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Mitchell et al.

(54) **BIOMARKERS FOR PROSTATE CANCER AND METHODS USING THE SAME**

(75) Inventors: **Matthew W. Mitchell**, Durham, NC (US); **Alvin Berger**, Raleigh, NC (US); **Kay A. Lawton**, Raleigh, NC (US)

Correspondence Address:
BRINKS, HOFER, GILSON & LIONE
P.O. BOX 110285
RESEARCH TRIANGLE PARK, NC 27709 (US)

(73) Assignee: **METABALON, INC.**, Durham, NC (US)

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A61K 31/132	(2006.01)
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(57) **ABSTRACT**

Methods for identifying and evaluating suites of biochemical and/or gene entities useful as biomarkers for early prediction of prostate cancer, disease grading, target identification/validation, and monitoring of drug efficacy are provided. Also provided are suites of small molecule entities as biomarkers for prostate cancer.

Figure 1

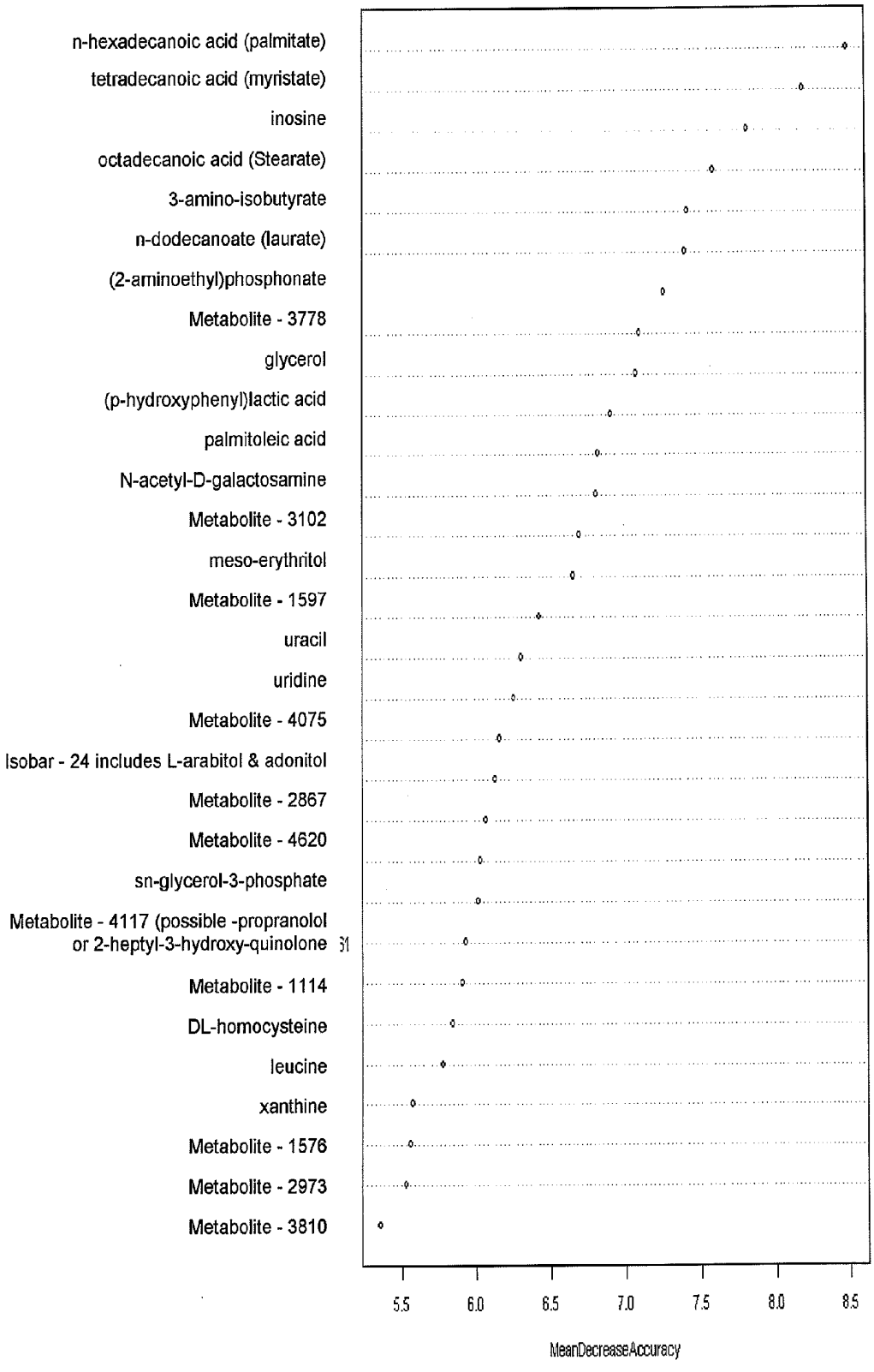

n-hexadecanoic acid (palmitate)
tetradecanoic acid (myristate)
inosine
octadecanoic acid (Stearate)
3-amino-isobutyrate
n-dodecanoate (laurate)
(2-aminoethyl)phosphonate
Metabolite - 3778
glycerol
(p-hydroxyphenyl)lactic acid
palmitoleic acid
N-acetyl-D-galactosamine
Metabolite - 3102
meso-erythritol
Metabolite - 1597
uracil
uridine
Metabolite - 4075
Isobar - 24 includes L-arabitol & adonitol
Metabolite - 2867
Metabolite - 4620
sn-glycerol-3-phosphate
Metabolite - 4117 (possible -propranolol or 2-heptyl-3-hydroxy-quinolone
Metabolite - 1114
DL-homocysteine
leucine
xanthine
Metabolite - 1576
Metabolite - 2973
Metabolite - 3810
5.5
6.0
6.5
7.0
7.5
8.0
8.5
MeanDecreaseAccuracy

Figure 2

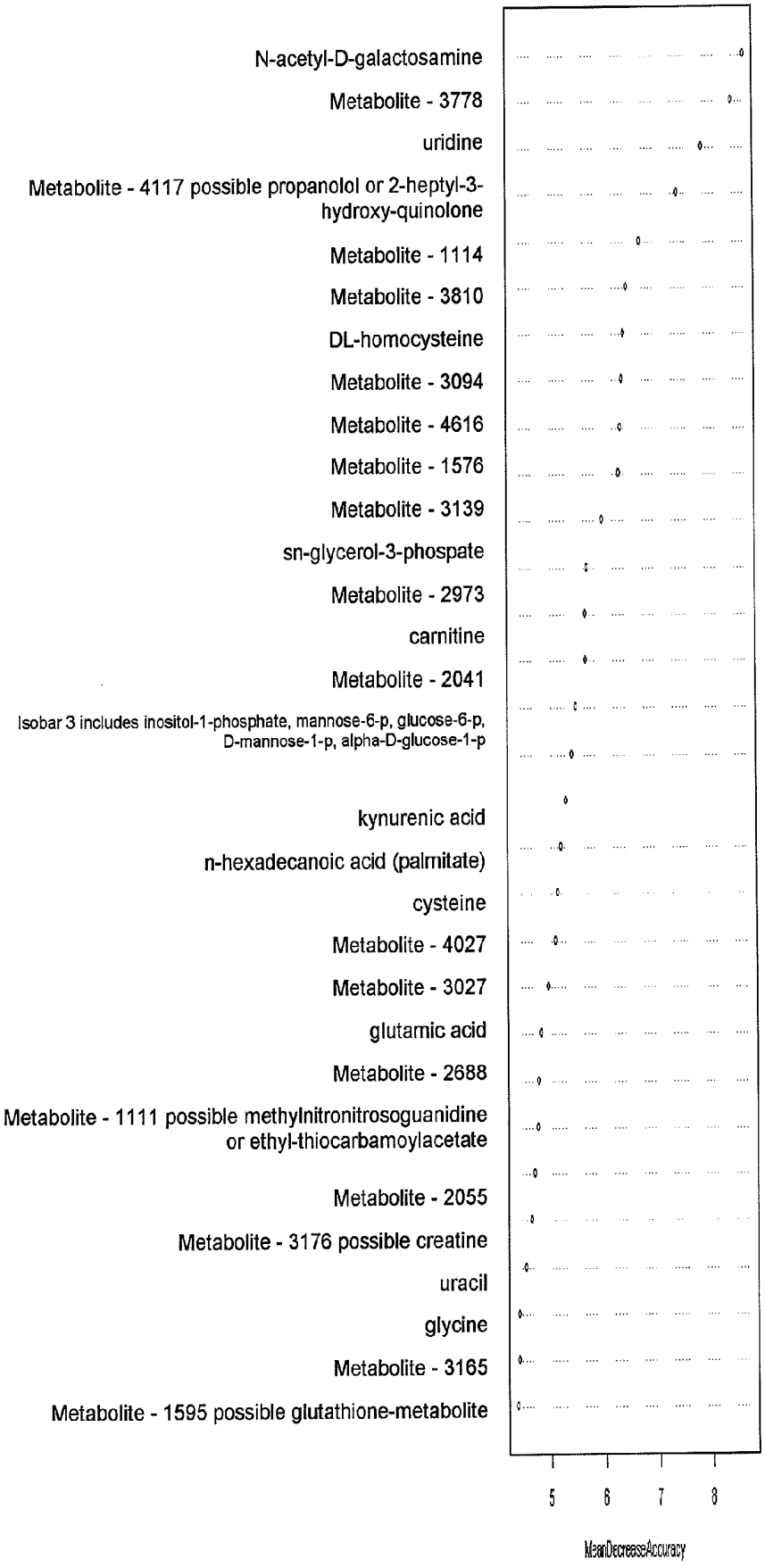

N-acetyl-D-galactosamine
Metabolite - 3778
uridine
Metabolite - 4117 possible propanolol or 2-heptyl-3-hydroxy-quinolone
Metabolite - 1114
Metabolite - 3810
DL-homocysteine
Metabolite - 3094
Metabolite - 4616
Metabolite - 1576
Metabolite - 3139
sn-glycerol-3-phospate
Metabolite - 2973
carnitine
Metabolite - 2041
Isobar 3 includes inositol-1-phosphate, mannose-6-p, glucose-6-p, D-mannose-1-p, alpha-D-glucose-1-p
kynurenic acid
n-hexadecanoic acid (palmitate)
cysteine
Metabolite - 4027
Metabolite - 3027
glutamic acid
Metabolite - 2688
Metabolite - 1111 possible methylnitronitrosoguanidine or ethyl-thiocarbamoylacetate
Metabolite - 2055
Metabolite - 3176 possible creatine
uracil
glycine
Metabolite - 3165
Metabolite - 1595 possible glutathione-metabolite
5
6
7
8
MeanDecreaseAccuracy

Figure 3

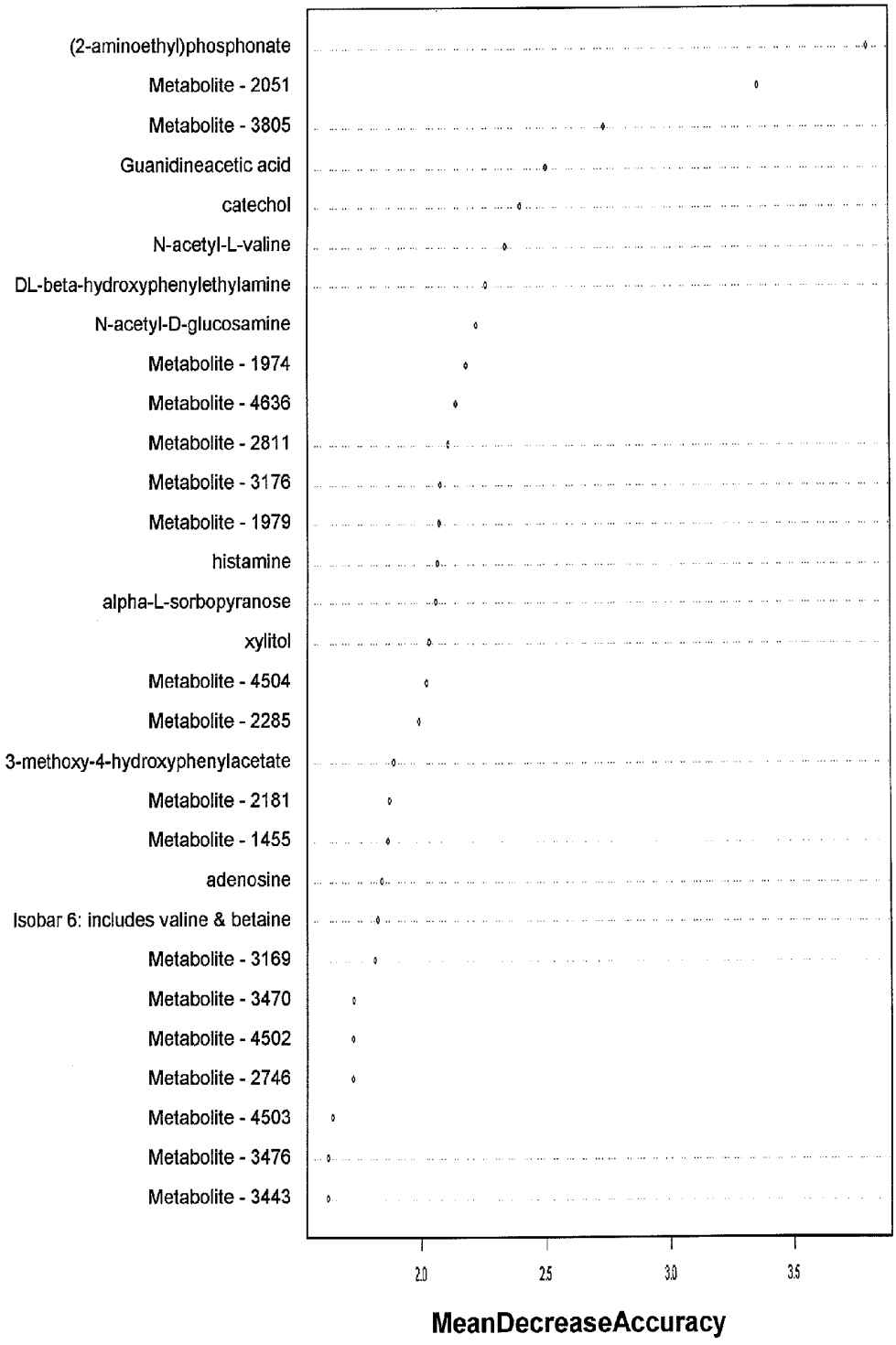

(2-aminoethyl)phosphonate
Metabolite - 2051
Metabolite - 3805
Guanidineacetic acid
catechol
N-acetyl-L-valine
DL-beta-hydroxyphenylethylamine
N-acetyl-D-glucosamine
Metabolite - 1974
Metabolite - 4636
Metabolite - 2811
Metabolite - 3176
Metabolite - 1979
histamine
alpha-L-sorbopyranose
xylitol
Metabolite - 4504
Metabolite - 2285
3-methoxy-4-hydroxyphenylacetate
Metabolite - 2181
Metabolite - 1455
adenosine
Isobar 6: includes valine & betaine
Metabolite - 3169
Metabolite - 3470
Metabolite - 4502
Metabolite - 2746
Metabolite - 4503
Metabolite - 3476
Metabolite - 3443
2.0
2.5
3.0
3.5
MeanDecreaseAccuracy

Figure 4


Metabolite - 3805
Histamine
Metabolite - 1455
Catechol
xylitol
Metabolite - 4636
Metabolite - 3691
Adenosine
Glycine
Metabolite - 3661
Metabolite - 3955
Methionine
Isobar 6 includes valine, betaine
guanidineacetic acid
Metabolite - 3817
N-acetyl-D-glucosamine
Metabolite - 3806
Metabolite - 2277
3-methoxy-4-hydroxyphenylacetate
Metabolite - 4502
Metabolite - 4519
Guanine
Metabolite - 2181
Alpha-L-sorbopyranose
Metabolite - 2270
Metabolite - 1498
Metabolite - 3443
tryptophan
Metabolite - 2051
gamma-L-glutamy-L-tyrosine
1.5
2.0
2.5
3.0
MeanDecreaseAccuracy

Figure 5

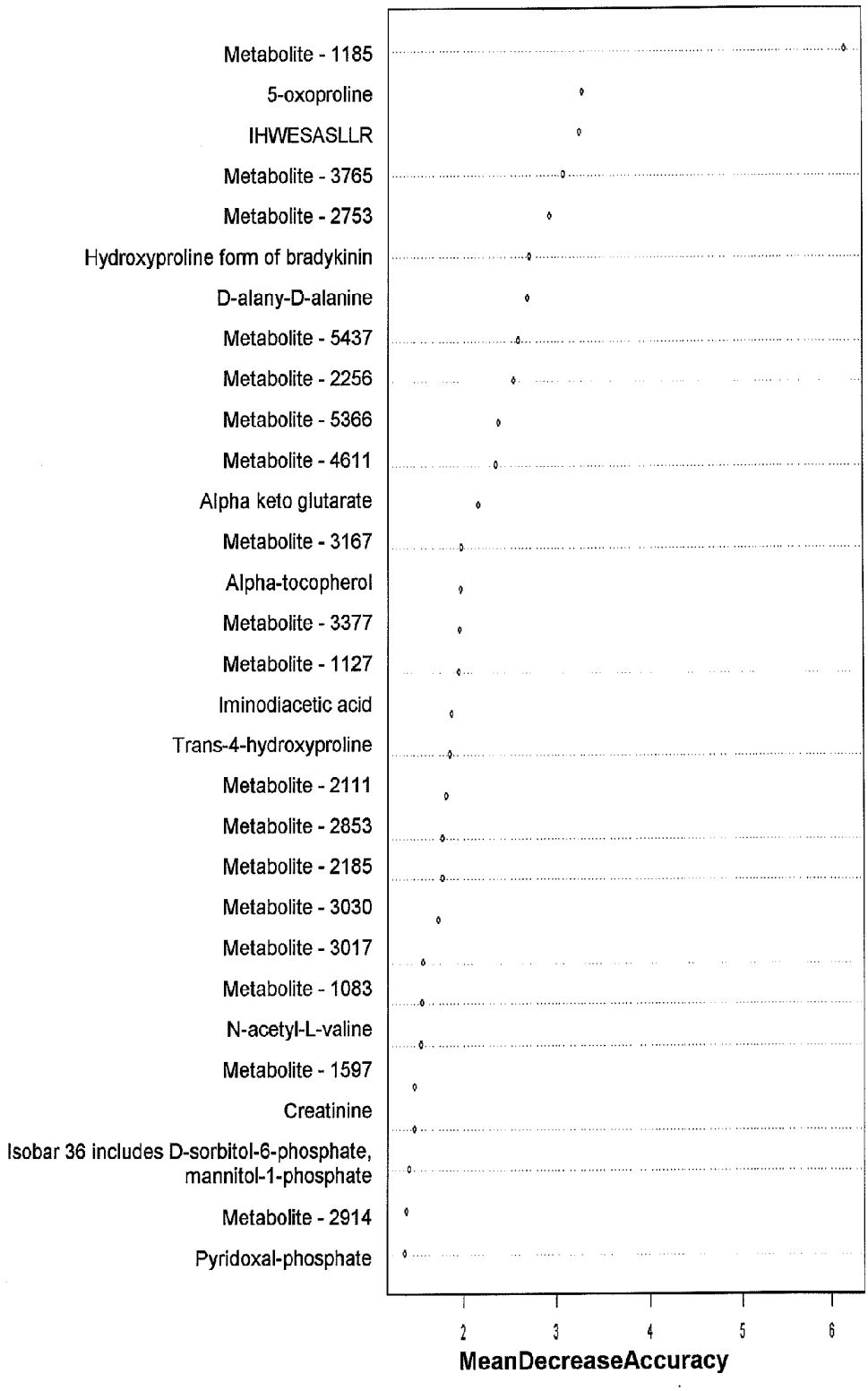

Metabolite - 1185
5-oxoproline
IHWESASLLR
Metabolite - 3765
Metabolite - 2753
Hydroxyproline form of bradykinin
D-alany-D-alanine
Metabolite - 5437
Metabolite - 2256
Metabolite - 5366
Metabolite - 4611
Alpha keto glutarate
Metabolite - 3167
Alpha-tocopherol
Metabolite - 3377
Metabolite - 1127
Iminodiacetic acid
Trans-4-hydroxyproline
Metabolite - 2111
Metabolite - 2853
Metabolite - 2185
Metabolite - 3030
Metabolite - 3017
Metabolite - 1083
N-acetyl-L-valine
Metabolite - 1597
Creatinine
Isobar 36 includes D-sorbitol-6-phosphate, mannitol-1-phosphate
Metabolite - 2914
Pyridoxal-phosphate
2
3
4
5
6
MeanDecreaseAccuracy

