

What is claimed is:

1. A method of identifying the presence or absence of prostate cancer in a subject in need thereof, the method comprising:

(a) determining the expression level of at least 24 biomarkers in a saliva sample from the subject, wherein the at least 24 biomarkers comprise *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, *XPC*, and a housekeeping gene;

(b) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*;

(c) inputting each normalized expression from step (b) into an algorithm to generate a score;

(d) comparing the score to a predetermined cutoff value; and

(e) identifying the presence of prostate cancer in the subject when the score is greater than or equal to the predetermined cutoff value or determining the absence of prostate cancer in the subject when the score is less than the predetermined cutoff value.

2. The method of claim 1, wherein the predetermined cutoff value is 23% on a scale of 0-100%.

3. A method of determining whether a prostate cancer in a subject is stable or progressive, the method comprising:

(a) determining the expression level of at least 24 biomarkers in a saliva sample from the subject, wherein the at least 24 biomarkers comprise *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, *XPC*, and a housekeeping gene;

(b) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*;

(c) inputting each normalized expression level from step (b) into an algorithm to generate a score;

(d) comparing the score to a predetermined cutoff value; and

(e) determining that the prostate cancer is progressive when the score is greater than or equal to the predetermined cutoff value or determining that the prostate cancer is stable when the score is less than the predetermined cutoff value.

4. The method of claim 3, wherein the predetermined cutoff value is 50% on a scale of 0-100%.

5. A method of determining whether a prostate cancer in a subject has a low Gleason score (≤ 6) or a high Gleason score (≥ 7), the method comprising:

(a) determining the expression level of at least 24 biomarkers in a saliva sample from the subject, wherein the at least 24 biomarkers comprise *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*, and a housekeeping gene;

(b) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*;

(c) inputting each normalized expression level from step (b) into an algorithm to generate a score;

(d) comparing the score to a predetermined cutoff value; and

(e) determining that the prostate cancer in the subject has a high Gleason score (≥ 7) when the score is greater than or equal to the predetermined cutoff value or determining that the prostate cancer in the subject has a low Gleason score (≤ 6) when the score is less than the predetermined cutoff value.

6. The method of claim 5, wherein the predetermined cutoff value is 50% on a scale of 0-100%.

7. A method of determining the completeness of surgery in a subject having a prostate cancer, the method comprising:

(a) determining the expression level of at least 24 biomarkers in a saliva sample from the subject after the surgery, wherein the 24 biomarkers comprise *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, *XPC*, and a housekeeping gene;

(b) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*;

(c) inputting each normalized expression level from step (b) into an algorithm to generate a score;

(d) comparing the score to a predetermined cutoff value; and

(e) identifying that the prostate cancer is not completely removed when the score is greater than or equal to the score or identifying that the prostate cancer is completely removed when the score is less than the predetermined cutoff value.

8. The method of claim 7, wherein the predetermined cutoff value is 50% on a scale of 0-100%.

9. A method of evaluating the response of a subject having a prostate cancer to an anti-prostate cancer therapy, the method comprising:

(a) at a first time point:

(i) determining the expression level of at least 24 biomarkers in a saliva sample from the subject, wherein the at least 24 biomarkers comprise *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, *XPC*, and a housekeeping gene;

(ii) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*; and

(iii) inputting each normalized expression level from step (a)(ii) into an algorithm to generate a first score;

(b) at a second time point, wherein the second time point is after the first time point and after the therapy has been administered to the subject:

(i) determining the expression level of the at least 24 biomarkers in a saliva sample from the subject;

(ii) normalizing the expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *AAMP*, *CHTOP*, *EDC4*, *FYCO1*, *HNRNPU*, *HPN*, *KRT23*, *MAN2B2*, *MAX*, *MRPS25*, *NDUFS2*, *PPRC1*, *RAD23A*, *REPIN1*, *SDR39U1*, *SETBP1*, *SLC18A2*, *SMC4*, *SPARC*, *SQLE*, *STRIP1*, *STX12*, *UNC45A*, and *XPC*; and

(iii) inputting each normalized expression level from step (b)(ii) into an algorithm to generate a second score;

(c) comparing the first score and second score; and

(d) identifying that the subject is responsive to the anti-prostate cancer therapy when the second score is decreased as compared to the first score or identifying that the subject is not responsive to the anti-prostate cancer therapy when the second score is not decreased as compared to the normalized expression levels from step (a)(ii).

10. The method of claim 9, wherein the first time point is before the therapy is to be administered to the subject.
11. The method of claim 9, wherein the first time point is after the therapy has been administered to the subject.
12. The method of any one of claims 9-11, wherein the subject is identified as responsive to the anti-neuroendocrine cancer therapy when the second is at least 5% less than the first score.
13. The method of any one of the preceding claims, wherein the housekeeping gene is selected from the group consisting of *ATG4B*, *RHOA*, *TOX4*, *TPT1*, and *TXNIP*.
14. The method of claim 13, wherein the housekeeping gene is *TOX4*.
15. The method of any one of the preceding claims, having:
 - i) a sensitivity of at least 90%; and/or
 - ii) a specificity of at least 90%.
16. The method of any one of the preceding claims, wherein at least one of the at least 24 biomarkers is RNA, cDNA, or protein.
17. The method of claim 16, wherein:
 - i) when the biomarker is RNA, the RNA is reverse transcribed to produce cDNA, and the produced cDNA expression level is detected;
 - ii) when the biomarker is protein, the protein detected by forming a complex between the protein and a labeled antibody; and/or
 - iii) when the biomarker is RNA or cDNA, the RNA or cDNA is detected by forming a complex between the RNA or cDNA and a labeled nucleic acid probe or primer.
18. The method of any one of the preceding claims, wherein the first predetermined cutoff value is derived from a plurality of reference samples obtained from subjects not having or not diagnosed with a neoplastic disease.

19. The method of claim 18, wherein the neoplastic disease is prostate cancer.
20. The method of any one of the preceding claims wherein the algorithm is XGB, RF, glmnet, cforest, CART, treebag, knn, nnet, SVM-radial, SVM-linear, NB, or mlp.
21. The method of claim 20, wherein the algorithm is Random Forest.
22. The method of claim 21, wherein the machine learning algorithm is trained using the expression levels or normalized expression levels of the at least 24 biomarkers obtained from a plurality of reference samples obtained from subjects not having a neuroendocrine cancer and the expression levels or normalized expression levels of the at least 24 biomarkers from a plurality of reference samples obtained from subjects having neuroendocrine cancer.
23. The method of any one of the preceding claims, further comprising treating the subject identified as having prostate cancer with at least one anti-prostate cancer therapy.
24. The method of any one of the preceding claims, wherein the anti-prostate cancer therapy comprises active surveillance, surgery, radiation therapy, cryotherapy, hormone therapy, chemotherapy, vaccine treatment, bone-directed treatment, or any combination thereof.
25. The method of claim 24, wherein:
 - i) the radiation therapy comprises external beam radiation, brachytherapy, radiopharmaceuticals or any combination thereof, preferably wherein the radiopharmaceuticals comprise ¹⁷⁷Lu-PSMA;
 - ii) the hormone therapy comprises androgen suppression therapy;
 - iii) the chemotherapy comprises docetaxel, cabazitaxel, mitoxantrone, estramustine, or any combination thereof;
 - iv) the vaccine treatment comprises Sipuleucel-T; and/or
 - v) the bone-directed treatment comprises a bisphosphonate, denosumab, a corticosteroid, or a combination thereof.