHCDR1 having the amino acid sequence GYTFSNYWIE (SEQ ID NO: 3); a VHCDR2 having the amino acid sequence EILPGSDSTNYNEKFKG (SEQ ID NO: 4), and a VHCDR3 having the amino acid sequence GGSNYGYYFDY (SEQ ID NO: 5); and (ii) a light chain variable domain comprising a VLCDR1 having the amino acid sequence KASQDVGTAVA (SEQ ID NO: 6), a VLCDR2 having the amino acid sequence WASTRHT (SEQ ID NO: 7), and a VLCDR3 having the amino acid sequence QQYSSYRT (SEQ ID NO: 8).

[0007a] In one aspect, there is provided an antigen-binding protein, or an antigen-binding fragment thereof, comprising (i) a heavy chain variable domain comprising a VHCDR1 having the amino acid sequence GYTFSNYWIE (SEQ ID NO: 3); a VHCDR2 having the amino acid sequence EILPGSDSTNYNEKFKG (SEQ ID NO: 4), and a VHCDR3 having the amino acid sequence GGSNYGYYFDY (SEQ ID NO: 5); and (ii) a light chain variable domain comprising a VLCDR1 having the amino acid sequence KASQDVGTAVA (SEQ ID NO: 6), a VLCDR2 having the amino acid sequence WASTRHT (SEQ ID NO: 7), and a VLCDR3 having the amino acid sequence QQYSSYRT (SEQ ID NO: 8), wherein the antigen-binding protein, or an antigen-binding fragment thereof, binds to ERBB2 receptor protein kinase.

[0008] In one aspect, there is provided an antigen-binding protein or an antigen-binding fragment thereof, that competes with the antigen binding protein as disclosed herein for binding to ErbB2 receptor protein kinase.

[0009] In one aspect, there is provided an antigen-binding protein, or an antigen-binding fragment thereof as disclosed herein comprising a radioisotope or a cytotoxin conjugated thereto.

[0010] In one aspect, there is provided a composition comprising a physiologically acceptable carrier and a therapeutically effective amount of the antigen-binding protein, or an antigen-binding fragment thereof as disclosed herein.

[0011] In one example, there is provided a use of an antigen-binding protein, or an antigen-binding fragment thereof as disclosed herein in the manufacture of a medicament for treating cancer.

[0011a] In one aspect, there is provided a use of an antigen-binding protein, or an antigen-binding fragment thereof as disclosed herein in the manufacture of a medicament for treating cancer, wherein the cancer is an ERBB2-associated cancer or a cancer that overexpresses ERBB2.

[0012] In one aspect, there is provided a method for detecting cancer in a subject, the method comprising: contacting a sample obtained from the subject with an antigen-binding protein, or an antigen-binding fragment thereof as disclosed herein *in vitro*; detecting the binding of the antigen-binding protein, or antigen-binding fragment thereof in the sample; correlating the binding with a level of binding in a control sample to determine the level of binding in the sample, wherein an increase in the level of binding in the sample relative to the control sample is indicative of cancer.

Claims

1. An antigen-binding protein, or an antigen-binding fragment thereof, comprising (i) a heavy chain variable domain comprising a VHCDR1 having the amino acid sequence GYTFSNYWIE (SEQ ID NO: 3); a VHCDR2 having the amino acid sequence EILPGSDSTNYNEKFKG (SEQ ID NO: 4), and a VHCDR3 having the amino acid sequence GGSNYGYYFDY (SEQ ID NO: 5); and (ii) a light chain variable domain comprising a VLCDR1 having the amino acid sequence KASQDVGTAVA (SEQ ID NO: 6), a VLCDR2 having the amino acid sequence WASTRHT (SEQ ID NO: 7), and a VLCDR3 having the amino acid sequence QQYSSYRT (SEQ ID NO: 8), wherein the antigen-binding protein, or an antigen-binding fragment thereof, binds to ERBB2 receptor protein kinase.

2. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:1.

3. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 1, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:2.

4. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in any one of claims 1 to 3, wherein the antigen binding protein is selected from the group consisting of monoclonal, recombinant, polyclonal, chimeric, humanised, bispecific and heteroconjugate antibodies; a single variable domain, a domain antibody, antigen binding fragments, immunologically effective fragments, single chain Fv, a single chain antibody, a univalent antibody lacking a hinge region, a minibody, diabodies, and Tandabs™.

5. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 6, wherein the binding protein is a monoclonal antibody.

6. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 5, wherein the monoclonal antibody is humanised.

7. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in any one of claims 1 to 6, wherein the antigen-binding protein, or an antigen-binding fragment thereof binds to isoform 4 of ERBB2 receptor protein kinase.

8. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 7, wherein the antigen-binding protein, or antigen-binding fragment thereof binds to a truncated isoform 4 of ERBB2 receptor protein kinase.

9. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 8, wherein the truncated isoform 4 does not comprise any hydrophobic regions.

10. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in any one of claims 6 to 9, wherein the antigen-binding protein, or antigen-binding fragment thereof binds to a glycan on the ERBB2 receptor protein kinase.

11. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 10, wherein the antigen-binding protein, or antigen-binding fragment thereof binds to an N-linked glycan on the ERBB2 receptor protein kinase.

12. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 11, wherein the antigen-binding protein, or antigen-binding fragment thereof binds to an N-linked glycan located at one or more of amino acid positions 66, 124, 187, 259, 530, 571 and 629 of ERBB2 receptor protein kinase.

13. An antigen-binding protein, or an antigen-binding fragment thereof, as claimed in any one of claims 1 to 12, comprising a radioisotope or a cytotoxin conjugated thereto.

14. The antigen-binding protein, or antigen-binding fragment thereof, as claimed in claim 13, wherein the antibody is conjugated with a cytotoxin selected from the group consisting of monomethyl auristatin E (MMEA-1), mertansine (DM-1) and saporin.

15. The antigen-binding protein, or antigen-binding fragment thereof as claimed in claim 13 or 14, wherein the antigen-binding protein, or an antigen-binding fragment comprising a radioisotope or cytotoxin conjugated thereto is internalized into a cell upon binding to ERBB2 receptor tyrosine kinase.

16. A composition comprising a physiologically acceptable carrier and a therapeutically effective amount of the antigen-binding protein, or an antigen-binding fragment thereof, as claimed in any one of claims 1 to 15.

17. The composition as claimed in claim 16, wherein the composition comprises a further active pharmaceutical ingredient selected from bevacizumab, carboplatin, herceptin or paclitaxel.

18. Use of an antigen-binding protein, or an antigen-binding fragment thereof, as claimed in any one of claims 13 to 15, in the manufacture of a medicament for treating cancer, wherein the cancer is an ERBB2-associated cancer or a cancer that overexpresses ERBB2.

19. Use of claim 18, wherein the cancer is selected from breast, colorectal, ovarian, lung, retinoblastoma, gastric, cervical and pancreatic cancer.

20. Use of claims 18 or 19, wherein the medicament is to be administered with a further active pharmaceutical ingredient.

21. Use of claim 18 or 19, wherein the medicament is to be administered with chemotherapy.

22. Use of claim 20 or 21, wherein the further pharmaceutical agent or chemotherapy is to be administered separately, simultaneously or sequentially.

23. A method for detecting cancer in a subject, the method comprising: contacting a sample obtained from the subject with an antigen-binding protein, or an antigen-binding fragment thereof as claimed in any one of claims 1 to 15 *in vitro*; detecting the binding of the antigen-binding protein, or antigen-binding fragment thereof in the sample; correlating the binding with a level of binding in a control sample to determine the level of binding in the sample, wherein an increase in the level of binding in the sample relative to the control sample is indicative of cancer.

24. The method according to claim 23, wherein the control sample is from the same subject.

25. The method according to claim 23, wherein the control sample is from a different subject.

26. The method according to any one of claims 23 to 25, wherein the antigen-binding protein, or antigen-binding fragment thereof, binds ERBB2 receptor protein kinase.

27. The method according to any one of claims 23 to 26, wherein the antigen-binding protein, or antigen-binding fragment thereof, comprises a detectable label.

28. The method according to claim 27, wherein the detectable label is selected from biotin, alkaline phosphatase, horseradish peroxidase, FITC, PE or Cy Dyes.

29. The method according to claims 27 or 28, wherein the detectable label is detected in an assay selected from flow cytometry, tissue section or immunohistochemistry.

30. The method as claimed in any one of claims 23 to 29, wherein the cancer is selected from breast, colorectal, ovarian, lung, retinoblastoma, gastric, cervical and pancreatic cancer.

31. A kit when used in the method of any one of claims 23 to 30, comprising an antigen-binding protein, or an antigen-binding fragment thereof as claimed in any one of claims 1 to 15, together with instructions for use.