Figure 6

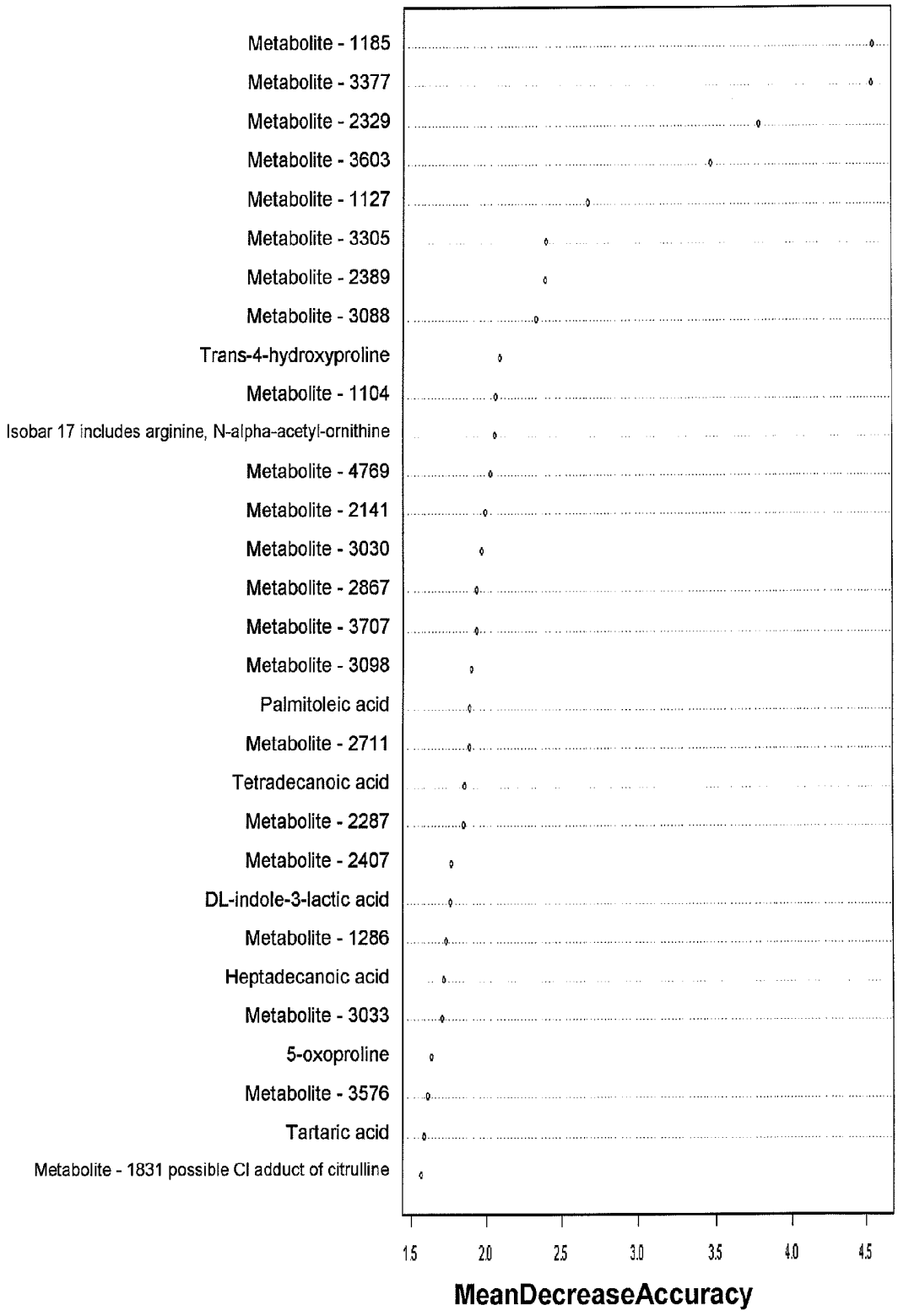
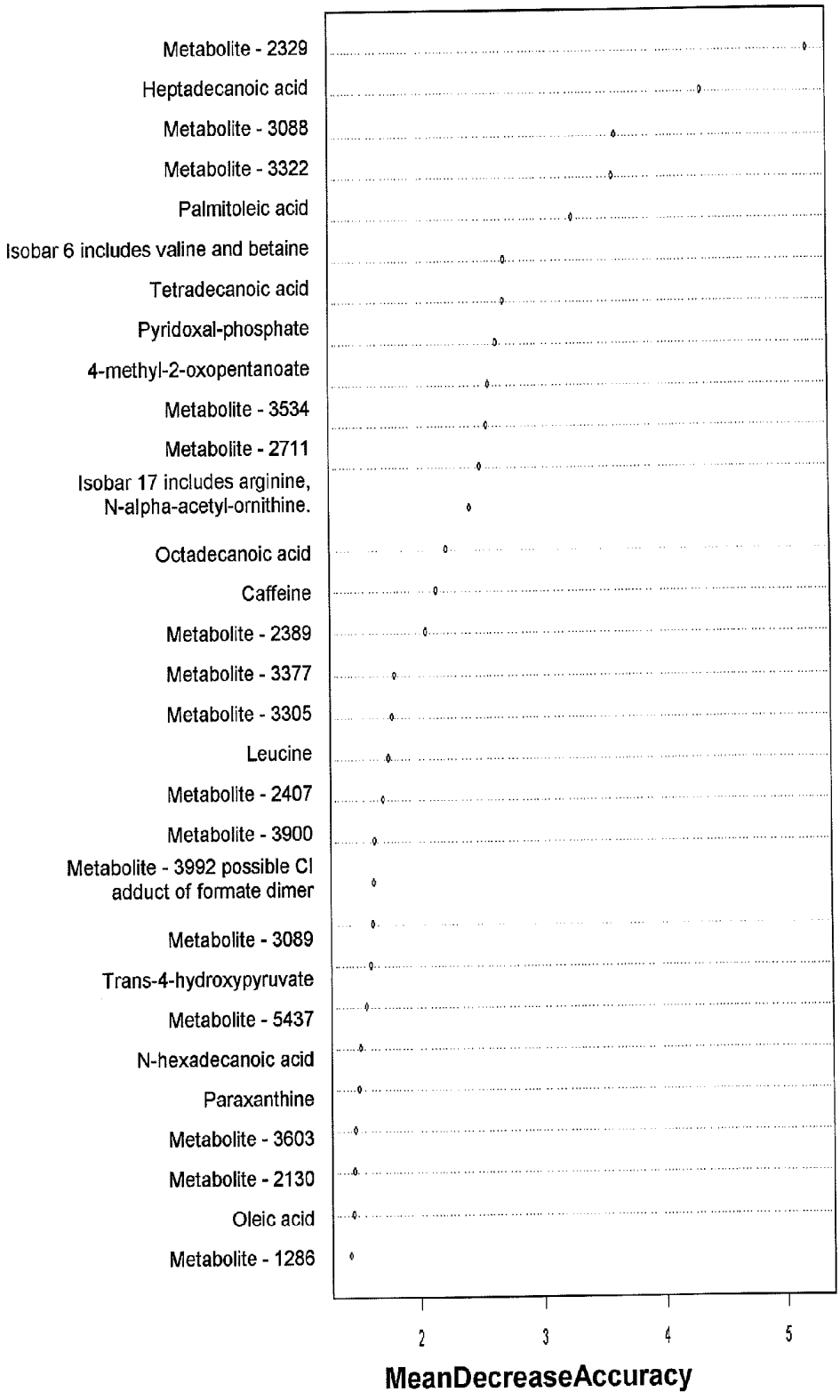

Metabolite - 1185
Metabolite - 3377
Metabolite - 2329
Metabolite - 3603
Metabolite - 1127
Metabolite - 3305
Metabolite - 2389
Metabolite - 3088
Trans-4-hydroxyproline
Metabolite - 1104
Isobar 17 includes arginine, N-alpha-acetyl-ornithine
Metabolite - 4769
Metabolite - 2141
Metabolite - 3030
Metabolite - 2867
Metabolite - 3707
Metabolite - 3098
Palmitoleic acid
Metabolite - 2711
Tetradecanoic acid
Metabolite - 2287
Metabolite - 2407
DL-indole-3-lactic acid
Metabolite - 1286
Heptadecanoic acid
Metabolite - 3033
5-oxoproline
Metabolite - 3576
Tartaric acid
Metabolite - 1831 possible Cl adduct of citrulline
1.5
2.0
2.5
3.0
3.5
4.0
4.5
MeanDecreaseAccuracy

Figure 7


Metabolite - 2329
Heptadecanoic acid
Metabolite - 3088
Metabolite - 3322
Palmitoleic acid
Isobar 6 includes valine and betaine
Tetradecanoic acid
Pyridoxal-phosphate
4-methyl-2-oxopentanoate
Metabolite - 3534
Metabolite - 2711
Isobar 17 includes arginine, N-alpha-acetyl-ornithine.
Octadecanoic acid
Caffeine
Metabolite - 2389
Metabolite - 3377
Metabolite - 3305
Leucine
Metabolite - 2407
Metabolite - 3900
Metabolite - 3992 possible Cl adduct of formate dimer
Metabolite - 3089
Trans-4-hydroxypyruvate
Metabolite - 5437
N-hexadecanoic acid
Paraxanthine
Metabolite - 3603
Metabolite - 2130
Oleic acid
Metabolite - 1286
2
3
4
5
MeanDecreaseAccuracy

BIOMARKERS FOR PROSTATE CANCER AND METHODS USING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 60/845,600, filed Sep. 19, 2006, the entire contents of which are hereby incorporated by reference herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[0002] This invention was made, in part, with Government support under Grant No. U01CA111275-01 from the National Institutes of Health. The U.S. Government may have certain rights in this invention.

FIELD

[0003] The invention generally relates to biomarkers for prostate cancer and methods based on the same biomarkers.

BACKGROUND

[0004] Prostate cancer is the leading cause of male cancer-related deaths and afflicts one out of nine men over the age of 65. The American Cancer Society estimates that over 200,000 American men will be diagnosed with prostate cancer and over 30,000 will die this year. While effective surgical and radiation treatments exist for localized prostate cancer, metastatic prostate cancer remains essentially incurable and most men diagnosed with metastatic disease will succumb over a period of months to years.

[0005] Prostate cancer is detected by either a digital rectal exam (DRE), or by the measurement of levels of prostate specific antigen (PSA), which has an unacceptably high rate of false-positives. The diagnosis of prostate cancer can be confirmed only by a biopsy. Radical prostatectomy, radiation and watchful waiting are generally effective for localized prostate cancer, but it is often difficult to determine which approach to use. Since it is not possible to distinguish between the indolent and more aggressive tumors current therapy takes a very conservative approach.

[0006] While imaging, X-rays, computerized tomography scans and further biopsies can help determine if prostate cancer has metastasized, they are not able to differentiate early stages. Understanding the progression of prostate cancer from a localized, early, indolent state, to an aggressive state, and, ultimately, to a metastatic state would allow the proper clinical management of this disease. Furthermore, early-indolent prostate cancer may be progressive or non-progressive toward aggressive forms.

SUMMARY

[0007] In one aspect, the present invention provides a method of diagnosing whether a subject has prostate cancer, comprising analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, where the one or more biomarkers are selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 and comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to diagnose whether the subject has prostate cancer.

[0008] In another aspect, the present invention also provides a method of determining whether a subject is predisposed to developing prostate cancer, comprising analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, where the one or more biomarkers are selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 20, 22, 24, and/or 26; and comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to determine whether the subject is predisposed to developing prostate cancer.

[0009] In yet another aspect, the invention provides a method of monitoring progression/regression of prostate cancer in a subject comprising analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, where the one or more biomarkers are selected from Tables 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 and the first sample is obtained from the subject at a first time point; analyzing a second biological sample from a subject to determine the level(s) of the one or more biomarkers, where the second sample is obtained from the subject at a second time point; and comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to monitor the progression/regression of prostate cancer in the subject.

[0010] In another aspect, the present invention provides a method of assessing the efficacy of a composition for treating prostate cancer comprising analyzing, from a subject having prostate cancer and currently or previously being treated with a composition, a biological sample to determine the level(s) of one or more biomarkers for prostate cancer selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 20, 22, 24, and/or 26; and comparing the level(s) of the one or more biomarkers in the sample to (a) levels of the one or more biomarkers in a previously-taken biological sample from the subject, where the previously-taken biological sample was obtained from the subject before being treated with the composition, (b) prostate cancer-positive reference levels of the one or more biomarkers, and/or (c) prostate cancer-negative reference levels of the one or more biomarkers.

[0011] In another aspect, the present invention provides a method for assessing the efficacy of a composition in treating prostate cancer, comprising analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26, the first sample obtained from the subject at a first time point; administering the composition to the subject; analyzing a second biological sample from the subject to determine the level(s) of the one or more biomarkers, the second sample obtained from the subject at a second time point after administration of the composition; comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the efficacy of the composition for treating prostate cancer.

[0012] In yet another aspect, the invention provides a method of assessing the relative efficacy of two or more compositions for treating prostate cancer comprising analyzing, from a first subject having prostate cancer and currently

or previously being treated with a first composition, a first biological sample to determine the level(s) of one or more biomarkers selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; analyzing, from a second subject having prostate cancer and currently or previously being treated with a second composition, a second biological sample to determine the level(s) of the one or more biomarkers; and comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the relative efficacy of the first and second compositions for treating prostate cancer.

[0013] In another aspect, the present invention provides a method for screening a composition for activity in modulating one or more biomarkers of prostate cancer, comprising contacting one or more cells with a composition; analyzing at least a portion of the one or more cells or a biological sample associated with the cells to determine the level(s) of one or more biomarkers of prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and comparing the level(s) of the one or more biomarkers with predetermined standard levels for the biomarkers to determine whether the composition modulated the level(s) of the one or more biomarkers.

[0014] In a further aspect, the present invention provides a method for identifying a potential drug target for prostate cancer comprising identifying one or more biochemical pathways associated with one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and identifying a protein affecting at least one of the one or more identified biochemical pathways, the protein being a potential drug target for prostate cancer.

[0015] In yet another aspect, the invention provides a method for treating a subject having prostate cancer comprising administering to the subject an effective amount of one or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 20, 22, 24, and/or 26 that are decreased in prostate cancer.

[0016] In another aspect, the invention also provides a method of distinguishing low grade prostate cancer from high grade prostate cancer in a subject having prostate cancer, comprising analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for low grade prostate cancer and/or high grade prostate cancer in the sample, where the one or more biomarkers are selected from Tables 3, 8, 11, 20 and/or 26 and comparing the level(s) of the one or more biomarkers in the sample to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or to high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer in order to determine whether the subject has low grade or high grade prostate cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. **1** provides an importance plot of one example of metabolites to distinguish Normal (N), Localized cancer tumor (T), and Metastatic tumor (M) tissue types.

[0018] FIG. **2** provides an importance plot of one example of metabolites to distinguish Normal prostate tissue (N) and Localized prostate tumor tissue (T).

[0019] FIG. **3** provides an importance plot of one example of metabolites to distinguish Non-cancer tissue (Control) and lower grade prostate cancer tissue (PCA) using urine samples.

[0020] FIG. **4** provides an importance plot of one example of metabolites to distinguish lower grade prostate cancer tissues and higher grade prostate cancer tissues from urine samples.

[0021] FIG. **5** provides an importance plot of one example of metabolites to distinguish non-cancer tissue (Control) and lower grade prostate cancer tissue (PCA) using plasma samples.

[0022] FIG. **6** provides an importance plot of one example of metabolites to distinguish lower grade prostate cancer tissues and higher grade prostate cancer tissues using plasma samples.

[0023] FIG. **7** provides an importance plot of one example of metabolites to distinguish subjects with lower grade prostate cancer and higher grade prostate cancer.

DETAILED DESCRIPTION

[0024] The present invention relates to biomarkers of prostate cancer, methods for diagnosis of prostate cancer, methods of distinguishing between low grade and high grade prostate cancer, methods of determining predisposition to prostate cancer, methods of monitoring progression/regression of prostate cancer, methods of assessing efficacy of compositions for treating prostate cancer, methods of screening compositions for activity in modulating biomarkers of prostate cancer, methods of treating prostate cancer, as well as other methods based on biomarkers of prostate cancer. Prior to describing this invention in further detail, however, the following terms will first be defined.

DEFINITIONS

[0025] "Biomarker" means a compound, preferably a metabolite, that is differentially present (i.e., increased or decreased) in a biological sample from a subject or a group of subjects having a first phenotype (e.g., having a disease) as compared to a biological sample from a subject or group of subjects having a second phenotype (e.g., not having the disease). A biomarker may be differentially present at any level, but is generally present at a level that is increased by at least 5%, by at least 10%, by at least 15%, by at least 20%, by at least 25%, by at least 30%, by at least 35%, by at least 40%, by at least 45%, by at least 50%, by at least 55%, by at least 60%, by at least 65%, by at least 70%, by at least 75%, by at least 80%, by at least 85%, by at least 90%, by at least 95%, by at least 100%, by at least 110%, by at least 120%, by at least 130%, by at least 140%, by at least 150%, or more; or is generally present at a level that is decreased by at least 5%, by at least 10%, by at least 15%, by at least 20%, by at least 25%, by at least 30%, by at least 35%, by at least 40%, by at least 45%, by at least 50%, by at least 55%, by at least 60%, by at least 65%, by at least 70%, by at least 75%, by at least 80%, by at least 85%, by at least 90%, by at least 95%, or by 100% (i.e., absent). A biomarker is preferably differentially present at a level that is statistically significant (i.e., a p-value less than 0.05 and/or a q-value of less than 0.10 as determined using either Welch's T-test or Wilcoxon's rank-sum Test).

[0026] The "level" of one or more biomarkers means the absolute or relative amount or concentration of the biomarker in the sample.

[0027] "Sample" or "biological sample" means biological material isolated from a subject. The biological sample may contain any biological material suitable for detecting the desired biomarkers, and may comprise cellular and/or non-

cellular material from the subject. The sample can be isolated from any suitable biological tissue or fluid such as, for example, prostate tissue, blood, blood plasma, urine, or cerebral spinal fluid (CSF).

[0028] "Subject" means any animal, but is preferably a mammal, such as, for example, a human, monkey, mouse, or rabbit.

[0029] A "reference level" of a biomarker means a level of the biomarker that is indicative of a particular disease state, phenotype, or lack thereof, as well as combinations of disease states, phenotypes, or lack thereof. A "positive" reference level of a biomarker means a level that is indicative of a particular disease state or phenotype. A "negative" reference level of a biomarker means a level that is indicative of a lack of a particular disease state or phenotype. For example, a "prostate cancer-positive reference level" of a biomarker means a level of a biomarker that is indicative of a positive diagnosis of prostate cancer in a subject, and a "prostate cancer-negative reference level" of a biomarker means a level of a biomarker that is indicative of a negative diagnosis of prostate cancer in a subject. A "reference level" of a biomarker may be an absolute or relative amount or concentration of the biomarker, a presence or absence of the biomarker, a range of amount or concentration of the biomarker, a minimum and/or maximum amount or concentration of the biomarker, a mean amount or concentration of the biomarker, and/or a median amount or concentration of the biomarker; and, in addition, "reference levels" of combinations of biomarkers may also be ratios of absolute or relative amounts or concentrations of two or more biomarkers with respect to each other. Appropriate positive and negative reference levels of biomarkers for a particular disease state, phenotype, or lack thereof may be determined by measuring levels of desired biomarkers in one or more appropriate subjects, and such reference levels may be tailored to specific populations of subjects (e.g., a reference level may be age-matched so that comparisons may be made between biomarker levels in samples from subjects of a certain age and reference levels for a particular disease state, phenotype, or lack thereof in a certain age group). Such reference levels may also be tailored to specific techniques that are used to measure levels of biomarkers in biological samples (e.g., LC-MS, GC-MS, etc.), where the levels of biomarkers may differ based on the specific technique that is used.

[0030] "Non-biomarker compound" means a compound that is not differentially present in a biological sample from a subject or a group of subjects having a first phenotype (e.g., having a first disease) as compared to a biological sample from a subject or group of subjects having a second phenotype (e.g., not having the first disease). Such non-biomarker compounds may, however, be biomarkers in a biological sample from a subject or a group of subjects having a third phenotype (e.g., having a second disease) as compared to the first phenotype (e.g., having the first disease) or the second phenotype (e.g., not having the first disease).

[0031] "Metabolite", or "small molecule", means organic and inorganic molecules which are present in a cell. The term does not include large macromolecules, such as large proteins (e.g., proteins with molecular weights over 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, or 10,000), large nucleic acids (e.g., nucleic acids with molecular weights of over 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, or 10,000), or large polysaccharides (e.g., polysaccharides with a molecular weights of over 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, or 10,000). The small molecules of the cell are generally found free in solution in the cytoplasm or in other organelles, such as the mitochondria, where they form a pool of intermediates which can be metabolized further or used to generate large molecules, called macromolecules. The term "small molecules" includes signaling molecules and intermediates in the chemical reactions that transform energy derived from food into usable forms. Examples of small molecules include sugars, fatty acids, amino acids, nucleotides, intermediates formed during cellular processes, and other small molecules found within the cell.

[0032] "Metabolic profile", or "small molecule profile", means a complete or partial inventory of small molecules within a targeted cell, tissue, organ, organism, or fraction thereof (e.g., cellular compartment). The inventory may include the quantity and/or type of small molecules present. The "small molecule profile" may be determined using a single technique or multiple different techniques.

[0033] "Metabolome" means all of the small molecules present in a given organism.

[0034] "Prostate cancer" refers to a disease in which cancer develops in the prostate, a gland in the male reproductive system. "Low grade" or "lower grade" prostate cancer refers to non-metastatic prostate cancer, including malignant tumors with low potential for metastisis (i.e. prostate cancer that is considered to be less aggressive). "High grade" or "higher grade" prostate cancer refers to prostate cancer that has metastasized in a subject, including malignant tumors with high potential for metastisis (prostate cancer that is considered to be aggressive).

I. Biomarkers

[0035] The prostate cancer biomarkers described herein were discovered using metabolomic profiling techniques. Such metabolomic profiling techniques are described in more detail in the Examples set forth below as well as in U.S. Pat. No. 7,005,255 and U.S. patent application Ser. Nos. 11/357,732, 10/695,265 (Publication No. 2005/0014132), 11/301,077 (Publication No. 2006/0134676), 11/301,078 (Publication No. 2006/0134677), 11/301,079 (Publication No. 2006/0134678), and 11/405,033, the entire contents of which are hereby incorporated herein by reference.

