Claims

1. A monoclonal antibody comprising:

(a) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:13, 14 and 15, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:16, 17 and 18; and/or

(b) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs: 19, 20 and 21, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:22, 23 and 24, respectively; and/or

(c) an amino acid sequence comprising SEQ ID NOs: 9 and 11 for the light and heavy chains, respectively; and/or

(d) an amino acid sequence comprising SEQ ID NOs:10 and 12 for the light and heavy chains, respectively.

2. A method of measuring and/or quantifying the presence and/or amount of Her-3 or Her-3 in a complex in a sample from a subject, the method comprising mixing the sample with an antibody of claim 1 and determining the presence and/or quantity of the antibody bound to Her-3 and/or Her-3 in a complex.

3. A method for determining whether a subject with a cancer is likely to respond to treatment with a Her family-targeted agent, for predicting a time course of disease and/or for predicting the probability of a significant event in the time course of the subject's cancer, comprising the method according to claim 2.

4. The method of claim 3, wherein if the level of Her-3 is high, the patient is less likely to respond to the Her family-targeted agent; and if the level of Her-3 is low, the patient is more likely to respond to the Her family-targeted agent.

5. The method of any of claims 2 to 4, wherein the method comprises measuring and/or quantifying the presence and/or amount of at least one of total Her-3, Her-3 homodimers, or Her-3 heterodimers.

6. The method of any one of claims 2 to 5, further comprising measuring the amount p95 in the sample.

7. The method of claim 6, wherein if the amount of p95 and Her-3 expression is low, then the patient is likely to respond to the Her-family targeted agent and/or the patient has a long time course.

8. The method of any one of claims 2 to 7, wherein the sample comprises a tumor sample.

9. The method of any one of any one of claims 2 to 8, wherein the sample comprises a tumor sample; and/or the sample comprises a breast cancer sample, a colorectal cancer sample, an ovarian cancer sample, a non-small cell lung cancer sample, or a gastric cancer sample.

10. The method of any one of claims 2 to 9, wherein the sample comprises a Her-2 positive sample.

11. The method of any one of claims 2 to 10, wherein the sample comprises breast cancer.

12. The method of any one of claims 2 to 11, wherein the sample comprises a Her-2 positive breast cancer sample.

13. The method of any of one of claims 2 to 12, wherein the sample comprises an early stage breast cancer sample or a metastatic breast cancer sample

14. The method of any one of claims 2 to 13, wherein the sample is an FFPE sample or solubilized FFPE sample.

15. The method of any one of claims 2 to 14, wherein the method comprises:

(a) mixing (i) the sample from the subject; (ii) a proximity probe that is capable of binding Her-3, the proximity probe having an effective proximity and (iii) at least one binding compound, the at least one binding compound being capable of

binding Her-3 and having one or more signaling molecules attached, wherein binding of the proximity probe and the binding compound within the effective proximity produces a signal from the molecular tags that correlates with the presence and/or quantity of Her-3 and/or Her-3 in a complex;

(b) detecting the signal from the molecular tags to determine the presence and/or quantity of Her-3 and/or Her-3 in a complex;,

wherein the proximity probe and/or the binding compound comprises the antibody of claim 1.

16. The method of claim 15, wherein the proximity probe comprises a cleaving probe that has a cleavage-inducing moiety and the at least one binding compound has one or more molecular tags attached to the binding compound by a cleavable linkage, wherein the cleavable linkage may be cleaved within the effective proximity, producing a signal that correlates with the presence and/or quantity of Her-3.

17. The method of any one of claims 2 to 14, wherein the method comprises the steps of:

(a) contacting the sample with a tagged Her-3 binding composition that specifically binds to Her-3 and has one or more molecular tags attached thereto via a cleavable linkage;

(b) contacting the sample with a cleaving agent;

(c) cleaving the cleavable linkage of the tagged Her-3 binding composition, thereby releasing the one or more molecular tag; and

(d) quantitating the released molecular tags to determine the presence and/or amount of Her-3 in the sample,

wherein the a tagged Her-3 binding composition comprises the Her-3 antibody of claim 1.

