

CLAIMS

1. An *in vitro* method of detecting a prostate cancer in a subject, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from the subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample;

wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction;

wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a prostate cancer .

2. The method according to claim 1, wherein the early endosomal marker is selected from APPL1 and EEA1, and the late endosomal marker is selected from SDC1 and RAB7.

3. The method according to claim 1 or claim 2, wherein the method further comprises detecting one or more of an early endosomal marker, a late endosomal marker, a marker associated with endosomal biogenesis, a marker associated with endosomal trafficking and a marker associated with endosomal recycling.

4. The method according to claim 3, wherein the selected marker comprises one or more of CATHEPSIN B, CATHEPSIN D, α -GALACTOSIDASE, LIMP-1, LIMP-2, TFR1, TFR2, STAMP2, SORT1 (SORTILIN), LAMP-1, RAB4, APPL2, RAB5, RAB11, MPR, PAP, ACTIN, M6PR, IGFR2, MYO1B, PDCD6IP, SDCBP, STX7, STX12, FGF1, FGF2, FGF3, FGFR1, FGFR2, FGFR3, NOX2, NOX4, and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

5. The method according to claim 4, wherein one or more of an altered presence, altered level, altered secretion and altered distribution of the selected marker is indicative of prostate cancer in the subject.

6. The method according to claim 5, wherein one or more of an increased level of RAB5 protein and/or mRNA, an increased secretion of RAB5 protein, an increased level of APPL1 protein and/or mRNA, an increased secretion of APPL1 protein, an increased level of

EEA1 protein and/or mRNA, an increased secretion of EEA1 protein, an increased level of LIMP-2 protein and/or mRNA, an increased level of TFR1 protein and/or mRNA, an increased level of TFR2 protein and/or mRNA, an increased level of RAB4 protein and/or mRNA, an increased secretion of RAB4 protein, an increased level of APPL2 protein and/or mRNA, a decreased level of LAMP1 protein and/or mRNA, an increased secretion of RAB11 protein, a decreased secretion of RAB7 protein, a decreased level of CATHEPSIN B protein or mRNA, a decreased level of CATHEPSIN D protein or mRNA, an increased level of α -GALACTOSIDASE protein or mRNA, a decreased level of STX7 protein or mRNA, a decreased level of STX12 protein or mRNA, an increased secretion of PDCD6IP protein, a decreased secretion of SDCBP protein, a decreased secretion of SORT1 protein, a decreased level of FGF1 protein or mRNA, a decreased level of FGF2 protein or mRNA, an increased level of FGF3 protein or mRNA, a decreased level of FGFR1 protein or mRNA, a decreased level of FGFR2 protein or mRNA, an increased level of FGFR3 protein or mRNA, an increased level of NOX2 protein or mRNA, and increased level of NOX4 protein or mRNA, an increased nuclear and/or nucleoli level of APPL1 protein, an increased nuclear membrane level of RAB7 protein, and an enlarged LIMP2 protein positive vesicles, is indicative of prostate cancer in the subject.

7. The method according to claim 5 or 6, wherein an altered presence, altered level, altered expression, altered secretion and altered distribution is as compared to one or more of non-malignant tissue, prostatic intraepithelial neoplasia, primary prostate cancer and metastatic prostate cancer.

8. The method according to claim 7, wherein LIMP2 protein or mRNA is increased in prostatic intraepithelial neoplasia as compared non-malignant prostate, LAMP1 protein or mRNA is decreased in metastatic prostate cancer as compared prostatic intraepithelial neoplasia, LAMP1 protein or mRNA is increased in primary prostate cancer as compared to metastatic prostate cancer, CATHEPSIN B protein or mRNA is decreased in primary prostate cancer as compared to non-malignant tissue, CATHEPSIN B protein or mRNA is decreased in metastatic prostate cancer as compared to non-malignant prostate, ACID CERAMIDASE protein or mRNA is increased in prostatic intraepithelial neoplasia as compared to non-malignant prostate, ACID CERAMIDASE protein or mRNA is increased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, ACID CERAMIDASE protein or mRNA is increased in primary prostate cancer as compared to metastatic prostate