[0036] Generally, metabolic profiles were determined for biological samples from human subjects diagnosed with prostate cancer as well as from one or more other groups of human subjects (e.g., healthy control subjects not diagnosed with prostate cancer), as well as from human subjects diagnosed with lower grade prostate cancer and human subjects diagnosed with metastatic/high grade prostate cancer. The metabolic profile for biological samples from a subject having prostate cancer was compared to the metabolic profile for biological samples from the one or more other groups of subjects. Those molecules differentially present, including those molecules differentially present at a level that is statistically significant, in the metabolic profile of samples from subjects with prostate cancer as compared to another group (e.g., healthy control subjects not diagnosed with prostate cancer) were identified as biomarkers to distinguish those groups. In addition, those molecules differentially present, including those molecules differentially present at a level that is statistically significant, in the metabolic profile of samples from subjects with low grade prostate cancer as compared to high grade prostate cancer were also identified as biomarkers to distinguish those groups.

[0037] The biomarkers are discussed in more detail herein. The biomarkers that were discovered correspond with the following group(s):

[0038] Biomarkers for distinguishing subjects having prostate cancer vs. control subjects not diagnosed with prostate cancer (see Tables 1, 2, 4, 5, 6, 7, 9, 10, 15, 18, 22, 24);

[0039] Biomarkers for distinguishing subjects having low grade prostate cancer vs. control subjects not diagnosed with prostate cancer (see Tables 1, 6, 9, 22);

[0040] Biomarkers for distinguishing subjects having metastatic/high grade prostate cancer vs. control subjects not diagnosed with prostate cancer (see Tables 2, 7, 10, 24);

[0041] Biomarkers for distinguishing subjects having metastatic/high grade prostate cancer vs. subjects having low grade prostate cancer (see Tables 3, 8, 11, 20, 26).

[0042] Although the identities of some of the biomarkers compounds are not known at this time, such identities are not necessary for the identification of the biomarkers in biological samples from subjects, as the "unnamed" compounds have been sufficiently characterized by analytical techniques to allow such identification. The analytical characterization of all such "unnamed" compounds is listed in the Examples. Such "unnamed" biomarkers are designated herein using the nomenclature "Metabolite" followed by a specific metabolite number.

IIA. Diagnosis of Prostate Cancer

[0043] The identification of biomarkers for prostate cancer allows for the diagnosis of (or for aiding in the diagnosis of) prostate cancer in subjects presenting one or more symptoms of prostate cancer. A method of diagnosing (or aiding in diagnosing) whether a subject has prostate cancer comprises (1) analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers of prostate cancer in the sample and (2) comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to diagnose (or aid in the diagnosis of) whether the subject has prostate cancer. The one or more biomarkers that are used are selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 and combinations thereof. When such a method is used to aid in the diagnosis of prostate cancer, the results of the method may be used along with other methods (or the results thereof) useful in the clinical determination of whether a subject has prostate cancer.

[0044] Any suitable method may be used to analyze the biological sample in order to determine the level(s) of the one or more biomarkers in the sample. Suitable methods include chromatography (e.g., HPLC, gas chromatography, liquid chromatography), mass spectrometry (e.g., MS, MS-MS), enzyme-linked immunosorbent assay (ELISA), antibody linkage, other immunochemical techniques, and combinations thereof. Further, the level(s) of the one or more biomarkers may be measured indirectly, for example, by using an assay that measures the level of a compound (or compounds) that correlates with the level of the biomarker(s) that are desired to be measured.

[0045] The levels of one or more of the biomarkers of Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 may be determined in the methods of diagnosing and methods of aiding in diagnosing whether a subject has prostate cancer. For example, the level(s) of one biomarker, two or more biomarkers, three or more biomarkers, four or more biomarkers, five or more biomarkers, six or more biomarkers, seven or more biomarkers, eight or more biomarkers, nine or more biomarkers, ten or more biomarkers, etc., including a combination of all of the biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 or any fraction thereof, may be determined and used in such methods. Determining levels of combinations of the biomarkers may allow greater sensitivity and specificity in diagnosing prostate cancer and aiding in the diagnosis of prostate cancer, and may allow better differentiation of prostate cancer from other prostate disorders (e.g. benign prostatic hypertrophy (BPH), prostatitis, etc.) or other cancers that may have similar or overlapping biomarkers to prostate cancer (as compared to a subject not having prostate cancer). For example, ratios of the levels of certain biomarkers (and non-biomarker compounds) in biological samples may allow greater sensitivity and specificity in diagnosing prostate cancer and aiding in the diagnosis of prostate cancer and may allow better differentiation of prostate cancer from other cancers or other disorders of the prostate that may have similar or overlapping biomarkers to prostate cancer (as compared to a subject not having prostate cancer).

[0046] One or more biomarkers that are specific for diagnosing prostate cancer (or aiding in diagnosing prostate cancer) in a certain type of sample (e.g., prostate tissue sample, urine sample, or blood plasma sample) may also be used. For example, when the biological sample is prostate tissue, one or more biomarkers listed in Tables 1, 2, 13, and/or 15, may be used to diagnose (or aid in diagnosing) whether a subject has prostate cancer. When the biological sample is blood plasma, one or more biomarkers listed in Tables 4, 6, 7, 22, and/or 24 may be used to diagnose (or aid in diagnosing) whether a subject has prostate cancer. When the biological sample is urine, one or more biomarkers listed in Tables 5, 9, 10, and/or 18 may be used to diagnose (or aid in diagnosing) whether a subject has prostate cancer.

[0047] After the level(s) of the one or more biomarkers in the sample are determined, the level(s) are compared to prostate cancer-positive and/or prostate cancer-negative reference levels to aid in diagnosing or to diagnose whether the subject has prostate cancer. Levels of the one or more biomarkers in a sample matching the prostate cancer-positive reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of a diagnosis of prostate cancer in the subject. Levels of the one or more biomarkers in a sample matching the prostate cancer-negative reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of a diagnosis of no prostate cancer in the subject. In addition, levels of the one or more biomarkers that are differentially present (especially at a level that is statistically significant) in the sample as compared to prostate cancer-negative reference levels are indicative of a diagnosis of prostate cancer in the subject. Levels of the one or more biomarkers that are differentially present (especially at a level that is statistically significant) in the sample as compared to prostate cancer-positive reference levels are indicative of a diagnosis of no prostate cancer in the subject.

[0048] The level(s) of the one or more biomarkers may be compared to prostate cancer-positive and/or prostate cancer-negative reference levels using various techniques, including a simple comparison (e.g., a manual comparison) of the level (s) of the one or more biomarkers in the biological sample to prostate cancer-positive and/or prostate cancer-negative reference levels. The level(s) of the one or more biomarkers in the biological sample may also be compared to prostate cancer-positive and/or prostate cancer-negative reference levels using one or more statistical analyses (e.g., t-test, Welch's T-test, Wilcoxon's rank sum test, random forest).

[0049] In addition, the biological samples may be analyzed to determine the level(s) of one or more non-biomarker compounds. The level(s) of such non-biomarker compounds may also allow differentiation of prostate cancer from other prostate disorders that may have similar or overlapping biomarkers to prostate cancer (as compared to a subject not having a prostate disorder). For example, a known non-biomarker compound present in biological samples of subjects having prostate cancer and subjects not having prostate cancer could be monitored to verify a diagnosis of prostate cancer as compared to a diagnosis of another prostate disorder when biological samples from subjects having the prostate disorder do not have the non-biomarker compound.

[0050] The methods of diagnosing (or aiding in diagnosing) whether a subject has prostate cancer may also be conducted specifically to diagnose (or aid in diagnosing) whether a subject has low grade prostate cancer and/or high grade prostate cancer. Such methods comprise (1) analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers of low grade prostate cancer (and/or high grade prostate cancer) in the sample and (2) comparing the level(s) of the one or more biomarkers in the sample to low grade prostate cancer-positive and/or low grade prostate cancer-negative reference levels (or high grade prostate cancer-positive and/or high grade prostate cancer-negative reference levels) in order to diagnose (or aid in the diagnosis of) whether the subject has low grade prostate cancer (or high grade prostate cancer). Biomarker specific for low grade prostate cancer are listed in Tables 1, 6, 9, 22 and biomarkers specific for high grade prostate cancer are listed in Tables 2, 7, 10, 24.

IIB. Methods of Distinguishing Low Grade Prostate Cancer from High Grade Prostate Cancer

[0051] The identification of biomarkers for distinguishing low grade prostate cancer versus high grade prostate cancer allows low grade prostate cancer and high grade prostate cancer to be distinguished in patients. A method of distinguishing low grade prostate cancer from high grade prostate cancer in a subject having prostate cancer comprises (1) analyzing a biological sample from a subject to determine the level(s) in the sample of one or more biomarkers of low grade prostate cancer that distinguish over high grade prostate cancer and/or one or more biomarkers of high grade prostate cancer that distinguish over low grade prostate cancer, and (2) comparing the level(s) of the one or more biomarkers in the sample to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer of the one or more biomarkers in order to determine whether the subject has low grade or high grade prostate cancer. The one or more biomarkers that are used are selected from Tables 3, 8, 11, 20, and/or 26 and combinations thereof.

[0052] Any suitable method may be used to analyze the biological sample in order to determine the level(s) of the one or more biomarkers in the sample. Suitable methods include chromatography (e.g., HPLC, gas chromatography, liquid chromatography), mass spectrometry (e.g., MS, MS-MS), enzyme-linked immunosorbent assay (ELISA), antibody linkage, other immunochemical techniques, and combinations thereof. Further, the level(s) of the one or more biomarkers may be measured indirectly, for example, by using an assay that measures the level of a compound (or compounds) that correlates with the level of the biomarker(s) that are desired to be measured.

[0053] The levels of one or more of the biomarkers of Tables 3, 8, 11, 20, and/or 26 may be determined in the methods of diagnosing and methods of aiding in diagnosing whether a subject has prostate cancer. For example, the level (s) of one biomarker, two or more biomarkers, three or more biomarkers, four or more biomarkers, five or more biomarkers, six or more biomarkers, seven or more biomarkers, eight or more biomarkers, nine or more biomarkers, ten or more biomarkers, etc., including a combination of all of the biomarkers in Tables 3, 8, 11, 20, and/or 26 or any fraction thereof, may be determined and used in such methods. Determining levels of combinations of the biomarkers may allow greater sensitivity and specificity in distinguishing between low grade and high grade prostate cancer.

[0054] One or more biomarkers that are specific for distinguishing between low grade and high grade prostate cancer in a certain type of sample (e.g., prostate tissue sample, urine sample, or blood plasma sample) may also be used. For example, when the biological sample is prostate tissue, one or more biomarkers listed in Table 3 may be used. When the biological sample is blood plasma, one or more biomarkers listed in Table 8 or 26 may be used. When the biological sample is urine, one or more biomarkers listed in Table 11 or 20 may be used.

[0055] After the level(s) of the one or more biomarkers in the sample are determined, the level(s) are compared to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer-negative and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer of the one or more biomarkers in order to determine whether the subject has low grade or high grade prostate cancer. Levels of the one or more biomarkers in a sample matching the low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of low-grade prostate cancer in the subject. Levels of the one or more biomarkers in a sample matching the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of high-grade prostate cancer in the subject. If the level(s) of the one or more biomarkers are more similar to the low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (or less similar to the high grade prostate cancer-positive reference levels), then the results are indicative of low grade prostate cancer in the subject. If the level(s)

of the one or more biomarkers are more similar to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer (or less similar to the low grade prostate cancer-positive reference levels), then the results are indicative of high grade prostate cancer in the subject.

[0056] The level(s) of the one or more biomarkers may be compared to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer using various techniques, including a simple comparison (e.g., a manual comparison) of the level(s) of the one or more biomarkers in the biological sample to low grade prostate cancer-positive and/or high grade prostate cancer-positive reference levels. The level(s) of the one or more biomarkers in the biological sample may also be compared to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer using one or more statistical analyses (e.g., t-test, Welch's T-test, Wilcoxon's rank sum test, random forest).

[0057] In addition, the biological samples may be analyzed to determine the level(s) of one or more non-biomarker compounds. The level(s) of such non-biomarker compounds may also allow differentiation of low grade prostate cancer from high grade prostate cancer.

III. Methods of Determining Predisposition to Prostate Cancer

[0058] The identification of biomarkers for prostate cancer also allows for the determination of whether a subject having no symptoms of prostate cancer is predisposed to developing prostate cancer. A method of determining whether a subject having no symptoms of prostate cancer is predisposed to developing prostate cancer comprises (1) analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers listed in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 in the sample and (2) comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to determine whether the subject is predisposed to developing prostate cancer. The results of the method may be used along with other methods (or the results thereof) useful in the clinical determination of whether a subject is predisposed to developing prostate cancer.

[0059] As described above in connection with methods of diagnosing (or aiding in the diagnosis of) prostate cancer, any suitable method may be used to analyze the biological sample in order to determine the level(s) of the one or more biomarkers in the sample.

[0060] As with the methods of diagnosing (or aiding in the diagnosis of) prostate cancer described above, the level(s) of one biomarker, two or more biomarkers, three or more biomarkers, four or more biomarkers, five or more biomarkers, six or more biomarkers, seven or more biomarkers, eight or more biomarkers, nine or more biomarkers, ten or more biomarkers, etc., including a combination of all of the biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 or any fraction thereof, may be determined and used in methods of determining whether a subject having no symptoms of prostate cancer is predisposed to developing prostate cancer.

[0061] After the level(s) of the one or more biomarkers in the sample are determined, the level(s) are compared to prostate cancer-positive and/or prostate cancer-negative reference levels in order to predict whether the subject is predisposed to developing prostate cancer. Levels of the one or more biomarkers in a sample matching the prostate cancer-positive reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the subject being predisposed to developing prostate cancer. Levels of the one or more biomarkers in a sample matching the prostate cancer-negative reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the subject not being predisposed to developing prostate cancer. In addition, levels of the one or more biomarkers that are differentially present (especially at a level that is statistically significant) in the sample as compared to prostate cancer-negative reference levels are indicative of the subject being predisposed to developing prostate cancer. Levels of the one or more biomarkers that are differentially present (especially at a level that is statistically significant) in the sample as compared to prostate cancer-positive reference levels are indicative of the subject not being predisposed to developing prostate cancer.

[0062] Furthermore, it may also be possible to determine reference levels specific to assessing whether or not a subject that does not have prostate cancer is predisposed to developing prostate cancer. For example, it may be possible to determine reference levels of the biomarkers for assessing different degrees of risk (e.g., low, medium, high) in a subject for developing prostate cancer. Such reference levels could be used for comparison to the levels of the one or more biomarkers in a biological sample from a subject.

[0063] As with the methods described above, the level(s) of the one or more biomarkers may be compared to prostate cancer-positive and/or prostate cancer-negative reference levels using various techniques, including a simple comparison, one or more statistical analyses, and combinations thereof.

[0064] As with the methods of diagnosing (or aiding in diagnosing) whether a subject has prostate cancer, the methods of determining whether a subject having no symptoms of prostate cancer is predisposed to developing prostate cancer may further comprise analyzing the biological sample to determine the level(s) of one or more non-biomarker compounds.

[0065] The methods of determining whether a subject having no symptoms of prostate cancer is predisposed to developing prostate cancer may also be conducted specifically to determine whether a subject having no symptoms of prostate cancer is predisposed to developing low grade prostate cancer and/or high grade prostate cancer. Biomarker specific for low grade prostate cancer are listed in Tables 1, 6, 9, and 22 and biomarkers specific for high grade prostate cancer are listed in Tables 2, 7, 10, and 24.

[0066] In addition, methods of determining whether a subject having low grade prostate cancer is predisposed to devel-

oping high grade prostate cancer may be conducted using one or more biomarkers selected from Tables 3, 8, 11, 20, and 26.

IV. Methods of Monitoring Progression/Regression of Prostate Cancer

[0067] The identification of biomarkers for prostate cancer also allows for monitoring progression/regression of prostate cancer in a subject. A method of monitoring the progression/regression of prostate cancer in a subject comprises (1) analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26, the first sample obtained from the subject at a first time point, (2) analyzing a second biological sample from a subject to determine the level(s) of the one or more biomarkers, the second sample obtained from the subject at a second time point, and (3) comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to monitor the progression/regression of prostate cancer in the subject. The results of the method are indicative of the course of prostate cancer (i.e., progression or regression, if any change) in the subject.

[0068] The change (if any) in the level(s) of the one or more biomarkers over time may be indicative of progression or regression of prostate cancer in the subject. In order to characterize the course of prostate cancer in the subject, the level (s) of the one or more biomarkers in the first sample, the level(s) of the one or more biomarkers in the second sample, and/or the results of the comparison of the levels of the biomarkers in the first and second samples may be compared to prostate cancer-positive, prostate cancer-negative, low grade prostate cancer-positive, low grade prostate cancer-negative, high-grade prostate cancer-positive, and/or high grade prostate cancer-negative reference levels as well as low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer. If the comparisons indicate that the level(s) of the one or more biomarkers are increasing or decreasing over time (e.g., in the second sample as compared to the first sample) to become more similar to the prostate cancer-positive reference levels (or less similar to the prostate cancer-negative reference levels), to the high grade prostate cancer reference levels, or, when the subject initially has low grade prostate cancer, to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer, then the results are indicative of prostate cancer progression. If the comparisons indicate that the level(s) of the one or more biomarkers are increasing or decreasing over time to become more similar to the prostate cancer-negative reference levels (or less similar to the prostate cancer-positive reference levels), or, when the subject initially has high grade prostate cancer, to low grade prostate cancer reference levels and/or to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer, then the results are indicative of prostate cancer regression.

[0069] As with the other methods described herein, the comparisons made in the methods of monitoring progression/regression of prostate cancer in a subject may be carried out using various techniques, including simple comparisons, one or more statistical analyses, and combinations thereof.

[0070] The results of the method may be used along with other methods (or the results thereof) useful in the clinical monitoring of progression/regression of prostate cancer in a subject.

[0071] As described above in connection with methods of diagnosing (or aiding in the diagnosis of) prostate cancer, any suitable method may be used to analyze the biological samples in order to determine the level(s) of the one or more biomarkers in the samples. In addition, the level(s) one or more biomarkers, including a combination of all of the biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 or any fraction thereof, may be determined and used in methods of monitoring progression/regression of prostate cancer in a subject.

[0072] Such methods could be conducted to monitor the course of prostate cancer in subjects having prostate cancer or could be used in subjects not having prostate cancer (e.g., subjects suspected of being predisposed to developing prostate cancer) in order to monitor levels of predisposition to prostate cancer.

V. Methods of Assessing Efficacy of Compositions for Treating Prostate Cancer

[0073] The identification of biomarkers for prostate cancer also allows for assessment of the efficacy of a composition for treating prostate cancer as well as the assessment of the relative efficacy of two or more compositions for treating prostate cancer. Such assessments may be used, for example, in efficacy studies as well as in lead selection of compositions for treating prostate cancer.

[0074] A method of assessing the efficacy of a composition for treating prostate cancer comprises (1) analyzing, from a subject having prostate cancer and currently or previously being treated with a composition, a biological sample to determine the level(s) of one or more biomarkers selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26, and (2) comparing the level(s) of the one or more biomarkers in the sample to (a) level(s) of the one or more biomarkers in a previously-taken biological sample from the subject, wherein the previously-taken biological sample was obtained from the subject before being treated with the composition, (b) prostate cancer-positive reference levels (including low grade prostate cancer-positive and/or high grade prostate cancer-positive reference levels) of the one or more biomarkers, (c) prostate cancer-negative reference levels (including low grade prostate cancer-negative and/or high grade prostate cancer-negative reference levels) of the one or more biomarkers, (d) low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer, and/or (e) high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer. The results of the comparison are indicative of the efficacy of the composition for treating prostate cancer.

[0075] Thus, in order to characterize the efficacy of the composition for treating prostate cancer, the level(s) of the one or more biomarkers in the biological sample are compared to (1) prostate cancer-positive reference levels, (2) prostate cancer-negative reference levels, (3) previous levels of the one or more biomarkers in the subject before treatment with the composition, (4) low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer, and/or (5) high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer.

[0076] When comparing the level(s) of the one or more biomarkers in the biological sample (from a subject having prostate cancer and currently or previously being treated with a composition) to prostate cancer-positive reference levels and/or prostate cancer-negative reference levels, level(s) in the sample matching the prostate cancer-negative reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the composition having efficacy for treating prostate cancer. Levels of the one or more biomarkers in the sample matching the prostate cancer-positive reference levels (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the composition not having efficacy for treating prostate cancer. The comparisons may also indicate degrees of efficacy for treating prostate cancer based on the level(s) of the one or more biomarkers.

[0077] When comparing the level(s) of the one or more biomarkers in the biological sample (from a subject having high grade prostate cancer and currently or previously being treated with a composition) low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer, level(s) in the sample matching the low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the composition having efficacy for treating prostate cancer. Levels of the one or more biomarkers in the sample matching the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer (e.g., levels that are the same as the reference levels, substantially the same as the reference levels, above and/or below the minimum and/or maximum of the reference levels, and/or within the range of the reference levels) are indicative of the composition not having efficacy for treating prostate cancer.

[0078] When the level(s) of the one or more biomarkers in the biological sample (from a subject having prostate cancer and currently or previously being treated with a composition) are compared to level(s) of the one or more biomarkers in a previously-taken biological sample from the subject before treatment with the composition, any changes in the level(s) of the one or more biomarkers are indicative of the efficacy of the composition for treating prostate cancer. That is, if the comparisons indicate that the level(s) of the one or more biomarkers have increased or decreased after treatment with the composition to become more similar to the prostate cancer-negative reference levels (or less similar to the prostate cancer-positive reference levels) or, when the subject initially has high grade prostate cancer, the level(s) have increased or decreased to become more similar to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (or less similar to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer), then the results are indicative of the composition having efficacy for treating prostate cancer. If the comparisons indicate that the level(s) of the one or more biomarkers have not increased or decreased after treatment with the composition to become more similar to the prostate cancer-negative reference levels (or less similar to the prostate cancer-positive reference levels) or, when the subject initially has high grade prostate cancer, the level(s) have not increased or decreased to become more similar to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (or less similar to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer), then the results are indicative of the composition not having efficacy for treating prostate cancer. The comparisons may also indicate degrees of efficacy for treating prostate cancer based on the amount of changes observed in the level(s) of the one or more biomarkers after treatment. In order to help characterize such a comparison, the changes in the level(s) of the one or more biomarkers, the level(s) of the one or more biomarkers before treatment, and/or the level(s) of the one or more biomarkers in the subject currently or previously being treated with the composition may be compared to prostate cancer-positive reference levels (including low grade and high grade prostate cancer-positive reference levels), prostate cancer-negative reference levels (including low grade and high grade prostate cancer-negative reference levels), low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer, and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer.

