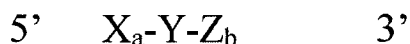


WHAT IS CLAIMED IS:

1. An ErbB3 gastrointestinal cancer detecting agent comprising a polynucleotide reagent capable of specifically binding to an ErbB3 mutation codon in an ErbB3 nucleic acid sequence, wherein the mutation codon encodes an amino acid mutation in SEQ ID NO:2 at a position selected from the group 104, 809, 232, 262, 284, 325, 846, 928, 60, 111, 135, 295, 406, 453, 1164, 193, 492, and 714.

2. The cancer detecting agent of claim 1, wherein the ErbB3 nucleic acid sequence comprises SEQ ID NO:230 or 1.

3. The cancer detecting agent of claim 1, wherein the reagent comprises a polynucleotide of formula



Formula I,

wherein

X is a nucleic acid sequence complementary to the ErbB3 nucleic acid sequence and a is between about 0 and about 250;

Y is the ErbB3 mutation codon; and

Z is a nucleic acid sequence complementary to the ErbB3 nucleic acid sequence and b is between about 0 and about 250.

4. The cancer detecting agent of any one of claims 1-3, further comprising a detectable label.

5. The cancer detecting agent of claim 4, wherein the detectable label is selected from the group radioisotope label, fluorescent label, bioluminescent label, and enzymatic label.

6. The cancer detecting agent of any one of claims 1-5, wherein the amino acid mutation is selected from V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, T1164A, a stop codon at position 193, D492H, and V714M.

7. A method of determining the presence of ErbB3 gastrointestinal cancer in a subject comprising detecting in a biological sample obtained from the subject a mutation in a nucleic acid sequence encoding ErbB3, wherein the mutation results in an amino acid change at a position of SEQ ID NO:2 selected from the group 104, 809, 232, 262, 284, 325, 846, 928, 60, 111, 135, 295, 406, 453, 498, 1164, 193, 492, and 714 and wherein the mutation is indicative of an ErbB3 gastrointestinal cancer in the subject.

8. The method of claim 7, wherein the amino acid mutation is selected from V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, K498I, T1164A, a stop codon at position 193, D492H, and V714M.

9. The method of claim 7 or 8, wherein administration of a therapeutic agent to said subject is contemplated.

10. The method of claim 9, wherein the therapeutic agent is an ErbB inhibitor.

11. The method of claim 10, wherein the ErbB inhibitor is selected from the group consisting of an EGFR antagonist, an ErbB2 antagonist, an ErbB3 antagonist, an ErbB4 antagonist, and an EGFR/ErbB3 antagonist.

12. The method of claim 11, wherein the inhibitor is a small molecule inhibitor.

13. The method of claim 11, wherein the antagonist is an antagonist antibody.

14. The method of claim 13, wherein the antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody, a chimeric antibody, a human antibody, a humanized antibody and an antibody fragment.

15. The detecting agent of claim 1, wherein the gastrointestinal cancer is gastric cancer or colon cancer.

16. The method of claim 7, wherein the gastrointestinal cancer is gastric cancer

or colon cancer.

17. The method of claim 7, further comprising obtaining the sample from the subject.

18. The method of claim 7, wherein the detecting comprises amplifying or sequencing the mutation and detecting the mutation or sequence thereof.

19. The method of claim 18, wherein the amplifying comprises admixing an amplification primer or amplification primer pair with a nucleic acid template isolated from the sample.

20. The method of claim 19, wherein the primer or primer pair is complementary or partially complementary to a region proximal to or including said mutation, and is capable of initiating nucleic acid polymerization by a polymerase on the nucleic acid template.

21. The method of claim 19, further comprising extending the primer or primer pair in a DNA polymerization reaction comprising a polymerase and the template nucleic acid to generate an amplicon.

22. The method of claim 18, wherein the mutation is detected by a process that includes one or more of: sequencing the mutation in a genomic DNA isolated from the biological sample, hybridizing the mutation or an amplicon thereof to an array, digesting the mutation or an amplicon thereof with a restriction enzyme, or real-time PCR amplification of the mutation.

23. The method of claim 18, comprising partially or fully sequencing the mutation in a nucleic acid isolated from the biological sample.

24. The method of claim 18, wherein the amplifying comprises performing a polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), or ligase chain reaction (LCR) using a nucleic acid isolated from the biological sample as a template in the

PCR, RT-PCR, or LCR.

25. Use of an ErbB inhibitor in a method of treating gastrointestinal cancer in a subject in need comprising

- a) detecting in a biological sample obtained from the subject a mutation in a nucleic acid sequence encoding ErbB3, wherein the mutation results in an amino acid change at a position of SEQ ID NO:2 selected from the group consisting of 104, 809, 232, 262, 284, 325, 846, 928, 60, 111, 135, 295, 406, 453, 498, 1164, 193, 491, and 714 and wherein the mutation is indicative of an ErbB3 gastrointestinal cancer in the subject; and
- b) administering the ErbB inhibitor to said subject.

26. The use of claim 25, wherein the amino acid mutation is selected from V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, K498I, T1164A, a stop codon at position 193, D492H, and V714M.

27. The use of claim 25 or 26, wherein the ErbB inhibitor is selected from the group consisting of an EGFR antagonist, an ErbB2 antagonist, an ErbB3 antagonist, an ErbB4 antagonist, and an EGFR/ErbB3 antagonist.

28. The use of claim 27, wherein the antagonist is a small molecule inhibitor.

29. The use of claim 27, wherein the antagonist is an antagonist antibody.

30. The use of claim 29, wherein the antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody, a chimeric antibody, a human antibody, a humanized antibody and an antibody fragment.