cancer, APPL1 protein or mRNA is increased in primary prostate cancer as compared to non-malignant tissue, APPL2 protein or mRNA is increased in prostatic intraepithelial neoplasia as compared to non-malignant prostate, APPL2 protein or mRNA is increased in primary prostate cancer as compared to non-malignant tissue, APPL2 protein or mRNA is increased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, APPL2 protein or mRNA is increased in primary prostate cancer as compared to metastatic prostate cancer, RAB5 protein or mRNA is decreased in metastatic prostate cancer as compared to non-malignant prostate, EEA1 protein or mRNA is decreased in metastatic prostate cancer as compared non-malignant prostate, EEA1 protein or mRNA is decreased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, RAB4A protein or mRNA is decreased in metastatic prostate cancer as compared to non-malignant prostate, RAB4A protein or mRNA is decreased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, RAB4A protein or mRNA is decreased in prostatic intraepithelial neoplasia as compared to primary prostatic cancer, RAB4A protein or mRNA is decreased in primary prostate cancer as compared to metastatic prostate cancer, MYO1B protein or mRNA is increased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, MYO1B protein or mRNA is decreased in metastatic prostate cancer as compared prostatic intraepithelial neoplasia, MYO1B protein or mRNA is decreased in metastatic prostate cancer as compared to primary prostate cancer, PDCD6IP protein or mRNA is decreased in prostatic intraepithelial neoplasia as compared to metastatic prostate cancer, PDCD6IP protein or mRNA is decreased in prostatic intraepithelial neoplasia as compared to non-malignant prostate, SDCBP protein or mRNA is decreased in metastatic prostate cancer as compared to primary prostate cancer, STX7 protein or mRNA is decreased in metastatic prostate cancer as compared to primary prostate cancer, FGFR1 protein or mRNA is increased in metastatic prostate cancer as compared prostatic intraepithelial neoplasia, FGFR2 protein or mRNA is decreased in primary prostate cancer as compared to non-malignant tissue, NOX2 protein or mRNA is increased in primary prostate cancer as compared to non-malignant tissue and NOX4 protein or mRNA is increased in metastatic prostate cancer as compared prostatic intraepithelial neoplasia.

9. The method according to any one of claims 1 to 8, wherein a biological sample is to be obtained from the subject and processed to allow detection of the selected markers.

10. The method according to claim 9, wherein the biological sample comprises one or more of a blood sample, a plasma sample, a serum sample, a biopsy and a prostate tissue sample.

11. The method according to any one of claims 3 to 10, wherein the method comprises comparing the presence and/or level of the selected markers with the presence and/or level of one or more other markers associated with an altered risk of prostate cancer and/or one or more other markers known to be indicative of the presence or absence of prostate cancer in the subject.

12. The method according to claim 11, wherein the one or more other markers comprises prostate specific antigen.

13. The method according to any one of claims 1 to 12, wherein the method further comprises obtaining information relating to one or more clinical characteristics of the subject and using the information in combination with one or more of the presence, level, secretion and distribution of the selected marker to detect prostate cancer in the subject.

14. The method according to any one of claims 1 to 13, wherein the method comprises using a computer processor means to process data associated with one or more of the presence, level, secretion and distribution of the selected marker, and optionally one or more clinical characteristics, to generate a likelihood and/or risk of the presence of prostate cancer in the subject.

15. The method according to any one of claims 1 to 14, wherein the prostate cancer is selected from a prostatic intraepithelial neoplasia, a primary prostate cancer, and a metastatic prostate cancer.

16. The method according to any one of claims 1 to 15, wherein the method is used to diagnose prostate cancer in the subject, to screen for prostate cancer in the subject, for assessing prognosis, to determine the metastatic potential of a prostate cancer, to identify a subject suffering from prostate cancer, to identify a subject susceptible to prostate cancer, to determine the rate of relapse of prostate cancer in the subject, to determine the risk of mortality from prostate cancer in the subject, to stratify the prostate cancer, to discriminate between prostate cancer and not having prostate cancer in the subject, to determine whether the prostate cancer is an organ confined cancer, to discriminate between prostate cancer and one or more of benign prostatic hyperplasia, prostatitis and an inflammatory condition of the prostate, to determine

pathogenic progression, to assess whether the prostate cancer is slowing growing, indolent, or aggressive, to exclude the presence of prostate cancer in the subject, to identify a subject suitable for treatment and/or surgery for prostate cancer, and to determine the likelihood or risk of a subject having prostate cancer.

17. An *in vitro* method of detecting a prostate cancer in a subject, the method comprising: processing a sample obtained from the subject to allow detection of an early endosomal marker and a late endosomal marker in a sample obtained from a subject; determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample; and identifying a prostate cancer in the subject, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.

18. An *in vitro* method of screening for a prostate cancer in a subject, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from a subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the subject, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.

19. The method according to claim 18, wherein the method is used to identify a subject suffering from, or susceptible to, a prostate cancer.

20. The method according to claim 19, wherein the method is used to exclude a subject not suffering from, or not susceptible to, a prostate cancer.

21. An *in vitro* method of identifying a subject suffering from, or susceptible to, a prostate cancer, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from the subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.