[0079] Another method for assessing the efficacy of a composition in treating prostate cancer comprises (1) analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26, the first sample obtained from the subject at a first time point, (2) administering the composition to the subject, (3) analyzing a second biological sample from a subject to determine the level(s) of the one or more biomarkers, the second sample obtained from the subject at a second time point after administration of the composition, and (4) comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the efficacy of the composition for treating prostate cancer. As indicated above, if the comparison of the samples indicates that the level(s) of the one or more biomarkers have increased or decreased after administration of the composition to become more similar to the prostate cancer-negative reference levels (or less similar to the prostate cancer-positive reference levels) or, when the subject initially has high grade prostate cancer, if the level(s) have increased or decreased to become more similar to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (or less similar to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer), then the results are indicative of the composition having efficacy for treating prostate cancer. If the comparisons indicate that the level(s) of the one or more biomarkers have not increased or decreased after treatment with the composition to become more similar to the prostate cancer-negative reference levels (or less similar to the prostate cancer-positive reference levels) or, when the subject initially has high grade prostate cancer, the level(s) have not increased or decreased to become more similar to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer (or less similar to the high grade prostate cancer-positive reference levels that distinguish over low grade prostate can-

cer), then the results are indicative of the composition not having efficacy for treating prostate cancer. The comparison may also indicate a degree of efficacy for treating prostate cancer based on the amount of changes observed in the level (s) of the one or more biomarkers after administration of the composition as discussed above.

[0080] A method of assessing the relative efficacy of two or more compositions for treating prostate cancer comprises (1) analyzing, from a first subject having prostate cancer and currently or previously being treated with a first composition, a first biological sample to determine the level(s) of one or more biomarkers selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 (2) analyzing, from a second subject having prostate cancer and currently or previously being treated with a second composition, a second biological sample to determine the level(s) of the one or more biomarkers, and (3) comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the relative efficacy of the first and second compositions for treating prostate cancer. The results are indicative of the relative efficacy of the two compositions, and the results (or the levels of the one or more biomarkers in the first sample and/or the level(s) of the one or more biomarkers in the second sample) may be compared to prostate cancer-positive reference levels (including low grade and high grade prostate cancer-positive reference levels), prostate cancer-negative reference levels (including low grade and high grade prostate cancer-negative reference levels), low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer, and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer to aid in characterizing the relative efficacy.

[0081] Each of the methods of assessing efficacy may be conducted on one or more subjects or one or more groups of subjects (e.g., a first group being treated with a first composition and a second group being treated with a second composition).

[0082] As with the other methods described herein, the comparisons made in the methods of assessing efficacy (or relative efficacy) of compositions for treating prostate cancer may be carried out using various techniques, including simple comparisons, one or more statistical analyses, and combinations thereof. Any suitable method may be used to analyze the biological samples in order to determine the level(s) of the one or more biomarkers in the samples. In addition, the level (s) of one or more biomarkers, including a combination of all of the biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 or any fraction thereof, may be determined and used in methods of assessing efficacy (or relative efficacy) of compositions for treating prostate cancer.

[0083] Finally, the methods of assessing efficacy (or relative efficacy) of one or more compositions for treating prostate cancer may further comprise analyzing the biological sample to determine the level(s) of one or more non-biomarker compounds. The non-biomarker compounds may then be compared to reference levels of non-biomarker compounds for subjects having (or not having) prostate cancer.

VI. Methods of Screening a Composition for Activity in Modulating Biomarkers Associated with Prostate Cancer

[0084] The identification of biomarkers for prostate cancer also allows for the screening of compositions for activity in modulating biomarkers associated with prostate cancer, which may be useful in treating prostate cancer. Methods of screening compositions useful for treatment of prostate cancer comprise assaying test compositions for activity in modulating the levels of one or more biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26. Such screening assays may be conducted in vitro and/or in vivo, and may be in any form known in the art useful for assaying modulation of such biomarkers in the presence of a test composition such as, for example, cell culture assays, organ culture assays, and in vivo assays (e.g., assays involving animal models).

[0085] In one embodiment, a method for screening a composition for activity in modulating one or more biomarkers of prostate cancer comprises (1) contacting one or more cells with a composition, (2) analyzing at least a portion of the one or more cells or a biological sample associated with the cells to determine the level(s) of one or more biomarkers of prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and (3) comparing the level(s) of the one or more biomarkers with predetermined standard levels for the one or more biomarkers to determine whether the composition modulated the level(s) of the one or more biomarkers. As discussed above, the cells may be contacted with the composition in vitro and/or in vivo. The predetermined standard levels for the one or more biomarkers may be the levels of the one or more biomarkers in the one or more cells in the absence of the composition. The predetermined standard levels for the one or more biomarkers may also be the level(s) of the one or more biomarkers in control cells not contacted with the composition.

[0086] In addition, the methods may further comprise analyzing at least a portion of the one or more cells or a biological sample associated with the cells to determine the level(s) of one or more non-biomarker compounds of prostate cancer. The levels of the non-biomarker compounds may then be compared to predetermined standard levels of the one or more non-biomarker compounds.

[0087] Any suitable method may be used to analyze at least a portion of the one or more cells or a biological sample associated with the cells in order to determine the level(s) of the one or more biomarkers (or levels of non-biomarker compounds). Suitable methods include chromatography (e.g., HPLC, gas chromatograph, liquid chromatography), mass spectrometry (e.g., MS, MS-MS), ELISA, antibody linkage, other immunochemical techniques, and combinations thereof. Further, the level(s) of the one or more biomarkers (or levels of non-biomarker compounds) may be measured indirectly, for example, by using an assay that measures the level of a compound (or compounds) that correlates with the level of the biomarker(s) (or non-biomarker compounds) that are desired to be measured.

VII. Method of Identifying Potential Drug Targets

[0088] The identification of biomarkers for prostate cancer also allows for the identification of potential drug targets for prostate cancer. A method for identifying a potential drug target for prostate cancer comprises (1) identifying one or more biochemical pathways associated with one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 and (2) identifying a protein (e.g., an enzyme) affecting at least one of the one or more identified biochemical pathways, the protein being a potential drug target for prostate cancer.

[0089] Another method for identifying a potential drug target for prostate cancer comprises (1) identifying one or more

biochemical pathways associated with one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 and one or more non-biomarker compounds of prostate cancer and (2) identifying a protein affecting at least one of the one or more identified biochemical pathways, the protein being a potential drug target for prostate cancer.

[0090] One or more biochemical pathways (e.g., biosynthetic and/or metabolic (catabolic) pathway) are identified that are associated with one or more biomarkers (or non-biomarker compounds). After the biochemical pathways are identified, one or more proteins affecting at least one of the pathways are identified. Preferably, those proteins affecting more than one of the pathways are identified.

[0091] A build-up of one metabolite (e.g., a pathway intermediate) may indicate the presence of a 'block' downstream of the metabolite and the block may result in a low/absent level of a downstream metabolite (e.g. product of a biosynthetic pathway). In a similar manner, the absence of a metabolite could indicate the presence of a 'block' in the pathway upstream of the metabolite resulting from inactive or non-functional enzyme(s) or from unavailability of biochemical intermediates that are required substrates to produce the product. Alternatively, an increase in the level of a metabolite could indicate a genetic mutation that produces an aberrant protein which results in the over-production and/or accumulation of a metabolite which then leads to an alteration of other related biochemical pathways and result in dysregulation of the normal flux through the pathway; further, the build-up of the biochemical intermediate metabolite may be toxic or may compromise the production of a necessary intermediate for a related pathway. It is possible that the relationship between pathways is currently unknown and this data could reveal such a relationship.

[0092] For example, the data indicates that metabolites in the biochemical pathways involving nitrogen excretion, amino acid metabolism, energy metabolism, oxidative stress, purine metabolism and bile acid metabolism are enriched in prostate cancer subjects. Further, polyamine levels are higher in cancer subjects, which indicates that the level and/or activity of the enzyme ornithine decarboxylase is increased. It is known that polyamines can act as mitotic agents and have been associated with free radical damage. These observations indicate that the pathways leading to the production of polyamines (or to any of the aberrant biomarkers) would provide a number of potential targets useful for drug discovery.

[0093] The proteins identified as potential drug targets may then be used to identify compositions that may be potential candidates for treating prostate cancer, including compositions for gene therapy.

VIII. Methods of Treating Prostate Cancer

[0094] The identification of biomarkers for prostate cancer also allows for the treatment of prostate cancer. For example, in order to treat a subject having prostate cancer, an effective amount of one or more prostate cancer biomarkers that are lowered in prostate cancer as compared to a healthy subject not having prostate cancer may be administered to the subject. The biomarkers that may be administered may comprise one or more of the biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 20, 22, 24, and/or 26 that are decreased in prostate cancer. In some embodiments, the biomarkers that are administered are one or more biomarkers listed in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 20, 22, 24, and/or 26 that are decreased in prostate cancer and that have a p-value less than 0.10. In other embodiments, the biomarkers that are administered are one or biomarkers listed in Tables 1, 2 and/or 3 that are decreased in prostate cancer by at least 5%, by at least 10%, by at least 15%, by at least 20%, by at least 25%, by at least 30%, by at least 35%, by at least 40%, by at least 45%, by at least 50%, by at least 55%, by at least 60%, by at least 65%, by at least 70%, by at least 75%, by at least 80%, by at least 85%, by at least 90%, by at least 95%, or by 100% (i.e., absent).

IX. Methods of Using the Prostate Cancer Biomarkers for Other Types of Prostate Cancer

[0095] It is believed that some of the biomarkers for major prostate cancer described herein may also be biomarkers for other types of cancer, including, for example, lung cancer or kidney cancer. Therefore, it is believed that at least some of the prostate cancer biomarkers may be used in the methods described herein for other types of cancer. That is, the methods described herein with respect to prostate cancer may also be used for diagnosing (or aiding in the diagnosis of) any type of cancer, methods of monitoring progression/regression of any type of cancer, methods of assessing efficacy of compositions for treating any type of cancer, methods of screening a composition for activity in modulating biomarkers associated with any type of cancer, methods of identifying potential drug targets for any type of cancer, and methods of treating any type of cancer. Such methods could be conducted as described herein with respect to prostate cancer.

X. Methods of Using the Prostate Cancer Biomarkers for Other Prostate Disorders

[0096] It is believed that some of the biomarkers for prostate cancer described herein may also be biomarkers for prostate disorders (e.g. prostatitis, benign prostate hypertrophy (BHP)) in general. Therefore, it is believed that at least some of the prostate cancer biomarkers may be used in the methods described herein for prostate disorders in general. That is, the methods described herein with respect to prostate cancer may also be used for diagnosing (or aiding in the diagnosis of) a prostate disorder, methods of monitoring progression/regression of a prostate disorder, methods of assessing efficacy of compositions for treating a prostate disorder, methods of screening a composition for activity in modulating biomarkers associated with a prostate disorder, methods of identifying potential drug targets for prostate disorder, and methods of treating a prostate disorder. Such methods could be conducted as described herein with respect to prostate cancer.

XI. Other Methods

[0097] Other methods of using the biomarkers discussed herein are also contemplated. For example, the methods described in U.S. Pat. No. 7,005,255 and U.S. patent application Ser. No. 10/695,265 may be conducted using a small molecule profile comprising one or more of the biomarkers disclosed herein.

[0098] In any of the methods listed herein, the biomarkers that are used may be selected from those biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 having p-values of less than 0.05 and/or those biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 having q-values of less than 0.10. The biomarkers

that are used in any of the methods described herein may also be selected from those biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 that are decreased in prostate cancer (as compared to the control) or that are decreased in remission (as compared to control or prostate cancer) by at least 5%, by at least 10%, by at least 15%, by at least 20%, by at least 25%, by at least 30%, by at least 35%, by at least 40%, by at least 45%, by at least 50%, by at least 55%, by at least 60%, by at least 65%, by at least 70%, by at least 75%, by at least 80%, by at least 85%, by at least 90%, by at least 95%, or by 100% (i.e., absent); and/or those biomarkers in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 that are increased in prostate cancer (as compared to the control or remission) or that are increased in remission (as compared to the control or prostate cancer) by at least 5%, by at least 10%, by at least 15%, by at least 20%, by at least 25%, by at least 30%, by at least 35%, by at least 40%, by at least 45%, by at least 50%, by at least 55%, by at least 60%, by at least 65%, by at least 70%, by at least 75%, by at least 80%, by at least 85%, by at least 90%, by at least 95%, by at least 100%, by at least 110%, by at least 120%, by at least 130%, by at least 140%, by at least 150%, or more.

EXAMPLES

[0099] The invention will be further explained by the following illustrative examples that are intended to be non-limiting.

I. General Methods

[0100] A. Identification of Metabolic Profiles for Prostate Cancer

[0101] Each sample was analyzed to determine the concentration of several hundred metabolites. Analytical techniques such as GC-MS (gas chromatography-mass spectrometry) and LC-MS (liquid chromatography-mass spectrometry) were used to analyze the metabolites. Multiple aliquots were simultaneously, and in parallel, analyzed, and, after appropriate quality control (QC), the information derived from each analysis was recombined. Every sample was characterized according to several thousand characteristics, which ultimately amount to several hundred chemical species. The techniques used were able to identify novel and chemically unnamed compounds.

[0102] B. Statistical Analysis

[0103] The data was analyzed using T-tests to identify molecules (either known, named metabolites or unnamed metabolites) present at differential levels in a definable population or subpopulation (e.g., biomarkers for prostate cancer biological samples compared to control biological samples or compared to patients in remission from prostate cancer) useful for distinguishing between the definable populations (e.g., prostate cancer and control, low grade prostate cancer and high grade prostate cancer). Other molecules (either known, named metabolites or unnamed metabolites) in the definable population or subpopulation were also identified.

[0104] Data was also analyzed using Random Forest Analysis. Random forests give an estimate of how well individuals in a new data set can be classified into existing groups. Random forest analysis creates a set of classification trees based on continual sampling of the experimental units and compounds. Then each observation is classified based on the majority votes from all the classification trees. In statistics, a classification tree classifies the observations into groups based on combinations of the variables (in this instance variables are metabolites or compounds). There are many variations on the algorithms used to create trees. A tree algorithm searches for the metabolite (compound) that provides the largest split between the two groups. This produces nodes. Then at each node, the metabolite that provides the best split is used and so on. If the node cannot be improved on, then it stops at that node and any observation in that node is classified as the majority group.

[0105] Random forests classify based on a large number (e.g. thousands) of trees. A subset of compounds and a subset of observations are used to create each tree. The observations used to create the tree are called the in-bag samples, and the remaining samples are called the out-of-bag samples. The classification tree is created from the in-bag samples, and the out-of-bag samples are predicted from this tree. To get the final classification for an observation, the "votes" for each group are counted based on the times it was an out-of-bag sample. For example, suppose observation **1** was classified as a "Control" by 2,000 trees, but classified as "Disease" by 3,000 trees. Using "majority wins" as the criterion, this sample is classified as "Disease."

[0106] The results of the random forest are summarized in a confusion matrix. The rows correspond to the true grouping, and the columns correspond to the classification from the random forest. Thus, the diagonal elements indicate the correct classifications. A 50% error would occur by random chance for 2 groups, 66.67% error for three groups by random chance, etc. The "Out-of-Bag" (OOB) Error rate gives an estimate of how accurately new observations can be predicted using the random forest model (e.g., whether a sample is from a diseased subject or a control subject).

[0107] It is also of interest to see which variables are more "important" in the final classifications. The "importance plot" shows the top compounds ranked in terms of their importance. There are different criteria for ranking the importance, but the general idea is that removing an important variable will cause a greater decrease in accuracy than a variable that is less important.

[0108] C. Biomarker Identification

[0109] Various peaks identified in the analyses (e.g. GC-MS, LC-MS, MS-MS), including those identified as statistically significant, were subjected to a mass spectrometry based chemical identification process.

Example 1

Tissue

[0110] Biomarkers were discovered by (1) analyzing tissue samples from different groups of human subjects to determine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0111] The tissue samples used for the analysis were 16 control tissues that were cancer free tissues derived from sections of prostate tissue not containing cancer cells (i.e. from cancerous prostate glands and that were determined to be free of cancerous cells), 12 prostate tissue samples from localized prostate cancer tumors (i.e. lower grade prostate cancer) and 14 prostate tissue samples from distal metastatic prostate cancer tumors (i.e. high grade prostate cancer). After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0112] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Lower Grade Prostate Cancer vs. Control, Metastatic/High Grade Prostate Cancer vs. Control, Metastatic/High Grade Prostate Cancer vs. Lower Grade Prostate Cancer).

Biomarkers:

[0113] As listed below in Table 1, biomarkers were discovered that were differentially present between tissue samples from lower grade, localized prostate cancer tumors and Control prostate tissue that was determined to be free of cancerous cells (i.e. sections of prostate tissue not containing cancerous cells from cancerous prostate glands removed from the patient). Table 2 lists biomarkers that were discovered that were differentially present between tissue from prostate tumor samples from subjects with metastatic prostate cancer (i.e. high grade prostate cancer) and Control prostate tissue. Table 3 lists biomarkers that were discovered that were differentially present between tissue samples from prostate tumor samples from subjects with metastatic prostate cancer (i.e. high grade prostate cancer) and tissue samples from lower grade, localized prostate cancer tumors.

[0114] Tables 1-3 include, for each listed biomarker, the p-value and the q-value determined in the statistical analysis of the data concerning the biomarkers and an indication of the percentage difference in the lower grade prostate cancer (PCA) mean level as compared to the control mean level (Table 1), the high grade prostate cancer mean level as compared to the control mean level (Table 2), and the high grade prostate cancer mean level as compared to the lower grade prostate cancer mean level (Table 3). The term "Isobar" as used in the tables indicates the compounds that could not be distinguished from each other on the analytical platform used in the analysis (i.e., the compounds in an isobar elute at nearly the same time and have similar (and sometimes exactly the same) quant ions, and thus cannot be distinguished). Library indicates the chemical library that was used to identify the compounds. The number 50 refer to the GC library and the number 61 refers to the LC library.

