Claims:

1. A method of detecting breast cancer or lung cancer in a patient comprising the steps of:

a) Measuring an amount of a polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in a first sample isolated from the patient; and

b) Comparing the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the sample to an amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in a second sample isolated from normal, non-cancerous cells,

wherein an amplified amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the first sample relative to the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the second sample indicates breast cancer or lung cancer is present in the first sample.

2. The method of claim 1 further comprising measuring the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y231 in the first and second sample wherein an amplified amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 and Y231 in the first sample relative to the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 and Y231 in the second sample indicates cancer is present in the first sample.

3. The method of claim 1 or 2 whereby the cancer is dependent on EGFR, c-Src, c-Yes, ER, Wnt , WBP2 or E2F.

4. The method of any one of claims 1 to 3 whereby the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine is measured with an isolated phosphorylation site-specific antibody that specifically binds to a WW-domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or the tyrosine Y192 and the tyrosine Y231 wherein the antibody does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.

5. The method of any one of claims 1 to 3 further comprising the steps of:

c) bringing the polypeptide of SEQ ID No. 1 into contact with a polynucleotide probe or primer comprising a polynucleotide sequence capable of hybridising selectively to the polypeptide of SEQ ID No. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or the tyrosine Y192 and the tyrosine Y231 under suitable hybridising conditions; and

d) detecting any duplex formed between the probe or primer and the polypeptide of SEQ ID No. 1 phosphorylated at said tyrosine.

6. The method of any one of claims 1 to 3 whereby the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine is measured with an isolated phosphorylation site-specific aptamers that specifically binds to a WW-domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or Y231 or the tyrosine Y192 and the tyrosine Y231 wherein the aptamers does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.

7. The method of any one of claims 1 to 6 whereby the first and second sample are isolated from a nuclear fraction of a cell.

8. An agent to interfere with phosphorylation of tyrosine Y192 and Y231 in the polypeptide of SEQ ID NO. 1, wherein the agent is selected from one of an antibody, a peptide an aptamers and a small interfering RNA.

9. The agent of claim 8 wherein said antibody is an immunoglobulin comprising an immunoglobulin heavy chain.

10. The agent of claim 8 wherein said antibody is an immunoglobulin comprising an immunoglobulin light chain.

11. The agent of claim 9 or 10 wherein the immunoglobulin is an IgG1 kappa immunoglobulin.

12. The agent of claim 11 wherein the immunoglobulin comprises a human IgG1 constant region within a heavy chain of the immunoglobulin and a human constant region within a light chain of the immunoglobulin.

13. The agent of claim 9 or 10 wherein the immunoglobulin comprises fully or partially human framework regions within the heavy chain and within the light chain.

14. The agent of claim 9 or 10 wherein the immunoglobulin comprises murine framework regions within the heavy chain and within the light chain.

15. The agent of claim 8 comprising a peptide capable of binding to a portion of SEQ ID. NO. 1 that includes the phosphorylated tyrosine Y192 and Y231 and the amino acids flanking either side of the phosphorylated tyrosine Y192 and Y231.

16. The agent of claim 15 wherein the peptide comprises SEQ ID. NO. 3; or SEQ ID. NO. 4 ; or SEQ ID. NO. 5; or SEQ ID. NO. 6 and a nuclear localization signal.

17. A cell line producing an agent of any one of claims 8 to 16.

18. The agent of claim 8 wherein the small interfering RNA comprises SEQ ID NO. 2.

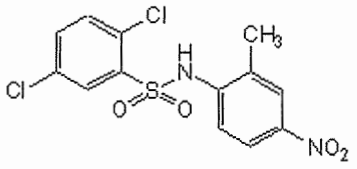
19. The agent or the cell line producing the agent of any one of claims 8 to 18 for use in the treatment of breast cancer or lung cancer.