22. An *in vitro* method of diagnosis for detecting a prostate cancer in a subject, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from the subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.
23. An *in vitro* method of determining the likelihood and/or risk of a subject suffering from, or being susceptible to, a prostate cancer, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from the subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of a likelihood and/or risk of the subject suffering from and being susceptible to a prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.
24. An *in vitro* method for determining the progression of a prostate cancer in a subject, the method comprising detecting an early endosomal marker and a late endosomal marker in a sample obtained from the subject, and determining the ratio of the level of the early endosomal marker to the late endosomal marker in the sample, wherein an increased ratio of the early endosomal marker to the late endosomal marker as compared to non-malignant tissue is indicative of the progression of prostate cancer; wherein the detection method is a detection method selected from polymerase chain reaction and immunological reaction.
25. The method according to claim 24, wherein the method comprises determining biochemical recurrence of the cancer, relapse rate and/or survival rate.
26. The method according to claim 25, wherein the level of the marker is indicative of a reduced relapse rate and/or increased survival rate.
27. The method according to claim 25, wherein the method further comprises detecting one or more of LIMP2, CATHEPSIN B, CAPTHESIN D, α -GALACTOSIDASE, RAB5A, EEA1, RAB7A, M6PR, IGFR2, SORT1, MYO1B, PDCD6IP, SDC1, STX12, FGF2, FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

28. The method according to claim 27, wherein the marker comprises one or more of decreased or lower LIMP2, increased or higher CATHEPSIN B, increased or higher CATHEPSIN D, increased or higher α -GALACTOSIDASE, decreased or lower RAB5A, decreased or lower EEA1, increased or higher RAB7A, increased or higher M6PR, decreased or lower IGFR2, decreased or lower SORT1, decreased or lower MYO1B, increased or higher PDCD6IP, increased or higher STX12, increased or higher FGF2, increased or higher FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

29. The method according to any one of claims 24 to 28, wherein the method further comprises identifying the level of PSA expression in the subject and stratifying the expression of the marker on the basis of the PSA expression level in the subject.

30. The method according to claim 29, wherein the PSA is a level indicative of a low risk of prostate cancer.

31. The method according to claim 30, wherein the PSA level is less than 10 ng/ml in blood, plasma and/or serum.

32. The method according to claim 30 or 31, wherein the PSA is a level of 7.8 ng/ml or less in blood, plasma and/or serum.

33. The method according to any one of claims 30 to 32, wherein the marker comprises one or more of LIMP2, CATHEPSIN B, α -GALACTOSIDASE, RAB5A, EEA1, M6PR, IGFR2, SORT1, MYO1B, PDCD6IP, SDC1, STX12, FGF2, FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

34. The method according to claim 33, wherein the marker comprises one or more of decreased or lower LIMP2, increased or higher CATHEPSIN B, increased or higher α -GALACTOSIDASE, decreased or lower RAB5A, decreased or lower EEA1, increased or higher M6PR, decreased or lower IGFR2, decreased or lower SORT1, decreased or lower MYO1B, increased or higher PDCD6IP, increased or higher SDC1, increased or higher STX12, increased or higher FGF2, increased or higher FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a

processed form of one of the aforementioned.

35. The method according to claim 25, wherein the level of the marker is indicative of an increased relapse rate and/or decreased survival rate.

36. The method according to claim 35, wherein the marker comprises one or more of LIMP2, CATHEPSIN B, CATHEPSIN D, α -GALACTOSIDASE, RAB5A, EEA1, RAB7A, M6PR, IGFR2, SORT1, MYO1B, PDCD6IP, SDC1, STX12, FGF2, FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

37. The method according to claim 35, wherein the marker comprises one or more of increased or higher LIMP2, decreased or lower CATHEPSIN B, decreased or lower CATHEPSIN D, decreased or lower α -GALACTOSIDASE, increased or higher RAB5A, increased or higher EEA1, decreased or lower RAB7A, decreased or lower M6PR, increased or higher IGFR2, increased or higher SORT1, increased or higher MYO1B, decreased or lower PDCD6IP, decreased or lower STX12, decreased or lower FGF2, decreased or lower FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

38. The method according to any one of claims 35 to 38, wherein the method further comprises identifying the level of PSA expression in the subject and stratifying the expression of the marker on the basis of the PSA expression level in the subject.

39. The method according to claim 38, wherein the PSA is a level indicative of a low risk of prostate cancer.

40. The method according to claim 39, wherein the PSA level is less than 10 ng/ml in blood, plasma and/or serum.

41. The method according to claim 39 or 40, wherein the PSA is a level of 7.8 ng/ml or less in blood, plasma and/or serum.

42. The method according to any one of claims 39 to 41, wherein the marker comprises one or more of LIMP2, CATHEPSIN B, α -GALACTOSIDASE, RAB5A, EEA1, M6PR, IGFR2, SORT1, MYO1B, PDCD6IP, SDC1, STX12, FGF2, FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned,

and a processed form of one of the aforementioned.

43. The method according to claim 42, wherein the marker comprises one or more of increased or higher LIMP2, decreased or lower CATHEPSIN B, decreased or lower α -GALACTOSIDASE, increased or higher RAB5A, increased or higher EEA1, decreased or lower M6PR, increased or higher IGFR2, increased or higher SORT1, increased or higher MYO1B, decreased or lower PDCD6IP, decreased or lower SDC1, decreased or lower STX12, decreased or lower FGF2, decreased or lower FGF3 and/or a mRNA encoding one of the aforementioned, a fragment of one of the aforementioned, a derivative of one of the aforementioned, and a processed form of one of the aforementioned.

44. A kit when used in performing the *in vitro* method of any one of claims 1 to 43.