TABLE 1

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3139	61	<0.0001	0.0019	147%
Metabolite - 1114	61	<0.0001	0.0053	55%
uridine	61	1.00E-04	0.0064	71%
Metabolite - 3778	61	1.00E-04	0.0064	-67%
dethiobiotin	50	1.00E-04	0.0064	62%
Metabolite - 3094	50	1.00E-04	0.0075	62%
N-acetyl-D-galactosamine	50	2.00E-04	0.0092	214%
4-hydroxy-2-quinolinecarboxylic acid	61	3.00E-04	0.0092	110%
Metabolite - 4019	50	3.00E-04	0.0092	104%
Metabolite - 2688	61	3.00E-04	0.0092	20%
proline	50	3.00E-04	0.0092	59%
Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	61	3.00E-04	0.0092	92%
glutamic acid	50	4.00E-04	0.0095	83%
3-hydroxy-3-methylglutarate	50	5.00E-04	0.0107	82%
Metabolite - 3810	61	6.00E-04	0.0119	-45%
Metabolite - 1576	61	6.00E-04	0.0119	116%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 4637	50	7.00E-04	0.0134	55%
Metabolite - 1595-possible-glutathione-metabolite	61	7.00E-04	0.0134	-58%
glycine	50	8.00E-04	0.0142	67%
leucine	50	9.00E-04	0.0145	61%
threonine	50	9.00E-04	0.0145	51%
histidine	50	0.001	0.0151	58%
anthranilic acid	50	0.0012	0.0167	53%
asparagine	50	0.0012	0.0167	81%
L-allo-threonine	50	0.0014	0.0177	48%
n-hexadecanoic acid	50	0.0014	0.0177	36%
1-7-dihydro-6h-purin-6-one	61	0.0016	0.0193	43%
N-acetyl-D-glucosamine	50	0.0016	0.0193	125%
DL-homocysteine	61	0.0019	0.021	118%
sn-Glycerol-3-phosphate	50	0.0019	0.021	98%
Isobar-2-includes-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-3-phospho-l-serine	61	0.0021	0.0219	58%
Isobar-27-includes-L-kynurenine-alpha-2-diamino-gamma-oxobenzenebutanoic acid	61	0.0023	0.0228	18%
Metabolite - 4051	50	0.0024	0.0228	90%
alpha-amino-adipate	50	0.0024	0.0228	108%
Metabolite - 4117-possible-propranolol-or-2-heptyl-3-hydroxy-quinolone	61	0.0026	0.0228	99%
cholesterol	50	0.0026	0.0228	163%
Metabolite - 5128	61	0.0027	0.0228	46%
Isobar-6-includes-valine-betaine	61	0.0027	0.0228	-85%
Metabolite - 4616	61	0.0029	0.0228	36%
Metabolite - 4015	50	0.0029	0.0228	269%
Metabolite - 2973	50	0.0029	0.0228	102%
valine	50	0.003	0.0233	-25%
malic acid	50	0.0032	0.0237	38%
Metabolite - 1211	61	0.0033	0.0241	62%
Isobar-22-includes-glutamic acid-O-acetyl-L-serine	61	0.0037	0.0263	-52%
tetradecanoic acid	50	0.0038	0.0263	44%
phosphate	50	0.0039	0.0265	59%
possible-ISOBAR-DL-aspartic acid-	50	0.004	0.0267	68%
Metabolite - 2466	61	0.0041	0.0271	71%
Metabolite - 2548	61	0.0044	0.0283	99%
Metabolite - 3848	61	0.0045	0.0283	-32%
Metabolite - 2109	61	0.0046	0.0283	117%
tryptophan	61	0.0046	0.0283	120%
2-acetamido-1-amino-1-2-dideoxy-beta-D-glucopyranose	50	0.0054	0.0324	38%
Metabolite - 3998	50	0.0057	0.0324	134%
5-oxoproline	50	0.0057	0.0324	53%
riboflavine	61	0.0058	0.0324	48%
phytonadione	50	0.0059	0.0324	67%
Metabolite - 2074	61	0.0059	0.0324	45%
9-12-octadecadienoic acid-z-z-	50	0.0061	0.0328	-42%
carnitine	61	0.0063	0.033	74%
Metabolite - 3370	61	0.0063	0.033	47%
uracil	50	0.0067	0.0343	37%
noradrenaline	50	0.0068	0.0344	129%
tyrosine	61	0.007	0.0348	50%
cysteine	50	0.0073	0.036	41%
25-hydroxycholesterol	50	0.0075	0.0364	800%
Metabolite - 4030-possible-glutethimide-or-securinine	61	0.0076	0.0366	18%
N-acetylserotonin	50	0.008	0.0376	109%
Metabolite - 2108	61	0.0081	0.0376	279%
phenylalanine	61	0.0082	0.0376	78%
				36%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Isobar-3-includes-inositol-1-phosphate-mannose-6-phosphate-glucose-6-phosphate-D-mannose-1-phosphate-alpha-D-glucose-1-phosphate-alpha-D-galactose-1-phosphate	61	0.0088	0.0395	63%
Metabolite - 1713	61	0.0089	0.0395	82%
Metabolite - 1977	61	0.0094	0.0412	218%
octadecanoic acid	50	0.0099	0.0429	25%
3-nitro-L-tyrosine	50	0.0101	0.0434	82%
Metabolite - 2064	61	0.0112	0.0472	44%
Metabolite - 2389	61	0.0123	0.051	36%
Metabolite - 4617	61	0.0124	0.051	53%
orotidine-5-phosphate	61	0.013	0.0528	125%
serine	50	0.0135	0.0542	40%
spermine	50	0.0143	0.0565	−78%
Metabolite - 2041	61	0.0145	0.0565	157%
Metabolite - 1465	61	0.0146	0.0565	174%
N-5-aminocarbonyl-L-ornithine	50	0.0158	0.0607	136%
2-deoxy-D-ribose	61	0.0164	0.062	44%
heptadecanoic acid	50	0.0168	0.0622	76%
Metabolite - 3165	61	0.0172	0.0622	26%
methionine	61	0.0173	0.0622	43%
S-adenosyl-l-homocysteine	61	0.0173	0.0622	41%
Isobar-24-includes-L-arabitol-adonitol	61	0.0174	0.0622	46%
glycerol	50	0.0175	0.0622	51%
Metabolite - 2690	61	0.019	0.0662	147%
Metabolite - 3176-possible-creatine	61	0.0191	0.0662	−22%
Metabolite - 4632	50	0.0197	0.0675	44%
aspartate	61	0.0207	0.0695	54%
Metabolite - 3027	50	0.0207	0.0695	108%
mannose-6-phosphate	50	0.022	0.0734	179%
Metabolite - 5215	50	0.0225	0.0742	−27%
Metabolite - 2055	61	0.0229	0.0744	−35%
uridine-5-monophosphate	61	0.023	0.0744	−38%
Metabolite - 4046	50	0.0249	0.0797	305%
Metabolite - 4355	50	0.0256	0.0797	36%
Metabolite - 4058	50	0.0256	0.0797	104%
Carnosine	61	0.0256	0.0797	−45%
Metabolite - 1070	61	0.0263	0.0811	109%
Metabolite - 5228	50	0.0279	0.0852	52%
Metabolite - 2753	61	0.0286	0.0861	224%
Metabolite - 4116	61	0.0289	0.0861	34%
Metabolite - 2272	61	0.0292	0.0861	152%
Metabolite - 4027	50	0.0294	0.0861	145%
xanthine	61	0.0298	0.0861	172%
Metabolite - 2924	50	0.0298	0.0861	51%
N-N-dimethylarginine	61	0.0318	0.0911	224%
Metabolite - 4017	50	0.0322	0.0915	52%
glutamine	50	0.0333	0.0924	39%
isoleucine	50	0.0335	0.0924	26%
Metabolite - 1498	61	0.0336	0.0924	48%
adenine	50	0.0336	0.0924	65%
Metabolite - 2005	61	0.0345	0.0941	45%
sarcosine	50	0.0354	0.0958	150%
Metabolite - 3498	61	0.0366	0.098	55%
Metabolite - 5210	50	0.0396	0.1052	−23%
arginino-succinate	61	0.043	0.1132	93%
Putrescine	50	0.0432	0.1132	−82%
Metabolite - 1104	61	0.0441	0.1144	−35%
taurine	61	0.0455	0.1171	−21%
Metabolite - 1597	61	0.0461	0.1178	29%
Metabolite - 4043	50	0.0469	0.119	33%
Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine-or-aspartame	61	0.0475	0.1195	107%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
N-6-trimethyl-l-lysine	61	0.0486	0.1215	35%
Metabolite - 2250	61	0.0508	0.1261	71%
creatinine	61	0.0514	0.1261	−25%
melatonin	50	0.0516	0.1261	111%
Metabolite - 2105	61	0.0541	0.1311	100%
2-deoxyuridine-5-triphosphate	61	0.0571	0.1375	−41%
tyramine	50	0.0591	0.1404	32%
inositol-1-phosphate	50	0.0592	0.1404	40%
4-methyl-2-oxopentanoate	61	0.0597	0.1405	162%
Metabolite - 5186	61	0.0601	0.1406	600%
fumaric acid	50	0.0638	0.1482	82%
2-deoxyuridine	61	0.0676	0.156	74%
Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	61	0.0688	0.1576	45%
Metabolite - 4868-possible-Bradykinin	61	0.0703	0.1598	114%
Metabolite - 2846	61	0.0753	0.1701	141%
arachidonic acid	50	0.0765	0.1705	52%
Metabolite - 1831-possible-Cl-adduct-of-citrulline	61	0.0769	0.1705	30%
Metabolite - 3099	50	0.0771	0.1705	43%
trans-4-hydroxyproline	50	0.0776	0.1705	63%
Metabolite - 3783	61	0.0782	0.1708	−39%
L-alpha-glycerophosphorylcholine	61	0.0793	0.172	58%
glycerate	61	0.0798	0.172	42%
cytidine	61	0.0819	0.1741	101%
Isobar-40-includes-Maltotetraose-stachyose	61	0.0825	0.1741	−41%
Metabolite - 1679	61	0.0831	0.1741	347%
Metabolite - 4032	50	0.0836	0.1741	108%
Metabolite - 3752	61	0.0841	0.1741	756%
Isobar-32-includes-N-acetyl-D-glucosamine-N-acetyl-D-mannosamine	61	0.0847	0.1741	34%
pantothenic acid	61	0.0849	0.1741	40%
glyceric acid	50	0.085	0.1741	27%
xylitol	50	0.0907	0.1831	65%
Metabolite - 2075	61	0.0915	0.1831	148%
Metabolite - 3430	61	0.0916	0.1831	63%
Metabolite - 3668	61	0.0917	0.1831	−47%
5-6-dihydrouracil	61	0.0928	0.1831	94%
Metabolite - 3138	61	0.0933	0.1831	62%
Metabolite - 2056	61	0.0933	0.1831	−20%
Metabolite - 4362	50	0.0944	0.1834	−41%
Metabolite - 4514	50	0.095	0.1834	−19%
Metabolite - 2607	61	0.0959	0.1834	−45%
Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	61	0.096	0.1834	70%
Isobar-5-includes-asparagine-ornithine	61	0.0963	0.1834	57%
Metabolite - 3957	61	0.0968	0.1834	43%
Isobar-30-includes-maltotetraose-stachyose	61	0.0993	0.1867	−35%
D-sorbitol-6-phosphate	50	0.0996	0.1867	53%
Metabolite - 2981	50	0.1017	0.1894	17%
ribulose-5-phosphate	50	0.1041	0.1929	−25%
Metabolite - 3123	61	0.1082	0.1987	−42%
Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	61	0.1085	0.1987	67%
Metabolite - 1593	61	0.111	0.2022	−44%
uric acid	61	0.1119	0.2027	−19%
Metabolite - 3178	61	0.1128	0.2027	−30%
Metabolite - 1455	61	0.1131	0.2027	−81%
Metabolite - 1286	61	0.1145	0.204	−16%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose	61	0.1166	0.2068	−35%
o-phosphoethanolamine	50	0.1196	0.211	44%
Metabolite - 1608	61	0.1206	0.2115	−59%
Metabolite - 3539	61	0.1217	0.2123	−57%
Metabolite - 4593	50	0.1257	0.217	37%
palmitoleic acid	50	0.1257	0.217	78%
Metabolite - 3896	61	0.1274	0.2176	65%
1-methyladenosine	61	0.1274	0.2176	100%
Metabolite - 1203-possible-acetylbrowniine-tricornine-germine-or-veracevine	61	0.1333	0.2253	86%
Metabolite - 3771	61	0.1338	0.2253	−18%
pyridoxamine-phosphate	61	0.1341	0.2253	−33%
Metabolite - 2212	61	0.135	0.2253	320%
Spermidine	50	0.1367	0.2253	−51%
Metabolite - 3992-	61	0.1375	0.2253	14%
Metabolite - 3044	61	0.1385	0.2253	30%
3-methyl-L-histidine	61	0.1389	0.2253	21%
Metabolite - 2546	61	0.1393	0.2253	−36%
fructose	50	0.1396	0.2253	−47%
Metabolite - 3816	61	0.1397	0.2253	−43%
Metabolite - 2255	61	0.1406	0.2253	44%
Metabolite - 3073	50	0.1407	0.2253	−39%
succinate	50	0.1456	0.2314	−54%
Metabolite - 2292	61	0.1459	0.2314	−35%
glutathione-reduced	61	0.1467	0.2314	−43%
alanine	50	0.1494	0.2346	21%
Metabolite - 4053	50	0.1527	0.2387	26%
Metabolite - 4567	61	0.1555	0.2419	−37%
Metabolite - 3832-possible-phenol-sulfate	61	0.1614	0.2499	−30%
Metabolite - 5189	61	0.1668	0.2571	263%
saccharopine	61	0.1679	0.2575	23%
Metabolite - 1216	61	0.1699	0.2577	53%
Metabolite - 5227	50	0.1704	0.2577	45%
citric acid	50	0.1708	0.2577	−37%
catechol	61	0.1712	0.2577	77%
Metabolite - 4615	61	0.1733	0.2594	−13%
Metabolite - 3808	61	0.1747	0.2594	−20%
Metabolite - 1609	61	0.1753	0.2594	−35%
D-allose	50	0.1754	0.2594	−37%
elaidic acid	50	0.1821	0.2681	84%
Metabolite - 2129	61	0.1835	0.269	110%
Metabolite - 2185	61	0.1864	0.2706	35%
azelaic acid	61	0.1875	0.2706	63%
Metabolite - 1088	61	0.1879	0.2706	81%
Metabolite - 5232	50	0.1879	0.2706	109%
Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	61	0.1887	0.2706	25%
hypotaurine	50	0.1917	0.2736	36%
Metabolite - 4150	50	0.1936	0.2744	−36%
Metabolite - 2111	61	0.1939	0.2744	33%
Metabolite - 1457	61	0.1957	0.2758	−35%
DL-cystathionine	50	0.1983	0.2783	22%
Metabolite - 5147	61	0.2019	0.2822	243%
Metabolite - 3476	61	0.2033	0.2828	−23%
benzoic acid	50	0.2043	0.2831	−14%
Metabolite - 5109	61	0.2069	0.2843	89%
Metabolite - 3102	50	0.2082	0.2843	25%
Metabolite - 3974	61	0.2083	0.2843	38%
Metabolite - 1351	61	0.2086	0.2843	19%
mannose	50	0.2108	0.2858	−32%
quinolinic acid	61	0.2114	0.2858	42%
gamma-L-glutamyl-L-glutamine	61	0.2161	0.2896	−28%
Metabolite - 1186	61	0.2164	0.2896	−54%
Metabolite - 2766	61	0.2183	0.2896	−34%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
phosphoenolpyruvate	50	0.2184	0.2896	105%
Metabolite - 4080	50	0.2187	0.2896	71%
Metabolite - 2139	61	0.221	0.2915	41%
Metabolite - 2900-	61	0.222	0.2915	24%
Metabolite - 2388	61	0.2232	0.2915	24%
2-deoxy-D-glucose	50	0.2236	0.2915	−30%
5-hydroxyindoleacetate	50	0.2255	0.2928	210%
Metabolite - 4869	61	0.2292	0.2964	−38%
Metabolite - 2774	61	0.2377	0.306	47%
Metabolite - 2232	61	0.2385	0.306	−36%
3-methoxy-L-tyrosine	50	0.2401	0.3069	−29%
inositol	50	0.2414	0.3071	−29%
glucono-gamma-lactone	50	0.2434	0.3071	−31%
Metabolite - 4133	50	0.2441	0.3071	34%
Metabolite - 4014	50	0.2444	0.3071	−17%
galactose	50	0.2449	0.3071	30%
Metabolite - 3813	61	0.248	0.3097	115%
Metabolite - 1980	61	0.2537	0.3151	119%
Metabolite - 5108	61	0.2542	0.3151	72%
Metabolite - 2703	61	0.2562	0.3165	31%
Metabolite - 5110	61	0.2632	0.3239	63%
Metabolite - 5207	50	0.2649	0.3247	13%
Metabolite - 2027	61	0.2671	0.3262	47%
2-keto-L-gulonic acid	50	0.2795	0.34	12%
Metabolite - 3064	61	0.2832	0.3434	50%
glucose-6-phosphate	50	0.2849	0.3439	−28%
Metabolite - 5166	61	0.2857	0.3439	49%
3-amino-isobutyrate	50	0.2892	0.3457	−27%
dulcitol	50	0.2894	0.3457	−27%
Metabolite - 3034	50	0.2933	0.349	22%
Metabolite - 4667	61	0.2942	0.349	18%
Metabolite - 2806	61	0.2996	0.3541	−12%
Metabolite - 5089	61	0.3011	0.3541	−65%
4-hydroxyphenylpyruvate	61	0.3034	0.3541	−17%
Metabolite - 4075	50	0.3039	0.3541	36%
Metabolite - 4235	61	0.3039	0.3541	−67%
glutarate	61	0.3122	0.358	47%
beta-nicotinamide-adenine-dinucleotide	61	0.3134	0.358	445%
Metabolite - 1327-possible-bilirubin	61	0.3175	0.358	30%
guanine	50	0.3177	0.358	26%
Metabolite - 1323-possible-4-sulfobenzyl-alcohol	61	0.3181	0.358	−31%
Metabolite - 3708	61	0.3196	0.358	−10%
Metabolite - 4706	61	0.3202	0.358	42%
Metabolite - 3545	61	0.3204	0.358	76%
Metabolite - 3132	61	0.3217	0.358	23%
niacinamide	61	0.3243	0.358	12%
Metabolite - 3514-retired-topiramate	61	0.3248	0.358	−89%
Metabolite - 5167	61	0.3248	0.358	43%
Metabolite - 5170	61	0.3251	0.358	854%
Metabolite - 3951	61	0.3267	0.358	13%
Metabolite - 2768	61	0.3321	0.358	798%
allantoin	61	0.3332	0.358	−15%
Metabolite - 2347	61	0.3332	0.358	−16%
Metabolite - 3436	61	0.3332	0.358	−21%
Metabolite - 5087	61	0.3338	0.358	−53%
Metabolite - 3576	61	0.3374	0.358	23%
Metabolite - 3694	61	0.3383	0.358	36%
Metabolite - 3522	61	0.3398	0.358	−85%
Metabolite - 2406	61	0.3409	0.358	31%
Metabolite - 3364	61	0.3409	0.358	12%
Metabolite - 3997	61	0.3409	0.358	43%
Metabolite - 4018	61	0.3409	0.358	38%
suberic acid	61	0.3409	0.358	15%
Metabolite - 3022	50	0.3409	0.358	8%
Metabolite - 1329	61	0.3409	0.358	10%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3756	61	0.3409	0.358	25%
Metabolite - 5086	61	0.3409	0.358	−41%
Metabolite - 1911	61	0.3431	0.3582	64%
gamma-glu-cys	61	0.3432	0.3582	60%
N-acetylneuraminate	61	0.3469	0.3609	−14%
Metabolite - 2691	61	0.3544	0.3669	33%
Metabolite - 3531	61	0.3572	0.3669	−70%
Metabolite - 3180	61	0.3575	0.3669	46%
L-homoserine-lactone	61	0.3583	0.3669	12%
Metabolite - 1974	61	0.3584	0.3669	−18%
Metabolite - 2141	61	0.3594	0.3669	29%
Metabolite - 1333	61	0.3625	0.3684	28%
GABA	50	0.3631	0.3684	−20%
adenosine	61	0.3676	0.3719	−18%
Metabolite - 5226	50	0.3709	0.3741	33%
Metabolite - 2036	61	0.3733	0.3748	−38%
Metabolite - 1616	61	0.3739	0.3748	76%
Metabolite - 3833	61	0.3752	0.375	20%
Metabolite - 2348	61	0.3836	0.3813	69%
S-5-adenosyl-L-methionine	61	0.3839	0.3813	30%
Metabolite - 4331	61	0.3854	0.3817	26%
Metabolite - 3475	61	0.3873	0.3824	−19%
n-dodecanoate	50	0.3957	0.3895	15%
Metabolite - 3952	61	0.399	0.3914	−14%
Metabolite - 3837	61	0.3999	0.3914	−33%
Metabolite - 1819	61	0.4015	0.3917	−15%
Metabolite - 2853	61	0.4036	0.3926	−20%
Metabolite - 3517	61	0.4048	0.3926	−34%
Metabolite - 3526	61	0.4155	0.4018	−23%
Metabolite - 2711	61	0.4182	0.4029	11%
5-s-methyl-5-thioadenosine	61	0.419	0.4029	33%
xanthosine	50	0.4265	0.4088	−18%
Metabolite - 5107	61	0.4345	0.4153	36%
Metabolite - 1248-possible-avermectin-aglycone	61	0.4438	0.421	22%
ornithine	50	0.4438	0.421	19%
Metabolite - 3984	61	0.4443	0.421	58%
Metabolite - 3215	61	0.4466	0.4219	−18%
Metabolite - 2181	61	0.45	0.423	23%
Metabolite - 1392	61	0.4505	0.423	−49%
Metabolite - 4512	50	0.4516	0.423	34%
Metabolite - 5209	50	0.4539	0.4241	−16%
Metabolite - 2198	61	0.4573	0.4251	−19%
Metabolite - 4931	61	0.4578	0.4251	11%
Metabolite - 3604	61	0.4589	0.4251	30%
maltose	50	0.4614	0.4253	−13%
Metabolite - 1330	61	0.4623	0.4253	−50%
Metabolite - 1843	61	0.4644	0.4253	35%
Metabolite - 5214	50	0.4665	0.4253	−19%
Metabolite - 3056	61	0.467	0.4253	−23%
Metabolite - 4084	50	0.468	0.4253	−5%
Metabolite - 2567	61	0.4682	0.4253	15%
Metabolite - 3893	61	0.4774	0.4323	−14%
Metabolite - 3543	61	0.4785	0.4323	−47%
Metabolite - 4503	50	0.4815	0.4338	21%
Isobar-31-includes-maltotriose-melezitose	61	0.4912	0.4406	−14%
histamine	61	0.4917	0.4406	−13%
D-ribose	50	0.4931	0.4407	−17%
Metabolite - 3390	61	0.4987	0.4445	−4%
6-phosphogluconic acid	61	0.5166	0.4592	−7%
Metabolite - 2319	61	0.5186	0.4597	24%
lactate	50	0.523	0.4624	8%
Metabolite - 4096-gamma-glu-gly-leu-	61	0.5325	0.4695	−7%
Metabolite - 4518	50	0.5347	0.4701	22%
Metabolite - 1129	61	0.536	0.4701	23%
Metabolite - 3003	50	0.5401	0.4724	15%
Metabolite - 5213	50	0.5456	0.476	−11%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 1069-possible-dehydroepiandrosterone-sulfate-	61	0.549	0.4771	25%
Metabolite - 1575	61	0.5511	0.4771	−16%
3-hydroxybutanoic acid	50	0.5512	0.4771	−22%
Metabolite - 4238	61	0.553	0.4773	14%
pyrophosphate	50	0.5551	0.4779	20%
Metabolite - 2867	61	0.5592	0.4788	25%
Metabolite - 1718	61	0.5602	0.4788	20%
arabinose	50	0.5604	0.4788	−14%
Metabolite - 3401	61	0.5676	0.4836	−18%
beta-alanine	50	0.5697	0.4842	−12%
Metabolite - 2897	61	0.5738	0.4856	−13%
Metabolite - 1394-possible-Losartan	61	0.5743	0.4856	23%
Metabolite - 4428	61	0.5759	0.4857	21%
Metabolite - 2099	61	0.5866	0.4924	26%
Metabolite - 3220	61	0.5868	0.4924	10%
Metabolite - 3317	61	0.5908	0.4932	19%
biliverdin	61	0.5908	0.4932	−12%
Metabolite - 3002	50	0.5925	0.4934	6%
Metabolite - 3955	61	0.5991	0.4976	−4%
Metabolite - 3020	50	0.6009	0.4979	12%
Metabolite - 3189	61	0.6061	0.5009	−23%
Metabolite - 1970	61	0.6121	0.5046	19%
Metabolite - 1963	61	0.6203	0.5078	−9%
Metabolite - 1113-possible-acetylcarnitine-or-isopentyl-adenine	61	0.6216	0.5078	−6%
Metabolite - 3016	50	0.6232	0.5078	−12%
caffeine	61	0.6241	0.5078	22%
ethylmalonic acid	61	0.6247	0.5078	38%
cystine	50	0.6255	0.5078	8%
Metabolite - 2558	61	0.6268	0.5078	−21%
uridine-5-diphosphoglucose	50	0.629	0.5084	8%
3-methyl-2-oxovaleric acid	61	0.634	0.5112	26%
dihydroxyacetone-phosphate	61	0.6396	0.5144	11%
Metabolite - 4497	50	0.6462	0.5184	−12%
Metabolite - 2313	61	0.649	0.5184	7%
Metabolite - 3085	50	0.6493	0.5184	−5%
Metabolite - 3996	50	0.6552	0.521	−9%
L-histidinol	61	0.6557	0.521	−9%
Metabolite - 1573	61	0.6598	0.5231	−9%
Metabolite - 2407	61	0.6624	0.5238	−18%
Metabolite - 5126	61	0.665	0.5246	11%
Metabolite - 4448	61	0.6685	0.5261	−8%
alpha-D-ribose-5-phosphate	50	0.6795	0.5319	9%
cytidine-5-monophosphate	61	0.6818	0.5319	11%
Metabolite - 1979-Cl-adduct-of-C6H10O5	61	0.6823	0.5319	5%
Metabolite - 2-Aminoethyl-phosphonate	61	0.6831	0.5319	4%
sorbitol	50	0.6839	0.5319	−21%
Metabolite - 2368	61	0.6862	0.5324	56%
Metabolite - 1961-retired-glycocholic acid	61	0.7054	0.5461	45%
Metabolite - 4523	50	0.7076	0.5464	7%
alpha-4-dihydroxybenzenepropanoic acid	50	0.7136	0.5498	20%
Metabolite - 1342-possible-phenylacetylglutamine	61	0.728	0.5591	−15%
Metabolite - 4020	50	0.7305	0.5591	9%
Metabolite - 3554	61	0.7316	0.5591	14%
Metabolite - 2174	61	0.7325	0.5591	9%
Metabolite - 4002	50	0.7391	0.5629	8%
DL-pipecolic acid	61	0.7474	0.5674	−8%
Metabolite - 2824	61	0.7484	0.5674	14%
Metabolite - 3807	61	0.7516	0.5685	−4%
Metabolite - 3129	61	0.7585	0.5724	−3%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 2194	61	0.7641	0.5735	−9%
ascorbic acid	50	0.7647	0.5735	−10%
biotin	61	0.7657	0.5735	−9%
Metabolite - 1975	61	0.7669	0.5735	−8%
Metabolite - 1349	61	0.7721	0.576	−6%
Metabolite - 2072	61	0.7799	0.5792	−9%
Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	61	0.7817	0.5793	4%
Metabolite - 4806	50	0.7875	0.581	3%
Metabolite - 4796	50	0.7882	0.581	−9%
4-Guanidinobutanoic acid	61	0.7894	0.581	6%
Metabolite - 3489	61	0.7984	0.5855	−7%
Metabolite - 1116	61	0.799	0.5855	−5%
Metabolite - 2827	61	0.8024	0.5867	13%
Metabolite - 3772	61	0.814	0.5923	4%
Metabolite - 2143	61	0.8147	0.5923	−12%
Metabolite - 3960	61	0.8168	0.5923	2%
Metabolite - 3040	50	0.8172	0.5923	3%
Metabolite - 3994	61	0.8202	0.5931	−8%
Metabolite - 2180	61	0.8237	0.5944	−7%
Metabolite - 2118	61	0.8311	0.5974	−3%
Metabolite - 4787	61	0.8315	0.5974	15%
Metabolite - 4516	50	0.8341	0.5979	−6%
Metabolite - 4168	61	0.8386	0.598	4%
uridine-5-diphosphoglucuronic acid	50	0.841	0.598	7%
Metabolite - 4134	50	0.8433	0.598	3%
Metabolite - 4271	50	0.8442	0.598	−17%
Metabolite - 2121	61	0.8444	0.598	8%
Metabolite - 4013	61	0.8451	0.598	5%
urea	50	0.8512	0.6007	−2%
Metabolite - 4272	50	0.8534	0.6007	−4%
Metabolite - 1653	61	0.855	0.6007	6%
Metabolite - 1183	61	0.8561	0.6007	9%
Metabolite - 5229	50	0.8587	0.6012	3%
glucarate	50	0.8678	0.6063	14%
Metabolite - 1187	61	0.8864	0.6163	5%
beta-D-lactose	50	0.8875	0.6163	3%
Metabolite - 2279	61	0.8877	0.6163	−4%
Metabolite - 5212	50	0.8914	0.617	3%
alpha-L-sorbopyranose	50	0.8925	0.617	−3%
Metabolite - 4354	50	0.9014	0.6219	−2%