20. The agent of claim 19 whereby the cancer is dependent on EGFR, c-Src, c-Yes, ER, Wnt, WBP2 or E2F.

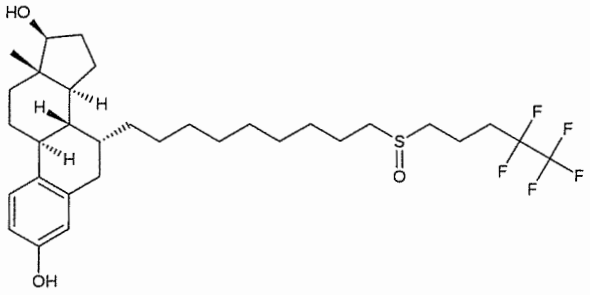
21. The agent of claim 8 or 19 further comprising a TCF/β-catenin inhibitor, anti-EGFR, anti-src, anti-c-Yes, anti-E2F, or anti-ERα compounds.

22. A composition comprising the agent or the cell line producing the agent of any one of claim 8 to 18 and a TCF/β-catenin inhibitor or an anti-estrogen receptor α compound for use in the treatment of breast cancer or lung cancer.

23. The agent of claim 21 or the composition of claim 22 wherein the TCF/β-catenin inhibitor is an FH535 of formula 1.



24. The agent of claim 21 or the composition of claim 22 wherein the anti-estrogen receptor α compound is a Fulvestrant of formula 2



25. Use of an agent to interfere with phosphorylation of tyrosine Y192 and Y231 in the polypeptide of SEQ ID NO. 1, wherein the agent is selected from one of an antibody, a peptide, an aptamer and a small interfering RNA in preparation of a medicament for the treatment of breast cancer or lung cancer.

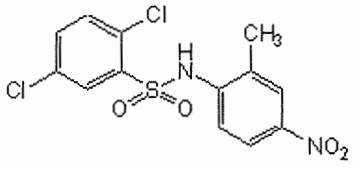
26. The use of claim 25 wherein the agent comprises any one of claims 8 to 18

27. Use of a composition comprising:

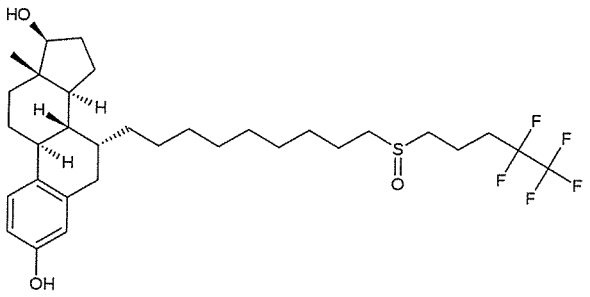
an agent to interfere with phosphorylation of tyrosine Y192 and Y231 in the polypeptide of SEQ ID NO. 1., wherein the agent is selected from one of an antibody, a peptide, an aptamer and a small interfering RNA; and

a TCF/ β-catenin inhibitor or an anti-estrogen receptorα compound in preparation of a medicament for the treatment of breast cancer or lung cancer.

28. The use of claim 27 wherein the TCF/β-catenin inhibitor is an FH535 of formula 1.



29. The use of claim 27 wherein the anti-estrogen receptor-α compound is a Fulvestrant of formula 2


HO
H
H
H
S
O
F
F
F
F
F
OH

Claims:

1. A method of detecting breast cancer or lung cancer in a patient comprising the steps of:

~~e~~a) Measuring an amount of a polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in a first sample isolated from the patient; and

~~f~~b) Comparing the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the sample to an amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in a second sample isolated from normal, non-cancerous cells,

wherein an amplified amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the first sample relative to the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 in the second sample indicates breast cancer or lung cancer is present in the first sample.

2. The method of claim 1 further comprising measuring~~whereby~~ the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at ~~Y192~~ Y231 in the first and second sample ~~also detects phosphorylation of tyrosine at Y231 of the polypeptide of SEQ ID No. 1~~ wherein an amplified amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 and Y231 in the first sample relative to the amount of polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine at Y192 and Y231 in the second sample indicates cancer is present in the first sample.