18. The method of any one of claims 3 to 17, wherein the Her family-targeted agent comprises a multi- or single-targeted agent.

19. The method of claim 18, wherein the Her family-targeted agent comprises a dual kinase inhibitor or a bispecific antibody.

20. The method of any one of claims 3 to 19, wherein the Her family-targeted agent comprises trastuzumab, lapatinib, pertuzumab, cetuximab, panitumumab, erlotinib, or gefitinib.

21. The method of claim 20, wherein the Her family-targeted agent comprises trastuzumab.

22. The method of any of claims 3 to 21, wherein likeliness to respond, likeliness to have a long time course and/or likeliness to have a significant event is measured as at least one of an overall survival rate, as time to progression, as disease-free survival, as progression-free survival, time to distant reoccurrence, hazard ratio and/or as objective tumor response or clinical benefit using the RECIST criteria.

23. An antibody according claim 1 for use in any one of the methods of claims 2 to 22.

Claims

1. A monoclonal antibody that binds specifically to a peptide having an amino acid sequence set forth in at least one of SEQ ID NOs:6-8.

2. The monoclonal antibody of claim 1, wherein the antibody binds specifically to a peptide having the amino acid sequence set forth in SEQ ID NO:6.

3. The monoclonal antibody of claim 1, wherein the monoclonal antibody comprises:

(a) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:13, 14 and 15, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:16, 17 and 18;

(b) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs: 19, 20 and 21, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:22, 23 and 24, respectively.

4. The antibody of claim 1, wherein the antibody:

(a) an amino acid sequence comprising SEQ ID NOs: 9 and 11 for the light and heavy chains, respectively; or

(b) an amino acid sequence comprising SEQ ID NOs:10 and 12 for the light and heavy chains, respectively.

5. A method of measuring and/or quantifying the presence and/or amount of Her-3 or Her-3 in a complex in a sample from a subject, the method comprising determining the presence and/or quantity of Her-3 and/or Her-3 in a complex in the sample using a Her-3 antibody that binds specifically to a peptide having an amino acid sequence set forth in at least one of SEQ ID NOs:6-8.

6. The method of claim 5, wherein the Her-3 antibody binds specifically

to a peptide having an amino acid sequence set forth in SEQ ID NO:6.

7. The method of any of claims 5 to 6, wherein the method comprises measuring and/or quantifying the presence and/or amount of at least one of total Her-3, Her-3 homodimers, or Her-3 heterodimers.

8. The method of any of claims 5-7, wherein the sample is a tumor sample.

9. The method of any of claims 5-8, wherein the sample is a breast cancer sample, a colorectal cancer sample, an ovarian cancer sample, a non-small cell lung cancer sample, or a gastric cancer sample.

10. The method of any of claims 5-9, wherein the sample is a breast cancer sample.

11. The method of any of claims 5-10, wherein the sample is an early stage breast cancer sample or a metastatic breast cancer sample.

12. The method of any of claims 5-11, wherein the sample is a Her-2 positive breast cancer sample.

13. The method of any of claims 5-12, wherein the sample comprises an FFPE sample or a solubilized FFPE sample.

14. The method of any of claims 5-13, wherein the measurement may be quantitative across a wide dynamic range.

15. The method of any of claims 5-14, wherein the Her-3 antibody comprises:

(a) a light chain variable region comprising CDR1, CDR2 and CDR3 having

sequences as set forth in SEQ ID NOs:13, 14 and 15, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:16, 17 and 18, respectively; or

(b) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs: 19, 20 and 21, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:22, 23 and 24, respectively.

16. The method of any of claims 5-15, wherein the Her-3 antibody comprises:

(a) an amino acid sequence having SEQ ID NOs:9 and 11 for the light and heavy chains, respectively, or

(b) an amino acid sequence having SEQ ID NOs:10 and 12 for the light and heavy chains, respectively.