TABLE 1-continued

Prostate Cancer Biomarkers from subjects with Lower Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3014	50	0.9104	0.6256	1%
Metabolite - 3534	61	0.9131	0.6256	−5%
Metabolite - 3966	61	0.9137	0.6256	−4%
Metabolite - 1497	61	0.9149	0.6256	−2%
Metabolite - 3379	61	0.9178	0.6256	−2%
Metabolite - 1288	61	0.9188	0.6256	3%
Metabolite - 2237	61	0.9222	0.6256	4%
Metabolite - 3755	61	0.9248	0.6256	2%
Metabolite - 3980	61	0.9253	0.6256	−3%
picolinic acid	61	0.9259	0.6256	3%
Metabolite - 2821	61	0.9284	0.6261	−2%
L-kynurenine	50	0.9317	0.627	−3%
inosine	61	0.9399	0.6272	−1%
Metabolite - 2724	61	0.9415	0.6272	−1%
Isobar-19-includes-D-saccharic acid-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	61	0.9431	0.6272	1%
Metabolite - 4510	50	0.9434	0.6272	−1%
alpha-keto-glutarate	61	0.9448	0.6272	−6%
3-methylglutaric acid	61	0.9453	0.6272	0%
Metabolite - 3051	61	0.9454	0.6272	2%
Metabolite - 3484	61	0.9472	0.6272	−3%
Metabolite - 1303	61	0.9513	0.6276	−2%
Metabolite - 3074	50	0.9517	0.6276	3%
guanosine	61	0.9553	0.6288	0%
hippuric acid	61	0.9589	0.6288	2%
Metabolite - 5211	50	0.9591	0.6288	3%
Metabolite - 5187	61	0.9644	0.6297	1%
Metabolite - 1496	61	0.9648	0.6297	0%
Metabolite - 4550	61	0.9663	0.6297	−2%
Metabolite - 3365	61	0.97	0.6309	1%
Metabolite - 4611	50	0.9734	0.6318	0%
Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	61	0.9753	0.6318	1%
1-methyladenine	50	0.979	0.633	2%
3-phospho-d-glycerate	61	0.9819	0.633	1%
Metabolite - 4365	50	0.9829	0.633	−1%
Metabolite - 4866	61	0.9912	0.6371	0%
Metabolite - 4003	61	0.9994	0.6412	0%