3. The method of claim 1 or 2 whereby the cancer is dependent on EGFR, c-Src, c-Yes, ER, Wnt , WBP2 or E2F.

~~4. The method of claim 3 whereby the cancer is breast cancer and lung cancer.~~

~~5~~4. The method of any one of claims 1 to ~~4~~3 whereby the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine is measured with an isolated phosphorylation site-specific antibody that specifically binds to a WW-domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or the tyrosine Y192 and the tyrosine Y231 wherein the antibody does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.

~~6~~5. The method of any one of claims 1 to ~~4~~3 further comprising the steps of:

e~~c~~) bringing the polypeptide of SEQ ID No. 1 into contact with a polynucleotide probe or primer comprising a polynucleotide sequence capable of hybridising selectively to the polypeptide of SEQ ID No. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or the tyrosine Y192 and the tyrosine Y231 under suitable hybridising conditions; and

f~~d~~) detecting any duplex formed between the probe or primer and the polypeptide of SEQ ID No. 1 phosphorylated at said tyrosine.

7~~6~~. The method of any one of claims 1 to 4~~-~~3 whereby the amount of the polypeptide of SEQ ID No. 1 with a phosphorylated tyrosine is measured with an isolated phosphorylation site-specific aptamers that specifically binds to a WW-domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or Y231 or the tyrosine Y192 and the tyrosine Y231 wherein the aptamers does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.

7. The method of any one of claims 1 to 6 whereby the first and second sample are isolated from a nuclear fraction of a cell.

8. An agent to interfere with phosphorylation of tyrosine Y192 and~~/or~~ Y231 in the polypeptide of SEQ ID NO. 1, wherein the agent is selected from one of an antibody, a peptide an aptamers and a small interfering RNA.

~~9. The agent of claim 8 comprising an isolated phosphorylation site-specific antibody that specifically binds to a WW-domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192, Y231 or the tyrosine Y192 and the tyrosine Y231 wherein the antibody does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.~~

10~~9~~. The agent of claim 9~~-~~8 wherein said antibody is an immunoglobulin comprising an immunoglobulin heavy chain.

11~~10~~. The agent of claim 9~~-~~8 wherein said antibody is an immunoglobulin comprising an immunoglobulin light chain.

~~12~~11. The agent of claim ~~10~~ 9 or ~~11~~ 10 wherein the immunoglobulin is an IgG1 kappa immunoglobulin.

~~13~~12. The agent of claim ~~12~~ 11 wherein the immunoglobulin comprises a human IgG1 constant region within a heavy chain of the immunoglobulin and a human constant region within a light chain of the immunoglobulin.

~~14~~13. The agent of claim ~~11~~ 9 or 10 wherein the immunoglobulin comprises fully or partially human framework regions within the heavy chain and within the light chain.

~~15~~14. The agent of claim ~~11~~ 9 or 10 wherein the immunoglobulin comprises murine framework regions within the heavy chain and within the light chain.

~~16~~15. The agent of claim 8 comprising a peptide capable of binding to a portion of SEQ ID. NO. 1 that includes the phosphorylated tyrosine ~~Y192 or, Y231 or~~ Y192 and Y231 and the amino acids flanking either side of the phosphorylated tyrosine ~~Y192 or, Y231 or~~ Y192 and Y231.

~~17~~16. The agent of claim ~~16~~ 15 wherein the peptide comprises SEQ ID. NO. 3; or SEQ ID. NO. 4 ; or SEQ ID. NO. 5; or SEQ ID. NO. 6 and a nuclear localization signal.

~~18~~17. A cell line producing an agent of any one of claims 8 to ~~17~~16.

~~19. The agent of claim 8 comprising an isolated phosphorylation site specific aptamers that specifically binds to a WW domain binding protein of SEQ ID. NO. 1 only when the polypeptide is phosphorylated at the tyrosine Y192 or the tyrosine Y192 and the tyrosine Y231 wherein the aptamers does not bind the polypeptide of SEQ ID No. 1 when it is not phosphorylated at said tyrosine.~~

~~20. The agent of claim 8 comprising a small interfering RNA.~~

~~21~~18. The agent of claim ~~20~~ 8 wherein the small interfering RNA comprises SEQ ID NO. 2.

