

Claims

1. An *in vitro* method for the prognosis of overall survival, cancer recurrence or response to treatment for a patient suffering from cancer, the method comprising:

5 (a) examining a sample from the patient to determine whether the patient is human epidermal growth factor receptor 2 (HER2) positive or negative based on a predetermined level of HER2; and

(b) measuring WW domain-binding protein 2 (WBP2) levels in the patient's sample,

10 wherein a result in step (a) and a result in step (b) are compared to a set of predetermined expression level results from a comparison population wherein the comparison population is stratified into a plurality of four subgroups determining the aggressiveness of a cancer and provides a prognosis of overall survival, cancer recurrence or response to treatment for the patient.

15 2. The method of claim 1, wherein each subgroup is referenced from a reference group of HER2 negative patients comprising WBP2 expression below a predetermined level.

20 3. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 4 to 5 times lower chance of overall survival compared to the reference group.

25 4. The method of claim 2, wherein a sample with WBP2 expression levels below the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 1 to 2 times lower chance of
30 overall survival compared to the reference group.

5. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 negative patient provides the prognosis that the patient has an approximate 2 to 3 times lower chance of overall survival compared to the reference group.

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6. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 2 to 3 times higher chance of cancer recurrence compared to the reference group.

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7. The method of claim 2, wherein a sample with WBP2 expression levels below the predetermined level and a HER2 positive patient provides the prognosis that the patient has an approximate 1 times higher chance of cancer recurrence compared to the reference group.

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8. The method of claim 2, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 negative patient provides the prognosis that the patient has an approximate 1 to 2 times higher chance of cancer recurrence compared to the reference group.

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9. The method of any one of claims 1 to 3, wherein a sample with WBP2 expression levels above the predetermined level and a HER2 positive result predicts that the patient is likely to respond to treatment.

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10. The method of any one of claims 1 to 3, wherein a sample with WBP2 expression levels below the predetermined level and a HER2 positive result predicts that the patient is less likely to respond to treatment.

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11. The method of claim 9 or 10, wherein the treatment comprises a HER2 antagonist.

12. The method of claim 11, wherein the HER2 antagonist comprises Herceptin (Trastuzumab), Pertuzumab, Lapatinib, Lapatinib in combination with capecitabine, Trastuzumab emtansin, Ado-trastuzumab, Neratinib, Amrubicin or Dasatinib.

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13. The method of any one of the preceding claims, wherein the WBP2 levels in the patient's sample are measured with at least one probe adapted to target a WBP2 protein.

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14. The method of claim 13, wherein the probe is an antibody.

15. The method of claim 13, wherein the probe is an aptamer.

16. The method of claim 13, wherein the probe is a peptide.

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17. The method of any one of the preceding claims, wherein the cancer is breast cancer.

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18. A kit for identifying in a sample the amount of human epidermal growth factor receptor 2 (HER2) and the amount of WW domain-binding protein 2 (WBP2), the kit comprising:

(a) at least one first probe adapted to detect and measure a human epidermal growth factor receptor 2 (HER2) level in the sample to determine whether the sample is HER2 positive or HER2 negative;

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(b) at least one second probe adapted to detect and measure WW domain-binding protein 2 (WBP2) levels in the sample; and

(c) written instructions for examining a sample to determine a population stratified into a plurality of four subgroups prognostic of overall survival, cancer recurrence or response to treatment for the patient.

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19. The kit of claim 18, wherein the first probe is adapted to target a HER2 gene.

20. The kit of claim 18, wherein the second probe is adapted to target
5 a WBP2 gene.

21. The kit of claim 18, wherein the first probe is adapted target a HER2 protein.

10 22. The kit of claim 18, wherein the second probe is adapted to target a WBP2 protein.

23. The kit of claim 21 or 22, wherein the first and second probe is an antibody.
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24. The kit of claim 21 or 22, wherein the first and second probe is an aptamer.

25. The kit of claim 21 or 22, wherein the first and second probe is a
20 peptide.

26. An *in vitro* method for determining the prognosis of overall survival, cancer recurrence or response to treatment, the method comprising:

25 (a) measuring the level of human epidermal growth factor receptor 2 (HER2) in a sample;

(b) measuring the level of WW domain-binding protein 2 (WBP2) in the sample; and

(c) determining whether the level of HER2 and WBP2 are above or
30 below a predetermined level

(d) stratifying the sample into one of four subgroups to provide a prognosis of overall cancer survival, cancer recurrence or response to cancer treatment.