TABLE 2

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
inosine	61	<0.0001	<0.0001	−269%
Metabolite - 2-Aminoethyl-phosphonate	61	<0.0001	<0.0001	−437%
Metabolite - 1597	61	<0.0001	<0.0001	110%
Metabolite - 1498	61	<0.0001	<0.0001	188%
octadecanoic acid	50	<0.0001	<0.0001	136%
Metabolite - 3390	61	<0.0001	<0.0001	−330%
riboflavine	61	<0.0001	<0.0001	196%
leucine	50	<0.0001	<0.0001	216%
phosphate	50	<0.0001	<0.0001	150%
anthranilic acid	50	<0.0001	<0.0001	140%
glycerol	50	<0.0001	<0.0001	352%
Metabolite - 3808	61	<0.0001	<0.0001	−452%
valine	50	<0.0001	<0.0001	103%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 1595-possible-glutathione-metabolite	61	<0.0001	<0.0001	−695%
n-hexadecanoic acid	50	<0.0001	<0.0001	365%
heptadecanoic acid	50	<0.0001	<0.0001	201%
Metabolite - 3998	50	<0.0001	<0.0001	101%
Metabolite - 1679	61	<0.0001	<0.0001	597%
phenylalanine	61	<0.0001	<0.0001	93%
Isobar-24-includes-L-arabitol-adonitol	61	<0.0001	<0.0001	313%
Metabolite - 2292	61	<0.0001	<0.0001	−644%
tryptophan	61	<0.0001	<0.0001	112%
Metabolite - 3893	61	<0.0001	<0.0001	−757%
xanthine	61	<0.0001	<0.0001	1072%
glycerate	61	<0.0001	<0.0001	375%
Metabolite - 3178	61	<0.0001	<0.0001	−1223%
ribulose-5-phosphate	50	<0.0001	<0.0001	−272%
noradrenaline	50	<0.0001	<0.0001	88%
Metabolite - 3085	50	<0.0001	<0.0001	−224%
Metabolite - 2272	61	<0.0001	<0.0001	594%
Metabolite - 4013	61	<0.0001	<0.0001	443%
taurine	61	<0.0001	<0.0001	−219%
uracil	50	<0.0001	<0.0001	933%
Metabolite - 3165	61	<0.0001	<0.0001	75%
Metabolite - 2973	50	<0.0001	<0.0001	−214%
histidine	50	<0.0001	<0.0001	120%
adenosine	61	<0.0001	1.00E−04	−276%
9-12-octadecadienoic acid-z-z-	50	<0.0001	1.00E−04	518%
isoleucine	50	<0.0001	1.00E−04	68%
Metabolite - 3772	61	<0.0001	1.00E−04	83%
DL-homocysteine	61	<0.0001	1.00E−04	216%
pantothenic acid	61	<0.0001	1.00E−04	164%
Metabolite - 3778	61	<0.0001	1.00E−04	−327%
Metabolite - 4611	50	<0.0001	1.00E−04	388%
Isobar-6-includes-valine-betaine	61	<0.0001	1.00E−04	78%
tetradecanoic acid	50	<0.0001	1.00E−04	810%
Metabolite - 3810	61	<0.0001	1.00E−04	−261%
proline	50	<0.0001	1.00E−04	209%
Metabolite - 1576	61	1.00E−04	1.00E−04	204%
Metabolite - 5210	50	1.00E−04	1.00E−04	−231%
4-hydroxyphenylpyruvate	61	1.00E−04	1.00E−04	−423%
Metabolite - 3102	50	1.00E−04	1.00E−04	918%
gamma-L-glutamyl-L-glutamine	61	1.00E−04	1.00E−04	−433%
Metabolite - 1977	61	1.00E−04	1.00E−04	382%
palmitoleic acid	50	1.00E−04	1.00E−04	1547%
n-dodecanoate	50	1.00E−04	1.00E−04	418%
Metabolite - 1114	61	1.00E−04	1.00E−04	106%
Metabolite - 4617	61	1.00E−04	1.00E−04	217%
Metabolite - 5107	61	1.00E−04	1.00E−04	268%
L-allo-threonine	50	1.00E−04	2.00E−04	86%
threonine	50	1.00E−04	2.00E−04	88%
Metabolite - 3138	61	1.00E−04	2.00E−04	268%
tyrosine	61	1.00E−04	2.00E−04	68%
Metabolite - 1349	61	1.00E−04	2.00E−04	−885%
arachidonic acid	50	1.00E−04	2.00E−04	164%
Metabolite - 4046	50	1.00E−04	2.00E−04	3090%
Metabolite - 4620	61	1.00E−04	2.00E−04	854%
Metabolite - 4075	50	1.00E−04	2.00E−04	971%
urea	50	2.00E−04	2.00E−04	234%
Metabolite - 2181	61	2.00E−04	2.00E−04	189%
Metabolite - 5209	50	2.00E−04	2.00E−04	−539%
Metabolite - 2108	61	2.00E−04	2.00E−04	155%
Metabolite - 1351	61	2.00E−04	2.00E−04	366%
glycine	50	2.00E−04	2.00E−04	101%
Metabolite - 3003	50	2.00E−04	2.00E−04	122%
Metabolite - 4134	50	2.00E−04	2.00E−04	458%
Metabolite - 1329	61	2.00E−04	2.00E−04	171%
Metabolite - 1394-possible-Losartan	61	2.00E−04	2.00E−04	158%
Metabolite - 3014	50	2.00E−04	2.00E−04	327%
Metabolite - 1116	61	3.00E−04	3.00E−04	446%
Metabolite - 5212	50	3.00E−04	3.00E−04	−488%
Metabolite - 1465	61	3.00E−04	3.00E−04	512%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 5228	50	3.00E−04	3.00E−04	86%
Isobar-2-includes-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	61	3.00E−04	3.00E−04	249%
glutathione-reduced	61	3.00E−04	3.00E−04	−819%
1-7-dihydro-6h-purin-6-one	61	3.00E−04	3.00E−04	63%
Metabolite - 2924	50	3.00E−04	3.00E−04	332%
methionine	61	3.00E−04	3.00E−04	68%
Metabolite - 4649	61	4.00E−04	3.00E−04	224%
fumaric acid	50	4.00E−04	3.00E−04	196%
Metabolite - 1593	61	4.00E−04	4.00E−04	−409%
inositol-1-phosphate	50	4.00E−04	4.00E−04	163%
Metabolite - 4051	50	4.00E−04	4.00E−04	663%
lactate	50	4.00E−04	4.00E−04	49%
Metabolite - 4117-possible-propranolol-or-2-heptyl-3-hydroxy-quinolone	61	4.00E−04	4.00E−04	267%
N-N-dimethylarginine	61	4.00E−04	4.00E−04	267%
Metabolite - 3370	61	4.00E−04	4.00E−04	79%
citric acid	50	5.00E−04	4.00E−04	−1943%
glyceric acid	50	5.00E−04	4.00E−04	125%
Metabolite - 3215	61	5.00E−04	4.00E−04	110%
1-methyladenosine	61	6.00E−04	5.00E−04	620%
5-hydroxyindoleacetate	50	6.00E−04	5.00E−04	−319%
S-5-adenosyl-L-methionine	61	6.00E−04	5.00E−04	230%
catechol	61	7.00E−04	5.00E−04	595%
Metabolite - 5110	61	7.00E−04	5.00E−04	278%
Metabolite - 1069-possible-dehydroepiandrosterone-sulfate-	61	7.00E−04	5.00E−04	−379%
Metabolite - 4593	50	7.00E−04	5.00E−04	113%
elaidic acid	50	7.00E−04	5.00E−04	526%
Metabolite - 3833	61	7.00E−04	6.00E−04	247%
Metabolite - 2711	61	8.00E−04	6.00E−04	84%
carnitine	61	8.00E−04	6.00E−04	155%
D-allose	50	8.00E−04	6.00E−04	−1265%
Metabolite - 3094	50	9.00E−04	6.00E−04	49%
Metabolite - 5108	61	9.00E−04	6.00E−04	237%
Metabolite - 3064	61	9.00E−04	6.00E−04	195%
L-alpha-glycerophosphorylcholine	61	9.00E−04	6.00E−04	361%
Metabolite - 5128	61	9.00E−04	6.00E−04	−2480%
Metabolite - 2567	61	9.00E−04	6.00E−04	132%
uric acid	61	9.00E−04	7.00E−04	142%
quinolinic acid	61	0.001	7.00E−04	173%
Metabolite - 4518	50	0.001	7.00E−04	618%
Metabolite - 4428	61	0.001	7.00E−04	210%
Metabolite - 5214	50	0.0011	7.00E−04	−421%
Metabolite - 3044	61	0.0011	7.00E−04	187%
Metabolite - 3816	61	0.0011	7.00E−04	−2267%
Metabolite - 1831-possible-Cl-adduct-of-citrulline	61	0.0011	7.00E−04	142%
guanosine	61	0.0012	7.00E−04	−191%
3-methyl-L-histidine	61	0.0012	8.00E−04	83%
Metabolite - 1843	61	0.0012	8.00E−04	524%
cysteine	50	0.0012	8.00E−04	988%
Metabolite - 5187	61	0.0012	8.00E−04	354%
ethylmalonic acid	61	0.0012	8.00E−04	1277%
Metabolite - 2766	61	0.0012	8.00E−04	−2129%
Metabolite - 1104	61	0.0014	8.00E−04	−200%
3-methoxy-L-tyrosine	50	0.0014	9.00E−04	−570%
Metabolite - 3807	61	0.0014	9.00E−04	346%
DL-pipecolic acid	61	0.0015	9.00E−04	296%
Metabolite - 2041	61	0.0015	9.00E−04	198%
malic acid	50	0.0015	9.00E−04	88%
Metabolite - 4331	61	0.0016	9.00E−04	97%
Metabolite - 5166	61	0.0017	0.001	157%
Metabolite - 2111	61	0.0018	0.001	134%
Metabolite - 5167	61	0.0018	0.001	146%
Metabolite - 2867	61	0.0018	0.001	−6300%
3-phospho-d-glycerate	61	0.0018	0.001	−210%
Metabolite - 2109	61	0.0019	0.001	179%
Metabolite - 5232	50	0.0019	0.0011	422%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
D-ribose	50	0.002	0.0011	−466%
Metabolite - 3771	61	0.002	0.0011	−163%
alanine	50	0.002	0.0011	86%
Metabolite - 2753	61	0.002	0.0011	227%
xanthosine	50	0.002	0.0011	−391%
arabinose	50	0.002	0.0011	−437%
Metabolite - 1323-possible-4-sulfobenzyl-alcohol	61	0.0021	0.0011	311%
Metabolite - 3489	61	0.0021	0.0011	−552%
trans-4-hydroxyproline	50	0.0022	0.0011	208%
Metabolite - 3966	61	0.0022	0.0012	159%
Metabolite - 1713	61	0.0025	0.0013	212%
Metabolite - 2237	61	0.0026	0.0013	307%
Metabolite - 2548	61	0.0026	0.0013	97%
Metabolite - 3364	61	0.0026	0.0013	272%
melatonin	50	0.0026	0.0013	227%
Isobar-5-includes-asparagine-ornithine	61	0.0028	0.0014	105%
Metabolite - 1819	61	0.0029	0.0014	69%
inositol	50	0.0029	0.0014	−541%
spermine	50	0.0029	0.0014	−5110%
Metabolite - 1288	61	0.003	0.0014	221%
Metabolite - 5109	61	0.0031	0.0015	385%
thymine	50	0.0031	0.0015	561%
Isobar-19-includes-D-saccharic acid-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	61	0.0031	0.0015	−213%
Metabolite - 2141	61	0.0032	0.0015	263%
Metabolite - 1327-possible-bilirubin	61	0.0033	0.0015	84%
Metabolite - 2900-alpha-4-dihydroxybenzenepropanoic acid	61 50	0.0034 0.0034	0.0016 0.0016	152% 2300%
Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine-or-aspartame	61	0.0035	0.0016	241%
glutamic acid	50	0.0036	0.0017	114%
5-s-methyl-5-thioadenosine	61	0.0036	0.0017	235%
2-deoxy-D-ribose	61	0.0037	0.0017	68%
4-hydroxy-2-quinolinecarboxylic acid	61	0.0037	0.0017	81%
Metabolite - 4869	61	0.0038	0.0017	184%
Metabolite - 4015	50	0.0038	0.0017	247%
N-acetylserotonin	50	0.0038	0.0017	1007%
allantoin	61	0.0039	0.0018	164%
Metabolite - 2118	61	0.0041	0.0018	−138%
Metabolite - 2323	61	0.0041	0.0018	111%
Isobar-22-includes-glutamic acid-O-acetyl-L-serine	61	0.0041	0.0018	52%
mercaptopyruvate	61	0.0043	0.0019	130%
3-methylglutaric acid	61	0.0044	0.0019	319%
Metabolite - 2139	61	0.0045	0.0019	165%
Spermidine	50	0.0045	0.0019	−2575%
Metabolite - 3974	61	0.0045	0.0019	114%
azelaic acid	61	0.0045	0.0019	90%
Metabolite - 5186	61	0.0048	0.002	6750%
4-acetamidobutyric acid	61	0.0048	0.002	754%
Metabolite - 5215	50	0.0049	0.002	−151%
dethiobiotin	50	0.0049	0.002	45%
Metabolite - 1496	61	0.0049	0.002	46%
Metabolite - 3955	61	0.0049	0.002	−138%
2-keto-L-gulonic acid	50	0.0054	0.0022	−167%
Metabolite - 5170	61	0.0055	0.0022	−600%
Metabolite - 2466	61	0.006	0.0024	−194%
caffeine	61	0.0064	0.0026	−287%
Isobar-40-includes-Maltotetraose-stachyose	61	0.0066	0.0027	−264%
Metabolite - 1211	61	0.0069	0.0027	−188%
Metabolite - 4706	61	0.0069	0.0027	304%
Metabolite - 4027	50	0.0069	0.0027	520%
Metabolite - 4150	50	0.007	0.0028	−483%
4-methyl-2-oxopentanoate	61	0.0072	0.0028	194%
Metabolite - 1216	61	0.0073	0.0028	109%
Metabolite - 3837	61	0.0074	0.0029	210%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
S-adenosyl-l-homocysteine	61	0.0075	0.0029	72%
Metabolite - 2768	61	0.0077	0.0029	−800%
suberic acid	61	0.008	0.0031	106%
Metabolite - 3554	61	0.0081	0.0031	272%
pyrophosphate	50	0.0081	0.0031	120%
Metabolite - 3996	50	0.0081	0.0031	86%
3-hydroxy-3-methylglutarate	50	0.0084	0.0031	123%
Metabolite - 4615	61	0.0084	0.0031	120%
4-Guanidinobutanoic acid	61	0.0084	0.0031	110%
Metabolite - 2348	61	0.0088	0.0032	151%
Metabolite - 1980	61	0.0088	0.0032	138%
N-5-aminocarbonyl-L-ornithine	50	0.0089	0.0033	177%
Metabolite - 3997	61	0.009	0.0033	1100%
fructose	50	0.0093	0.0034	−336%
Metabolite - 1286	61	0.0093	0.0034	−127%
Metabolite - 1342-possible-phenylacetylglutamine	61	0.0094	0.0034	229%
Metabolite - 4866	61	0.0099	0.0036	−479%
Metabolite - 3020	50	0.0103	0.0037	97%
Metabolite - 2607	61	0.0103	0.0037	147%
Metabolite - 1609	61	0.0104	0.0037	−227%
Metabolite - 4516	50	0.0115	0.0041	−213%
1-methyladenine	50	0.0116	0.0041	−580%
Metabolite - 2232	61	0.0116	0.0041	−242%
picolinic acid	61	0.0118	0.0041	137%
Metabolite - 2774	61	0.0126	0.0044	96%
Metabolite - 2690	61	0.0127	0.0044	2080%
Metabolite - 3221	61	0.0128	0.0044	107%
Isobar-30-includes-maltotetraose-stachyose	61	0.0132	0.0045	−202%
Metabolite - 3180	61	0.0134	0.0046	174%
Metabolite - 3220	61	0.0134	0.0046	267%
Metabolite - 3752	61	0.0135	0.0046	1122%
Metabolite - 4787	61	0.0135	0.0046	−540%
Metabolite - 4365	50	0.0146	0.0049	−229%
Metabolite - 3957	61	0.0147	0.0049	59%
DL-cystathionine	50	0.0148	0.0049	271%
2-deoxyuridine	61	0.0149	0.0049	128%
Metabolite - 3379	61	0.0151	0.005	−138%
sarcosine	50	0.0153	0.005	2138%
Metabolite - 4018	61	0.0155	0.0051	813%
cholesterol	50	0.0162	0.0053	33%
5-6-dihydrouracil	61	0.017	0.0055	154%
5-oxoproline	50	0.0174	0.0057	55%
3-amino-isobutyrate	50	0.0177	0.0057	1561%
Metabolite - 1961-retired-glycocholic acid	61	0.0179	0.0058	691%
Metabolite - 4043	50	0.0185	0.0059	38%
Metabolite - 2981	50	0.0186	0.0059	27%
Metabolite - 3984	61	0.0186	0.0059	800%
tyramine	50	0.0186	0.0059	38%
Metabolite - 3526	61	0.0194	0.0061	127%
Metabolite - 4168	61	0.0198	0.0062	54%
Putrescine	50	0.0199	0.0062	−2967%
Metabolite - 2099	61	0.0204	0.0064	−247%
pyridoxamine-phosphate	61	0.0205	0.0064	−197%
sn-Glycerol-3-phosphate	50	0.0214	0.0066	738%
GABA	50	0.022	0.0068	−192%
Metabolite - 4362	50	0.0223	0.0069	−215%
uridine-5-diphosphoglucose	50	0.0226	0.0069	−142%
saccharopine	61	0.0231	0.007	81%
Metabolite - 3132	61	0.0231	0.007	−195%
Metabolite - 4550	61	0.0234	0.0071	92%
asparagine	50	0.0235	0.0071	81%
Metabolite - 2143	61	0.0238	0.0071	345%
Metabolite - 1970	61	0.0253	0.0076	141%
L-kynurenine	50	0.0258	0.0077	335%
Metabolite - 1129	61	0.0259	0.0077	−183%
Metabolite - 1333	61	0.0263	0.0078	−268%
Metabolite - 2406	61	0.0264	0.0078	238%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 4632	50	0.0266	0.0078	53%
Metabolite - 3123	61	0.0267	0.0078	87%
Metabolite - 1911	61	0.0274	0.008	100%
Metabolite - 2806	61	0.0277	0.0081	−154%
Metabolite - 4014	50	0.0292	0.0085	69%
Metabolite - 1608	61	0.0295	0.0085	−605%
Metabolite - 1974	61	0.0295	0.0085	218%
Metabolite - 3708	61	0.0297	0.0085	46%
Metabolite - 3896	61	0.0297	0.0085	360%
Metabolite - 1303	61	0.0303	0.0086	−256%
Metabolite - 2212	61	0.0308	0.0087	453%
glutarate	61	0.0309	0.0087	155%
Metabolite - 3436	61	0.0316	0.0089	148%
D-sorbitol-6-phosphate	50	0.0319	0.009	−190%
Metabolite - 3430	61	0.0324	0.0091	110%
Metabolite - 3992-	61	0.033	0.0092	−132%
Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose	61	0.034	0.0094	−187%
Metabolite - 2390	61	0.0345	0.0096	343%
Metabolite - 3002	50	0.0346	0.0096	33%
Metabolite - 3545	61	0.0354	0.0097	165%
Metabolite - 1186	61	0.0373	0.0102	−1210%
Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	61	0.0375	0.0103	50%
Metabolite - 5207	50	0.0377	0.0103	−136%
Metabolite - 3016	50	0.0379	0.0103	−184%
Metabolite - 1963	61	0.0393	0.0106	−151%
xylitol	50	0.0393	0.0106	123%
Metabolite - 3022	50	0.0396	0.0107	92%
Metabolite - 2897	61	0.0416	0.0112	92%
uridine-5-monophosphate	61	0.0433	0.0116	−161%
Metabolite - 2027	61	0.044	0.0117	490%
2-deoxyuridine-5-triphosphate	61	0.0444	0.0118	−174%
Metabolite - 3034	50	0.0448	0.0119	67%
3-hydroxybutanoic acid	50	0.0476	0.0125	218%
3-methyl-2-oxovaleric acid	61	0.0477	0.0125	241%
Metabolite - 3980	61	0.0484	0.0127	−169%
niacinamide	61	0.052	0.0135	−138%
Isobar-27-includes-L-kynurenine-alpha-2-diamino-gamma-oxobenzenebutanoic acid	61	0.052	0.0135	645%
Metabolite - 4133	50	0.0522	0.0135	120%
Metabolite - 2827	61	0.0526	0.0136	−202%
Metabolite - 5189	61	0.0536	0.0138	110%
Metabolite - 2778	61	0.0537	0.0138	269%
Metabolite - 3027	50	0.0537	0.0138	130%
biliverdin	61	0.0539	0.0138	−151%
Metabolite - 3813	61	0.0547	0.0139	146%
uridine-5-diphosphoglucuronic acid	50	0.055	0.014	129%
Metabolite - 3951	61	0.0551	0.014	64%
phytonadione	50	0.0554	0.014	29%
Metabolite - 3139	61	0.0565	0.0142	71%
Metabolite - 3176-possible-creatine	61	0.0567	0.0142	−129%
Metabolite - 1718	61	0.0568	0.0142	−169%
Metabolite - 3783	61	0.0574	0.0143	−174%
Metabolite - 4616	61	0.0585	0.0145	210%
sorbitol	50	0.0592	0.0147	841%
Metabolite - 2064	61	0.0623	0.0154	54%
cytidine	61	0.0628	0.0155	181%
Metabolite - 5126	61	0.0633	0.0156	−145%
beta-alanine	50	0.0642	0.0157	52%
Metabolite - 4567	61	0.066	0.0161	632%
glucarate	50	0.0686	0.0166	−326%
Metabolite - 3539	61	0.0687	0.0166	143%
Metabolite - 3056	61	0.0688	0.0166	1354%
Metabolite - 2072	61	0.0689	0.0166	368%
Metabolite - 4032	50	0.0745	0.0179	162%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 5229	50	0.0758	0.0182	−144%
beta-nicotinamide-adenine-dinucleotide	61	0.0761	0.0182	2363%
Metabolite - 3960	61	0.0763	0.0182	−140%
Metabolite - 2121	61	0.0771	0.0183	98%
Metabolite - 3238	61	0.0778	0.0185	247%
Metabolite - 3129	61	0.0848	0.02	−118%
25-hydroxycholesterol	50	0.0913	0.0215	11%
Metabolite - 5226	50	0.0977	0.023	100%
Metabolite - 1575	61	0.1	0.0234	−188%
3-nitro-L-tyrosine	50	0.1027	0.024	96%
Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	61	0.104	0.0242	428%
Metabolite - 2250	61	0.1053	0.0245	−150%
gamma-glu-cys	61	0.1128	0.0261	−229%
Metabolite - 2853	61	0.1138	0.0263	79%
Metabolite - 3756	61	0.1144	0.0264	593%
Metabolite - 2368	61	0.115	0.0264	−507%
o-phosphoethanolamine	50	0.1171	0.0268	70%
Metabolite - 1497	61	0.1186	0.0271	−135%
Metabolite - 3475	61	0.1222	0.0278	−148%
Metabolite - 2185	61	0.1229	0.0279	61%
alpha-L-sorbopyranose	50	0.1302	0.0295	−139%
Metabolite - 4512	50	0.1307	0.0295	−167%
histamine	61	0.1324	0.0298	−130%
Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	61	0.135	0.0303	34%
Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	61	0.1383	0.0309	52%
Metabolite - 2824	61	0.1384	0.0309	125%
Metabolite - 3848	61	0.1384	0.0309	55%
biotin	61	0.1397	0.0311	−169%
L-homoserine-lactone	61	0.1404	0.0311	−118%
cytidine-5-monophosphate	61	0.1411	0.0312	41%
Metabolite - 3952	61	0.1461	0.0322	−144%
Metabolite - 3576	61	0.1462	0.0322	26%
Metabolite - 2821	61	0.1476	0.0324	291%
Metabolite - 2255	61	0.1483	0.0324	−169%
mannose	50	0.1503	0.0328	−147%
alpha-amino-adipate	50	0.1518	0.033	113%
Metabolite - 3696-retired-isobar-glycocheBenignoxycholic acid-glycodeoxycholic acid	61	0.152	0.033	230%
glucose-6-phosphate	50	0.153	0.0331	−144%
Metabolite - 2724	61	0.1543	0.0333	51%
Metabolite - 1616	61	0.1552	0.0334	−158%
Metabolite - 2347	61	0.1567	0.0337	42%
Metabolite - 2313	61	0.1604	0.0344	22%
Metabolite - 2389	61	0.1657	0.0354	22%
mannose-6-phosphate	50	0.1678	0.0357	−200%
Metabolite - 4503	50	0.1692	0.036	426%
serine	50	0.1707	0.0362	22%
Metabolite - 2005	61	0.172	0.0364	52%
Metabolite - 4806	50	0.1728	0.0364	22%
Metabolite - 4030-possible-glutethimide-or-securinine	61	0.1763	0.0371	52%
Metabolite - 3832-possible-phenol-sulfate	61	0.1775	0.0372	199%
glucono-gamma-lactone	50	0.1776	0.0372	−143%
Metabolite - 1070	61	0.1836	0.0383	23%
Metabolite - 4019	50	0.1844	0.0384	32%
Metabolite - 4355	50	0.1854	0.0385	22%
N-acetyl-D-glucosamine	50	0.186	0.0385	31%
Metabolite - 2198	61	0.1861	0.0385	−144%
Metabolite - 4053	50	0.1928	0.0397	45%
Isobar-3-includes-inositol-1-phosphate-mannose-6-phosphate-glucose-6-phosphate-D-mannose-1-phosphate-	61	0.1941	0.0399	−127%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
alpha-D-glucose-1-phosphate-alpha-D-galactose-1-phosphate				
maltose	50	0.1978	0.0406	426%
Metabolite - 4868-possible-Bradykinin	61	0.1998	0.0409	−120%
Metabolite - 4497	50	0.2013	0.0411	−132%
Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	61	0.2053	0.0418	−129%
Metabolite - 1457	61	0.2062	0.0419	41%
Metabolite - 2691	61	0.2102	0.0426	48%
Metabolite - 2075	61	0.2122	0.0428	−161%
dulcitol	50	0.2122	0.0428	−146%
Metabolite - 4931	61	0.2153	0.0433	30%
orotidine-5-phosphate	61	0.2187	0.0439	81%
Metabolite - 3074	50	0.2196	0.0439	86%
hypotaurine	50	0.221	0.044	60%
N-acetyl-D-galactosamine	50	0.2211	0.044	33%
Metabolite - 4116	61	0.2274	0.0452	16%
Metabolite - 3476	61	0.2356	0.0467	−137%
adenine	50	0.2383	0.0471	58%
N-6-trimethyl-l-lysine	61	0.2389	0.0471	−132%
2-deoxy-D-glucose	50	0.2399	0.0472	−142%
Metabolite - 3317	61	0.2414	0.0474	42%
glutamine	50	0.2426	0.0475	55%
Metabolite - 1573	61	0.247	0.0482	42%
Isobar-32-includes-N-acetyl-D-glucosamine-N-acetyl-D-mannosamine	61	0.2551	0.0497	24%
Metabolite - 1248-possible-avermectin-aglycone	61	0.2596	0.0505	−135%
Metabolite - 2388	61	0.2679	0.052	19%
Metabolite - 2546	61	0.2715	0.0525	91%
Metabolite - 1113-possible-acetylcarnitine-or-isopentyl-adenine	61	0.28	0.054	23%
alpha-D-ribose-5-phosphate	50	0.2826	0.0544	−129%
Metabolite - 5227	50	0.2888	0.0555	1117%
Metabolite - 3534	61	0.2998	0.0575	58%
2-acetamido-1-amino-1-2-dideoxy-beta-D-glucopyranose	50	0.3037	0.0581	25%
Metabolite - 5211	50	0.3045	0.0581	−184%
Metabolite - 1653	61	0.3126	0.0595	−127%
Metabolite - 2036	61	0.3211	0.061	115%
Metabolite - 4003	61	0.3245	0.0615	−124%
Metabolite - 4058	50	0.3276	0.0619	27%
Metabolite - 2055	61	0.3345	0.0631	−122%
3-phospho-l-serine	61	0.3436	0.0646	−109%
Metabolite - 3073	50	0.3654	0.0686	45%
Metabolite - 4272	50	0.3717	0.0696	−119%
Metabolite - 1203-possible-acetylbrowniine-tricornine-germine-or-veracevine	61	0.3764	0.0703	−140%
Metabolite - 4448	61	0.4001	0.0746	−116%
Metabolite - 2846	61	0.4122	0.0767	80%
Metabolite - 5213	50	0.4147	0.077	−118%
galactose	50	0.4216	0.0781	17%
hippuric acid	61	0.4252	0.0786	−139%
Metabolite - 3514-retired-topiramate	61	0.4327	0.0798	−341%
Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	61	0.4395	0.0808	37%
uridine	61	0.4426	0.0812	−108%
Metabolite - 1330	61	0.4441	0.0813	57%
Metabolite - 3994	61	0.4454	0.0814	−128%
Metabolite - 4017	50	0.4508	0.0822	16%
Metabolite - 5147	61	0.461	0.0838	196%
Metabolite - 4637	50	0.4761	0.0864	12%
Metabolite - 3668	61	0.477	0.0864	23%
Metabolite - 3365	61	0.4807	0.0868	−127%
Metabolite - 1455	61	0.4815	0.0868	−171%
Metabolite - 4096-gamma-glu-gly-leu-	61	0.4858	0.0874	−109%
Metabolite - 1187	61	0.4937	0.0886	−126%
Metabolite - 2194	61	0.5147	0.0922	30%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3543	61	0.5175	0.0925	44%
possible-ISOBAR-DL-aspartic acid-	50	0.519	0.0925	22%
Metabolite - 3522	61	0.5205	0.0925	−231%
Metabolite - 2105	61	0.521	0.0925	15%
dihydroxyacetone-phosphate	61	0.532	0.0942	−116%
Metabolite - 3051	61	0.5346	0.0945	29%
Metabolite - 3755	61	0.5481	0.0967	12%
Metabolite - 3604	61	0.5512	0.097	−129%
Metabolite - 4238	61	0.5582	0.098	23%
Metabolite - 4523	50	0.5592	0.098	13%
Metabolite - 2407	61	0.5602	0.098	−133%
Metabolite - 4354	50	0.5857	0.1021	−112%
Metabolite - 2129	61	0.5869	0.1021	17%
Metabolite - 4002	50	0.5873	0.1021	13%
Metabolite - 1392	61	0.5947	0.1031	36%
6-phosphogluconic acid	61	0.5976	0.1034	8%
phosphoenolpyruvate	50	0.6017	0.1039	16%
Carnosine	61	0.6048	0.1042	−112%
alpha-keto-glutarate	61	0.6073	0.1044	47%
Metabolite - 3484	61	0.6115	0.1049	27%
Metabolite - 2279	61	0.6193	0.1061	−115%
Metabolite - 2074	61	0.6245	0.1067	−118%
Isobar-31-includes-maltotriose-melezitose	61	0.6315	0.1077	−115%
N-acetylneuraminate	61	0.639	0.1088	11%
ascorbic acid	50	0.6412	0.1089	18%
Metabolite - 4084	50	0.6527	0.1106	−104%
Metabolite - 1088	61	0.6537	0.1106	16%
Metabolite - 4020	50	0.6567	0.1108	12%
creatinine	61	0.6624	0.1116	6%
Metabolite - 2174	61	0.6687	0.1124	15%
Metabolite - 3498	61	0.6739	0.1129	12%
Metabolite - 3401	61	0.6742	0.1129	16%
succinate	50	0.6845	0.1144	−120%
L-histidinol	61	0.6889	0.1149	−108%
Metabolite - 4667	61	0.6922	0.1152	−109%
Metabolite - 4510	50	0.6961	0.1156	9%
Metabolite - 3099	50	0.6979	0.1157	7%
Metabolite - 2056	61	0.7004	0.1158	−106%
Metabolite - 1183	61	0.7152	0.118	−118%
beta-D-lactose	50	0.7236	0.1192	14%
Metabolite - 4796	50	0.7305	0.1201	14%
Metabolite - 4235	61	0.7549	0.1238	−126%
Metabolite - 4514	50	0.7707	0.1262	−105%
Metabolite - 3531	61	0.7817	0.1277	−126%
Metabolite - 5089	61	0.783	0.1277	−121%
benzoic acid	50	0.797	0.1297	−103%
Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	61	0.808	0.1312	6%
ornithine	50	0.8172	0.1325	−106%
Metabolite - 2319	61	0.8211	0.1328	−111%
cystine	50	0.8239	0.1329	−104%
Metabolite - 5086	61	0.8247	0.1329	−110%
Metabolite - 3189	61	0.8275	0.1331	7%
guanine	50	0.8461	0.1356	8%
Metabolite - 3517	61	0.8465	0.1356	9%
Metabolite - 3040	50	0.8495	0.1358	−104%
Metabolite - 2558	61	0.8782	0.1401	7%
Metabolite - 2180	61	0.8839	0.1408	−104%
arginino-succinate	61	0.8933	0.1419	−103%
Metabolite - 4080	50	0.8946	0.1419	4%
Metabolite - 2688	61	0.9212	0.1459	−101%
aspartate	61	0.9268	0.1463	2%
Metabolite - 2703	61	0.9278	0.1463	−103%
Metabolite - 5087	61	0.9434	0.1485	−104%
Metabolite - 3694	61	0.9614	0.1509	−102%
Metabolite - 1979-Cl-adduct-of-C6H10O5	61	0.9624	0.1509	−101%

TABLE 2-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 1975	61	0.9674	0.1514	1%
Metabolite - 4271	50	0.9952	0.1555	1%