~~22~~19. The agent or the cell line producing the agent of any one of claims 8 to ~~21~~ 18 for use in the treatment of breast cancer or lung cancer.

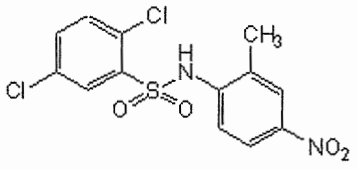
~~23~~20. The agent of claim ~~22~~ 19 whereby the cancer is dependent on EGFR, c-Src, c-Yes, ER, Wnt, WBP2 or E2F.

~~24. The agent of claim 22 or 23 wherein the cancer is breast cancer and lung cancer.~~

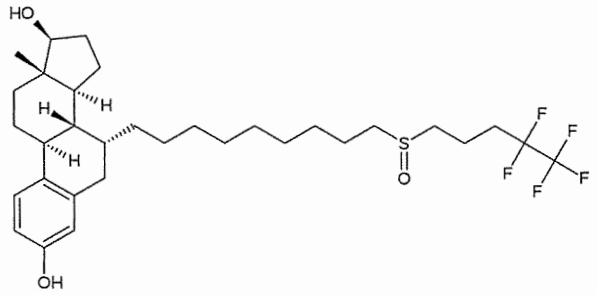
~~25~~21. The agent of claim 8 or ~~24~~ 19 further comprising a TCF/β-catenin inhibitor~~n anti- wnt pathway~~, anti-EGFR, anti-src, anti-c-Yes, anti-E2F, ~~anti-WBP2 and~~ or anti-ERα compounds.

~~26~~22. A composition comprising the agent or the cell line producing the agent of any one of claim 8 to ~~24~~ 18 and a TCF/β-catenin inhibitor or an anti-estrogen receptor α compound for use in the treatment of breast cancer or lung cancer.

~~27~~23. The agent of claim ~~25~~ 21 or the composition of claim ~~26~~ 22 wherein the TCF/β-catenin inhibitor~~anti-Wnt pathway compound~~ is an FH535 of formula 1.



~~28~~24. The agent of claim ~~25~~ 21 or the composition of claim ~~26~~ 22 wherein the anti-estrogen receptor α compound is a Fulvestrant of formula 2



~~29~~25. Use of ~~A method of treating a patient afflicted with cancer, comprising the steps of:~~

~~(a) administering to the patient~~ an agent to interfere with phosphorylation of tyrosine Y192 and/~~or~~ Y231 in the polypeptide of SEQ ID NO. 1, wherein the agent is selected from one of an antibody, a peptide, an aptamer and a small interfering RNA in preparation of a medicament for the treatment of breast cancer or lung cancer.

~~30~~26. The ~~method~~ use of claim ~~29~~ 25 wherein the agent comprises any one of claims 8 to ~~24~~18

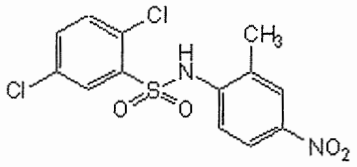
~~31~~27. Use of ~~A method of treating a patient afflicted with cancer, comprising the steps of:~~

~~(a) administering to the patient~~ a composition comprising:

an agent to interfere with phosphorylation of tyrosine Y192 and~~/or~~ Y231 in the polypeptide of SEQ ID NO. 1., wherein the agent is selected from one of an antibody, a peptide, an aptamer and a small interfering RNA; and

a TCF/ β-catenin inhibitor or an anti-estrogen receptor-α compound in preparation of a medicament for the treatment of breast cancer or lung cancer.

~~32~~28. The ~~method~~ use of claim ~~31~~ 27 wherein the TCF/β-catenin inhibitor ~~anti-estrogen receptor compound~~ is an FH535 of formula 1.



~~33~~29. The ~~method~~ use of claim ~~31~~ 27 wherein the anti-estrogen receptor-α compound is a Fulvestrant of formula 2