31. The use of claim 25, wherein the gastrointestinal cancer is gastric cancer or colon cancer.

WHAT IS CLAIMED IS:

1. An ErbB3 gastrointestinal cancer detecting agent comprising a polynucleotide reagent capable of specifically binding to an ErbB3 mutation codon in an ErbB3 nucleic acid sequence, wherein the mutation codon encodes an amino acid mutation in SEQ ID NO:2 at a position selected from the group 104, 809, 232, 262, 284, 325, 846, 928, 60, 111, 135, 295, 406, 453, 1164, 193, 492, and 714.

2. The cancer detecting agent of claim 1, wherein the ErbB3 nucleic acid sequence comprises SEQ ID NO:230 or 1.

3. The cancer detecting agent of claim 1, wherein the reagent comprises a polynucleotide of formula



wherein

X is a nucleic acid sequence complementary to the ErbB3 nucleic acid sequence and a is between about 0 and about 250;

Y is the ErbB3 mutation codon; and

Z is a nucleic acid sequence complementary to the ErbB3 nucleic acid sequence and b is between about 0 and about 250.

4. The cancer detecting agent of any one of claims 1-3, further comprising a detectable label.

5. The cancer detecting agent of claim 4, wherein the detectable label is selected from the group radioisotope label, fluorescent label, bioluminescent label, and enzymatic label.

6. The cancer detecting agent of any one of claims 1-5, wherein the amino acid mutation is selected from V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, T1164A, a stop codon at position 193, D492H, and V714M.

7. A method of determining the presence of ErbB3 gastrointestinal cancer in a subject comprising detecting in a biological sample obtained from the subject a mutation in a nucleic acid sequence encoding ErbB3, wherein the mutation results in an amino acid change at a position of SEQ ID NO:2 selected from the group V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, K498I, T1164A, a stop codon at position 193, D492H, and V714M and wherein the mutation is indicative of an ErbB3 gastrointestinal cancer in the subject.

8. The method of claim 7, further comprising administration of a therapeutic agent to said subject.

9. The method of claim 8, wherein the therapeutic agent is an ErbB inhibitor.

10. The method of claim 9, wherein the ErbB inhibitor is selected from the group consisting of an EGFR antagonist, an ErbB2 antagonist, an ErbB3 antagonist, an ErbB4 antagonist, and an EGFR/ErbB3 antagonist.

11. The method of claim 10, wherein the inhibitor is a small molecule inhibitor.

12. The method of claim 10, wherein the antagonist is an antagonist antibody.

13. The method of claim 12, wherein the antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody, a chimeric antibody, a human antibody, a humanized antibody and an antibody fragment.

14. The detecting agent of claim 1, wherein the gastrointestinal cancer is gastric cancer or colon cancer.

15. The method of claim 7, wherein the gastrointestinal cancer is gastric cancer or colon cancer.

16. The method of claim 7, wherein the detecting comprises amplifying or sequencing the mutation and detecting the mutation or sequence thereof.

17. The method of claim 16, wherein the amplifying comprises admixing an amplification primer or amplification primer pair with a nucleic acid template isolated from the sample.

18. The method of claim 17, wherein the primer or primer pair is complementary or partially complementary to a region proximal to or including said mutation, and is capable of initiating nucleic acid polymerization by a polymerase on the nucleic acid template.

19. The method of claim 17, further comprising extending the primer or primer pair in a DNA polymerization reaction comprising a polymerase and the template nucleic acid to generate an amplicon.

20. The method of claim 16, wherein the mutation is detected by a process that includes one or more of: sequencing the mutation in a genomic DNA isolated from the biological sample, hybridizing the mutation or an amplicon thereof to an array, digesting the mutation or an amplicon thereof with a restriction enzyme, or real-time PCR amplification of the mutation.

21. The method of claim 16, comprising partially or fully sequencing the mutation in a nucleic acid isolated from the biological sample.

22. The method of claim 16, wherein the amplifying comprises performing a polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), or ligase chain reaction (LCR) using a nucleic acid isolated from the biological sample as a template in the PCR, RT-PCR, or LCR.

23. Use of an ErbB inhibitor for the manufacture of a medicament for treating gastrointestinal cancer in a subject in need comprising

a) detecting in a biological sample obtained from the subject a mutation in a nucleic

acid sequence encoding ErbB3, wherein the mutation results in an amino acid change at a position of SEQ ID NO:2 selected from the group consisting of V104M, V104L, Q809R, A232V, P262H, P262S, G284R, G325R, S846I, E928G, M60K, Y111C, R135L, V295A, M406K, M406T, R453H, K498I, T1164A, a stop codon at position 193, D492H, and V714M and wherein the mutation is indicative of an ErbB3 gastrointestinal cancer in the subject.

24. The use of claim 22 or 23, wherein the ErbB inhibitor is selected from the group consisting of an EGFR antagonist, an ErbB2 antagonist, an ErbB3 antagonist, an ErbB4 antagonist, and an EGFR/ErbB3 antagonist.

25. The use of claim 24, wherein the antagonist is a small molecule inhibitor.

26. The use of claim 24, wherein the antagonist is an antagonist antibody.

27. The use of claim 26, wherein the antibody is selected from the group consisting of a monoclonal antibody, a bispecific antibody, a chimeric antibody, a human antibody, a humanized antibody and an antibody fragment.

28. The use of claim 22, wherein the gastrointestinal cancer is gastric cancer or colon cancer.