17. The method of any of claims 5-16, wherein the method comprises:

(a) mixing (i) the sample from the subject; (ii) a proximity probe that is capable of binding Her-3, the proximity probe having an effective proximity and (iii) at least one binding compound, the at least one binding compound being capable of binding Her-3 and having one or more signaling molecules attached, wherein binding of the proximity probe and the binding compound within the effective proximity produces a signal from the molecular tags that correlates with the presence and/or quantity of Her-3 and/or Her-3 in a complex;

(b) detecting the signal from the molecular tags to determine the presence and/or quantity of Her-3 and/or Her-3 in a complex

18. The method of claim 17, wherein the proximity probe and/or the binding compound is capable of binding specifically to Her-3 or the at least one other analyte.

19. The method of claim 18, wherein the proximity probe and/or binding

compound comprises the Her-3 antibody.

20. The method of claim 18, wherein the proximity probe comprises a cleaving probe that has a cleavage-inducing moiety and the at least one binding compound has one or more molecular tags attached to the binding compound by a cleavable linkage, wherein the cleavable linkage may be cleaved within the effective proximity, producing a signal that correlates with the presence and/or quantity of Her-3.

21. The method of any of claims 5-17, wherein the method comprises the steps of:

(a) contacting the sample with a tagged Her-3 binding composition that specifically binds to Her-3 and has one or more molecular tags attached thereto via a cleavable linkage;

(b) contacting the sample with a cleaving agent;

(c) cleaving the cleavable linkage of the tagged Her-3 binding composition, thereby releasing the one or more molecular tag; and

(d) quantitating the released molecular tags to determine the presence and/or amount of Her-3 in the sample,

wherein the a tagged Her-3 binding composition comprises the Her-3 antibody.

22. The method of any of claims 5-17 and 21, wherein the method comprises measuring and/or quantifying the presence and/or amount of Her-3 by immunohistochemistry.

23. A method of using the level of Her-3 as indicative of whether a subject with a cancer is likely to respond to treatment with a targeted therapy, a time course of disease and/or the probability of a significant event in the time course of the subject's cancer, comprising:

(a) measuring in a biological sample from the subject's cancer an amount of Her-3 using a Her-3 antibody that binds specifically to a peptide having an amino

acid sequence set forth in at least one of SEQ ID NOs:6-8; and

(b) the amount of Her-3 is correlated to whether the subject is likely to respond to treatment with a targeted therapy, the time course of the subject's disease and/or the probability of a significant event in the time course of the subject's cancer,

wherein a high level of Her-3 in the biological sample indicates that the subject is less like to respond to a targeted therapy, less likely to have a long time course, and more likely to have a significant event, and wherein a low level of Her-3 in the biological sample is indicative that the subject is more like to respond to a targeted therapy, more likely to have a long time course, and less likely to have a significant event.

24. The method of claim 23, wherein the Her-3 antibody binds specifically to a peptide having an amino acid sequence set forth in SEQ ID NO:6.

25. The method of any of claims 23-24, wherein the subject's cancer is breast cancer, colorectal cancer, ovarian cancer, non-small cell lung cancer or gastric cancer.

26. The method of claim 23, wherein the subject's cancer is breast cancer.

27. The method of any of claims 23-25, wherein the subject's cancer is early stage breast cancer or metastatic breast cancer.

28. The method of any of claims 23-25 and 27, wherein the subject's cancer is a Her-2 positive breast cancer.

29. The method of any of claims 23-25, 27 and 28, wherein the biological sample is an FFPE sample or a solubilized FFPE sample.

30. The method of any of claims 23-25 and 27-29, wherein the targeted therapy comprises at least one Her family-targeted agent.

31. The method of claim 30, wherein at least one Her family-targeted agent is a multi-targeted agent or a single-targeted agent.

32. The method of claim 31, wherein at least one Her family-targeted agent is a dual kinase inhibitor or a bispecific antibody.

33. The method of claim 30, wherein at least one Her family-targeted agent is trastuzumab, lapatinib, pertuzumab, cetuximab, panitumumab, erlotinib, or gefitinib.

34. The method of claim 30, wherein at least one Her family-targeted agent is trastuzumab.

35. The method of any of claims 23-25 and 27-30, wherein likeliness to respond, likeliness to have a long time course and/or likeliness to have a significant event is measured as at least one of overall survival rate, time to progression, disease-free survival, progression-free survival, time to distant reoccurrence, hazard ratio and/or as objective tumor response or clinical benefit using the RECIST criteria.

36. The method of any of claims 23-25, 27-30 and 35, wherein the method comprises measuring and/or quantifying the presence and/or amount of at least one of total Her-3, Her-3 homodimers, or Her-3 heterodimers.

37. The method of any of claims 23-25, 27-30, 35 and 36, wherein the Her-3 antibody comprises:

(a) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:13, 14 and 15, respectively, and a heavy chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:16, 17 and 18, respectively; or

(b) a light chain variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs: 19, 20 and 21, respectively, and a heavy chain

variable region comprising CDR1, CDR2 and CDR3 having sequences as set forth in SEQ ID NOs:22, 23 and 24, respectively.

38. The method of any of claims 23-25, 27-30, and 35-37, wherein the Her-3 antibody comprises:

(a) an amino acid sequence having SEQ ID NOs:9 and 11 for the light and heavy chains, respectively, or

(b) an amino acid sequence having SEQ ID NOs:10 and 12 for the light and heavy chains, respectively.

39. The method of any of claims 23-25, 27-30, and 35-38, wherein the method of measuring the amount of Her-3 comprises:

(a) mixing (i) the sample from the subject; (ii) a proximity probe that is capable of binding Her-3, the proximity probe having an effective proximity and (iii) at least one binding compound, the at least one binding compound being capable of binding Her-3 and having one or more signaling molecules attached, wherein binding of the proximity probe and the binding compound within the effective proximity produces a signal from the molecular tags that correlates with the presence and/or quantity of Her-3 and/or Her-3 in a complex;

(b) detecting the signal from the molecular tags to determine the presence and/or quantity of Her-3 and/or Her-3 in a complex.

40. The method of claim 39, wherein the proximity probe and/or the binding compound is capable of binding specifically to Her-3 or the at least one other analyte.

41. The method of claim 39, wherein the proximity probe and/or binding compound comprises the Her-3 antibody.

42. The method of claim 39, wherein the proximity probe comprises a cleaving probe that has a cleavage-inducing moiety and the at least one binding compound has one or more molecular tags attached to the binding compound by a

cleavable linkage, wherein the cleavable linkage may be cleaved within the effective proximity, producing a signal that correlates with the presence and/or quantity of Her-3.

43. The method of any of claims 23-25, 27-30, and 35-39, wherein the method comprises the steps of:

(a) contacting the sample with a tagged Her-3 binding composition that specifically binds to Her-3 and has one or more molecular tags attached thereto via a cleavable linkage;

(b) contacting the sample with a cleaving agent;

(c) cleaving the cleavable linkage of the tagged Her-3 binding composition, thereby releasing the one or more molecular tag; and

(d) quantitating the released molecular tags to determine the presence and/or amount of Her-3 in the sample,

wherein the a tagged Her-3 binding composition comprises the Her-3 antibody.

44. The method of any of claims 23-25, 27-30, 35-39 and 43, wherein the method comprises measuring and/or quantifying the presence and/or amount of Her-3 by immunohistochemistry.

45. The method of any of claims 23-25, 27-30, 35-39, 43 and 44, wherein the method further comprises:

(a) measuring the amount of p95 in the biological sample; and

(b) the amount of Her-3 and p95 is correlated to whether the subject is likely to respond to treatment with a targeted therapy, the time course of the subject's disease and/or the probability of a significant event in the time course of the subject's cancer,

wherein the subject is less like to respond to a targeted therapy, less likely to have a long time course, and more likely to have a significant event if the levels of Her-3 and p95 in the biological sample are high, and wherein the subject is more like to respond to a targeted therapy, more likely to have a long time course, and less likely to have a significant event if the levels of Her-3 and p95 in the biological sample are low.

46. A composition comprising the monoclonal antibody of any one of claims 1-4, characterized in that the composition is used for measuring and/or quantifying the presence and/or amount of Her-3 or Her-3 in the complex in a sample from a subject.