TABLE 3

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
inosine	61	<0.0001	<0.0001	−63%
Metabolite - 3390	61	<0.0001	<0.0001	−69%
octadecanoic acid	50	<0.0001	<0.0001	89%
Metabolite - 2-Aminoethyl-phosphonate	61	<0.0001	<0.0001	−78%
glycerol	50	<0.0001	<0.0001	200%
n-hexadecanoic acid	50	<0.0001	<0.0001	241%
leucine	50	<0.0001	1.00E−04	96%
Metabolite - 1498	61	<0.0001	2.00E−04	95%
Metabolite - 4013	61	<0.0001	2.00E−04	418%
Isobar-24-includes-L-arabitol-adonitol	61	<0.0001	2.00E−04	183%
4-hydroxyphenylpyruvate	61	<0.0001	2.00E−04	−71%
Putrescine	50	<0.0001	2.00E−04	−81%
glycerate	61	<0.0001	2.00E−04	235%
xanthine	61	<0.0001	2.00E−04	331%
uridine	61	<0.0001	2.00E−04	−46%
Metabolite - 1597	61	<0.0001	3.00E−04	63%
Metabolite - 4611	50	<0.0001	3.00E−04	388%
uracil	50	1.00E−04	5.00E−04	351%
3-phospho-d-glycerate	61	1.00E−04	6.00E−04	−53%
tetradecanoic acid	50	1.00E−04	6.00E−04	472%
Metabolite - 3102	50	1.00E−04	6.00E−04	716%
inositol	50	1.00E−04	6.00E−04	−74%
riboflavine	61	1.00E−04	6.00E−04	77%
Metabolite - 3772	61	1.00E−04	6.00E−04	76%
Metabolite - 3085	50	1.00E−04	6.00E−04	−53%
9-12-octadecadienoic acid-z-z-	50	1.00E−04	6.00E−04	256%
anthranilic acid	50	1.00E−04	6.00E−04	57%
n-dodecanoate	50	1.00E−04	6.00E−04	351%
Metabolite - 3215	61	1.00E−04	6.00E−04	157%
palmitoleic acid	50	1.00E−04	6.00E−04	825%
urea	50	1.00E−04	6.00E−04	241%
Metabolite - 4620	61	1.00E−04	6.00E−04	854%
valine	50	2.00E−04	7.00E−04	47%
Metabolite - 2466	61	2.00E−04	7.00E−04	−74%
Metabolite - 1349	61	2.00E−04	7.00E−04	−88%
Metabolite - 4075	50	2.00E−04	8.00E−04	689%
Metabolite - 3808	61	2.00E−04	8.00E−04	−72%
Metabolite - 5209	50	2.00E−04	8.00E−04	−78%
Metabolite - 4134	50	2.00E−04	8.00E−04	444%
Metabolite - 1116	61	2.00E−04	8.00E−04	476%
Metabolite - 4150	50	2.00E−04	8.00E−04	−68%
Metabolite - 3014	50	3.00E−04	9.00E−04	322%
Metabolite - 2548	61	3.00E−04	9.00E−04	189%
Metabolite - 3178	61	3.00E−04	0.001	−88%
uric acid	61	3.00E−04	0.001	200%
Metabolite - 1351	61	3.00E−04	0.001	291%
Metabolite - 4046	50	3.00E−04	0.001	688%
Metabolite - 1329	61	4.00E−04	0.001	147%
Metabolite - 4649	61	4.00E−04	0.0011	224%
Metabolite - 3992-	61	4.00E−04	0.0011	−33%
Metabolite - 2272	61	4.00E−04	0.0012	176%
Metabolite - 2181	61	5.00E−04	0.0013	135%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 4869	61	5.00E−04	0.0013	361%
arabinose	50	5.00E−04	0.0013	−73%
D-ribose	50	5.00E−04	0.0013	−74%
xanthosine	50	5.00E−04	0.0013	−69%
Isobar-19-includes-D-saccharic acid-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	61	6.00E−04	0.0015	−53%
3-methoxy-L-tyrosine	50	6.00E−04	0.0015	−75%
2-keto-L-gulonic acid	50	6.00E−04	0.0015	−47%
Metabolite - 2766	61	7.00E−04	0.0015	−93%
lactate	50	7.00E−04	0.0017	38%
Metabolite - 3893	61	7.00E−04	0.0017	−85%
tryptophan	61	8.00E−04	0.0017	53%
phenylalanine	61	8.00E−04	0.0017	43%
Metabolite - 1819	61	8.00E−04	0.0018	99%
Metabolite - 1323-possible-4-sulfobenzyl-alcohol	61	9.00E−04	0.0019	495%
Metabolite - 3123	61	0.001	0.0021	223%
guanosine	61	0.001	0.0022	−48%
proline	50	0.0011	0.0022	94%
N-acetyl-D-galactosamine	50	0.0011	0.0022	−58%
Metabolite - 2255	61	0.0011	0.0022	−59%
pantothenic acid	61	0.0011	0.0022	89%
Metabolite - 5212	50	0.0011	0.0022	−80%
DL-pipecolic acid	61	0.0012	0.0023	329%
Metabolite - 5187	61	0.0012	0.0023	348%
Metabolite - 5207	50	0.0012	0.0023	−35%
creatinine	61	0.0013	0.0023	41%
Metabolite - 4518	50	0.0013	0.0024	490%
Metabolite - 3807	61	0.0013	0.0024	363%
Metabolite - 2924	50	0.0014	0.0024	187%
Metabolite - 4617	61	0.0014	0.0024	107%
Metabolite - 3165	61	0.0014	0.0024	39%
Metabolite - 4428	61	0.0014	0.0024	155%
Metabolite - 5107	61	0.0014	0.0024	170%
Metabolite - 3833	61	0.0015	0.0024	188%
Metabolite - 2607	61	0.0015	0.0024	348%
ethylmalonic acid	61	0.0015	0.0024	894%
Metabolite - 3837	61	0.0017	0.0028	363%
Metabolite - 3132	61	0.0017	0.0028	−58%
Metabolite - 4051	50	0.0018	0.0028	266%
Isobar-3-includes-inositol-1-phosphate-mannose-6-phosphate-glucose-6-phosphate-D-mannose-1-phosphate-alpha-D-glucose-1-phosphate-alpha-D-galactose-1-phosphate	61	0.0018	0.0029	−52%
Metabolite - 3003	50	0.0019	0.0029	94%
allantoin	61	0.002	0.0031	211%
Metabolite - 3138	61	0.0021	0.0032	128%
catechol	61	0.0021	0.0032	292%
heptadecanoic acid	50	0.0022	0.0032	71%
Metabolite - 1843	61	0.0022	0.0033	361%
N-6-trimethyl-l-lysine	61	0.0023	0.0033	−44%
phosphate	50	0.0024	0.0034	49%
Isobar-2-includes-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-niacinamide	61	0.0025	0.0035	121%
	61	0.0025	0.0036	−35%
Metabolite - 2237	61	0.0026	0.0037	291%
Metabolite - 2567	61	0.0028	0.0038	101%
S-5-adenosyl-L-methionine	61	0.0028	0.0038	153%
Metabolite - 3489	61	0.0028	0.0038	−81%
Metabolite - 2867	61	0.0029	0.0039	−99%
1-methyladenosine	61	0.0029	0.0039	260%
thymine	50	0.0031	0.0041	561%
Metabolite - 3543	61	0.0032	0.0041	174%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
D-sorbitol-6-phosphate	50	0.0032	0.0041	−66%
Metabolite - 2250	61	0.0033	0.0042	−61%
citric acid	50	0.0034	0.0043	−92%
L-alpha-glycerophosphorylcholine	61	0.0035	0.0043	192%
Metabolite - 1288	61	0.0035	0.0043	212%
elaidic acid	50	0.0035	0.0044	241%
alpha-4-dihydroxybenzenepropanoic acid	50	0.0036	0.0044	1900%
Metabolite - 3996	50	0.0036	0.0044	104%
Metabolite - 2711	61	0.0037	0.0044	65%
mannose-6-phosphate	50	0.0038	0.0045	−82%
Metabolite - 1457	61	0.0038	0.0045	115%
Metabolite - 3364	61	0.0039	0.0046	232%
glyceric acid	50	0.0039	0.0046	78%
Metabolite - 4615	61	0.004	0.0046	154%
uridine-5-diphosphoglucose	50	0.004	0.0046	−35%
Metabolite - 2323	61	0.0041	0.0047	111%
Metabolite - 1333	61	0.0042	0.0047	−71%
Metabolite - 3966	61	0.0042	0.0047	171%
3-methylglutaric acid	61	0.0043	0.0047	319%
mercaptopyruvate	61	0.0043	0.0047	130%
D-allose	50	0.0043	0.0047	−87%
Metabolite - 1342-possible-phenylacetylglutamine	61	0.0043	0.0047	286%
isoleucine	50	0.0044	0.0047	33%
Metabolite - 3044	61	0.0046	0.0049	120%
4-acetamidobutyric acid	61	0.0048	0.0051	754%
3-phospho-l-serine	61	0.0051	0.0053	−22%
Metabolite - 3531	61	0.0051	0.0053	160%
Metabolite - 3514-retired-topiramate	61	0.0053	0.0055	170%
inositol-1-phosphate	50	0.0054	0.0055	88%
Metabolite - 1392	61	0.0057	0.0059	164%
Metabolite - 2973	50	0.006	0.006	−38%
Metabolite - 5214	50	0.0062	0.0062	−71%
Metabolite - 1394-possible-Losartan	61	0.0063	0.0063	109%
Metabolite - 4550	61	0.0065	0.0064	95%
Metabolite - 3816	61	0.0065	0.0064	−92%
Metabolite - 2141	61	0.0068	0.0066	181%
Metabolite - 3526	61	0.0075	0.0072	196%
Metabolite - 1831-possible-Cl-adduct-of-citrulline	61	0.0078	0.0075	86%
Metabolite - 1330	61	0.0079	0.0076	216%
spermine	50	0.0085	0.0081	−91%
Metabolite - 5186	61	0.0087	0.0081	879%
Metabolite - 4637	50	0.0087	0.0081	−28%
Metabolite - 3708	61	0.0087	0.0081	61%
Metabolite - 1496	61	0.0087	0.0081	46%
3-methyl-L-histidine	61	0.009	0.0082	51%
Metabolite - 3668	61	0.009	0.0082	132%
taurine	61	0.0091	0.0083	−42%
Metabolite - 5210	50	0.0092	0.0083	−44%
histidine	50	0.0093	0.0083	39%
Metabolite - 3522	61	0.0094	0.0084	182%
Metabolite - 4014	50	0.01	0.0088	104%
quinolinic acid	61	0.0101	0.0088	93%
Metabolite - 1465	61	0.0101	0.0088	124%
Metabolite - 3539	61	0.0102	0.0089	460%
Metabolite - 1186	61	0.0105	0.0091	−82%
arachidonic acid	50	0.0106	0.0091	74%
Metabolite - 3998	50	0.0108	0.0092	32%
carnitine	61	0.0111	0.0094	74%
Metabolite - 2900-alanine	61	0.0111	0.0094	103%
Isobar-6-includes-valine-betaine	50	0.0115	0.0096	54%
Metabolite - 3997	61	0.0115	0.0096	30%
Metabolite - 3554	61	0.0116	0.0096	740%
Metabolite - 2111	61	0.0121	0.0099	226%
	61	0.0121	0.0099	76%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 4019	50	0.0125	0.0102	−35%
Metabolite - 3221	61	0.0128	0.0103	107%
Metabolite - 5110	61	0.0132	0.0107	131%
N-acetyl-D-glucosamine	50	0.0134	0.0107	−42%
4-Guanidinobutanoic acid	61	0.0136	0.0108	98%
5-s-methyl-5-thioadenosine	61	0.0137	0.0108	152%
Metabolite - 5087	61	0.014	0.011	105%
ribulose-5-phosphate	50	0.014	0.011	−51%
Metabolite - 3020	50	0.0146	0.0114	76%
Metabolite - 3436	61	0.0152	0.0118	213%
3-amino-isobutyrate	50	0.0162	0.0125	2172%
Metabolite - 3955	61	0.0171	0.0131	−25%
Metabolite - 2897	61	0.0171	0.0131	121%
Metabolite - 3220	61	0.0175	0.0133	235%
Metabolite - 5089	61	0.0177	0.0134	133%
Metabolite - 2690	61	0.0191	0.0142	784%
suberic acid	61	0.0191	0.0142	79%
Metabolite - 2688	61	0.0191	0.0142	−18%
Metabolite - 4235	61	0.0193	0.0142	140%
Metabolite - 1974	61	0.0194	0.0142	289%
gamma-L-glutamyl-L-glutamine	61	0.0195	0.0142	−68%
Metabolite - 2347	61	0.02	0.0145	69%
Metabolite - 4706	61	0.0201	0.0145	184%
picolinic acid	61	0.0201	0.0145	131%
Metabolite - 2143	61	0.0204	0.0146	408%
Metabolite - 4866	61	0.0209	0.0149	−79%
Metabolite - 4018	61	0.0212	0.015	564%
2-acetamido-1-amino-1-2-dideoxy-beta-D-glucopyranose	50	0.0214	0.0151	−46%
adenosine	61	0.022	0.0155	−56%
sarcosine	50	0.0225	0.0157	795%
Metabolite - 1069-possible-dehydroepiandrosterone-sulfate-	61	0.0229	0.0159	−79%
DL-cystathionine	50	0.0233	0.0161	203%
Metabolite - 5086	61	0.0236	0.0163	53%
Metabolite - 3064	61	0.0242	0.0166	96%
L-kynurenine	50	0.0252	0.0172	347%
pyrophosphate	50	0.0256	0.0173	84%
Spermidine	50	0.0257	0.0173	−92%
Metabolite - 1961-retired-glycocholic acid	61	0.0257	0.0173	444%
Metabolite - 1608	61	0.0261	0.0174	−60%
Metabolite - 5109	61	0.0261	0.0174	156%
3-hydroxybutanoic acid	50	0.0263	0.0174	305%
Metabolite - 1114	61	0.0264	0.0174	33%
Metabolite - 5232	50	0.0267	0.0176	150%
N-acetylserotonin	50	0.0272	0.0178	192%
Metabolite - 3984	61	0.0287	0.0187	468%
Metabolite - 1595-possible-glutathione-metabolite	61	0.0293	0.019	−66%
trans-4-hydroxyproline	50	0.0308	0.0199	89%
Metabolite - 4593	50	0.0311	0.02	56%
Carnosine	61	0.0326	0.0209	63%
Metabolite - 2139	61	0.0342	0.0218	88%
beta-alanine	50	0.0345	0.0218	74%
Metabolite - 2390	61	0.0345	0.0218	343%
Metabolite - 2292	61	0.035	0.022	−76%
Metabolite - 2075	61	0.0355	0.0222	−75%
Metabolite - 4331	61	0.0357	0.0222	56%
Metabolite - 2108	61	0.0374	0.0232	44%
Metabolite - 3370	61	0.0394	0.0242	31%
Metabolite - 4168	61	0.0394	0.0242	49%
Metabolite - 4868-possible-Bradykinin	61	0.0397	0.0243	−61%
DL-homocysteine	61	0.0409	0.0249	45%
sn-Glycerol-3-phosphate	50	0.0414	0.0251	322%
Metabolite - 3139	61	0.0421	0.0254	−31%
Metabolite - 5126	61	0.0422	0.0254	−38%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 1129	61	0.0427	0.0256	−56%
Metabolite - 1203-possible-acetylbrowniine-tricornine-germine-or-veracevine	61	0.0434	0.0258	−62%
Metabolite - 5108	61	0.0435	0.0258	95%
Metabolite - 4027	50	0.0437	0.0259	153%
Metabolite - 2099	61	0.0442	0.0261	−68%
arginino-succinate	61	0.0455	0.0267	−50%
L-allo-threonine	50	0.0477	0.0279	26%
Metabolite - 2853	61	0.0497	0.029	124%
Metabolite - 1576	61	0.0509	0.0295	41%
Metabolite - 1303	61	0.0513	0.0296	−60%
noradrenaline	50	0.0515	0.0296	26%
Metabolite - 1713	61	0.0518	0.0297	71%
Metabolite - 2778	61	0.0537	0.0305	269%
sorbitol	50	0.0539	0.0305	1085%
Metabolite - 1718	61	0.0539	0.0305	−51%
Metabolite - 4567	61	0.0542	0.0305	1058%
gamma-glu-cys	61	0.0543	0.0305	−73%
caffeine	61	0.0545	0.0305	−71%
Metabolite - 5167	61	0.0553	0.0308	72%
fumaric acid	50	0.0577	0.032	63%
Metabolite - 3379	61	0.0578	0.032	−26%
Metabolite - 1970	61	0.059	0.0324	102%
Metabolite - 2406	61	0.0591	0.0324	159%
threonine	50	0.0604	0.033	24%
Metabolite - 2072	61	0.0621	0.0338	417%
Metabolite - 5229	50	0.0624	0.0339	−32%
Metabolite - 3960	61	0.0638	0.0343	−30%
Metabolite - 3022	50	0.0639	0.0343	79%
Metabolite - 5166	61	0.064	0.0343	72%
Metabolite - 3056	61	0.0644	0.0344	1785%
Metabolite - 2027	61	0.0656	0.0349	301%
Metabolite - 4015	50	0.0678	0.0359	72%
Metabolite - 2118	61	0.0694	0.0366	−26%
Metabolite - 1070	61	0.0695	0.0366	−41%
Metabolite - 4516	50	0.0724	0.038	−50%
Metabolite - 4365	50	0.0728	0.038	−56%
Metabolite - 2806	61	0.0732	0.038	−26%
Metabolite - 3896	61	0.0733	0.038	179%
glutathione-reduced	61	0.0737	0.0381	−78%
Metabolite - 3180	61	0.0751	0.0387	88%
3-methyl-2-oxovaleric acid	61	0.0755	0.0388	170%
Metabolite - 3073	50	0.0767	0.0392	138%
Metabolite - 1327-possible-bilirubin	61	0.0774	0.0395	41%
Metabolite - 3238	61	0.0778	0.0395	247%
L-homoserine-lactone	61	0.0786	0.0398	−24%
uridine-5-diphosphoglucuronic acid	50	0.0813	0.041	114%
Metabolite - 1248-possible-avermectin-aglycone	61	0.0825	0.0414	−39%
Metabolite - 3974	61	0.0853	0.0427	55%
Isobar-27-includes-L-kynurenine-alpha-2-diamino-gamma-oxobenzenebutanoic acid	61	0.0883	0.0441	293%
tyrosine	61	0.0893	0.0444	19%
Metabolite - 2105	61	0.0921	0.0456	−42%
Metabolite - 4017	50	0.0939	0.0462	−24%
saccharopine	61	0.094	0.0462	47%
Metabolite - 3002	50	0.0977	0.0479	25%
Metabolite - 4512	50	0.0991	0.0484	−55%
Metabolite - 1977	61	0.1008	0.0491	51%
Metabolite - 3771	61	0.1044	0.0506	−25%
Metabolite - 3498	61	0.1048	0.0506	−28%
aspartate	61	0.1051	0.0506	−34%
Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	61	0.1082	0.0519	407%
Metabolite - 4058	50	0.1102	0.0528	−38%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 3980	61	0.1154	0.0551	−39%
Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	61	0.1163	0.0552	−22%
5-hydroxyindoleacetate	50	0.1165	0.0552	−90%
Metabolite - 2121	61	0.1176	0.0556	84%
Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine-or-aspartame	61	0.1218	0.0574	64%
Metabolite - 3951	61	0.1225	0.0575	45%
Metabolite - 3832-possible-phenol-sulfate	61	0.1246	0.0583	327%
Metabolite - 2703	61	0.1261	0.0588	−26%
Metabolite - 3756	61	0.1282	0.0596	454%
Metabolite - 2546	61	0.1302	0.0603	197%
Metabolite - 3016	50	0.1372	0.0633	−39%
Metabolite - 3810	61	0.1419	0.0653	−31%
Metabolite - 3534	61	0.1426	0.0654	67%
melatonin	50	0.1438	0.0657	55%
Metabolite - 2821	61	0.1453	0.0662	300%
Metabolite - 1497	61	0.1469	0.0668	−25%
alpha-L-sorbopyranose	50	0.1505	0.0682	−26%
Metabolite - 3696-retired-isobar-glycochenodeoxycholic acid-glycodeoxycholic acid	61	0.152	0.0686	230%
Metabolite - 2724	61	0.1527	0.0687	52%
Metabolite - 4787	61	0.1533	0.0688	−84%
Metabolite - 4117-possible-propranolol-or-2-heptyl-3-hydroxy-quinolone	61	0.1541	0.0689	39%
Metabolite - 1573	61	0.1548	0.069	56%
beta-nicotinamide-adenine-dinucleotide	61	0.1581	0.0702	352%
alpha-D-ribose-5-phosphate	50	0.1585	0.0702	−29%
Metabolite - 1593	61	0.16	0.0707	−56%
glycine	50	0.1614	0.0711	20%
glutarate	61	0.1633	0.0717	73%
succinate	50	0.1697	0.074	84%
Metabolite - 1113-possible-acetylcarnitine-or-isopentyl-adenine	61	0.1697	0.074	30%
Metabolite - 3034	50	0.1726	0.0751	38%
Metabolite - 3848	61	0.1771	0.0767	−29%
Metabolite - 5228	50	0.1777	0.0767	22%
Metabolite - 3099	50	0.1779	0.0767	−25%
GABA	50	0.1788	0.0768	−35%
serine	50	0.1792	0.0768	−13%
Metabolite - 4133	50	0.1803	0.077	64%
Metabolite - 2036	61	0.1835	0.078	246%
Metabolite - 2824	61	0.1838	0.078	98%
possible-ISOBAR-DL-aspartic acid-maltose	50	0.1848	0.0782	−29%
	50	0.1852	0.0782	504%
Metabolite - 4503	50	0.1887	0.0794	335%
Metabolite - 2827	61	0.1937	0.0813	−56%
Metabolite - 3129	61	0.1989	0.0832	−13%
Metabolite - 1616	61	0.1999	0.0834	−64%
Metabolite - 3604	61	0.2032	0.0845	−40%
Metabolite - 5128	61	0.2076	0.0861	−72%
Isobar-5-includes-asparagine-ornithine	61	0.2092	0.0865	30%
1-7-dihydro-6h-purin-6-one	61	0.2113	0.0867	14%
1-methyladenine	50	0.2113	0.0867	−83%
Metabolite - 4030-possible-glutethimide-or-securinine	61	0.2115	0.0867	−28%
ornithine	50	0.2134	0.0872	−20%
Metabolite - 1679	61	0.2163	0.0881	56%
methionine	61	0.218	0.0886	17%
biotin	61	0.2198	0.0891	−35%
Metabolite - 4116	61	0.2206	0.0892	−13%
Metabolite - 1963	61	0.229	0.0923	−27%
Metabolite - 1575	61	0.2338	0.0938	−37%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
S-adenosyl-l-homocysteine	61	0.234	0.0938	22%
dethiobiotin	50	0.2429	0.0971	−11%
Metabolite - 1216	61	0.2446	0.0975	36%
Metabolite - 1455	61	0.2458	0.0977	206%
Metabolite - 4080	50	0.2467	0.0977	−39%
biliverdin	61	0.2525	0.0998	−25%
Metabolite - 5226	50	0.2569	0.1012	50%
25-hydroxycholesterol	50	0.258	0.1014	−6%
Metabolite - 2129	61	0.2623	0.1028	−44%
N-acetylneuraminate	61	0.265	0.1036	29%
Metabolite - 2109	61	0.2658	0.1036	27%
Metabolite - 3517	61	0.2721	0.1057	67%
Metabolite - 4667	61	0.2746	0.1064	−22%
cytidine-5-monophosphate	61	0.2754	0.1064	27%
Metabolite - 4003	61	0.276	0.1064	−19%
Metabolite - 3074	50	0.2779	0.1069	80%
Metabolite - 2774	61	0.2815	0.1079	34%
Metabolite - 5170	61	0.2827	0.1081	−98%
Metabolite - 2768	61	0.285	0.1087	−99%
dihydroxyacetone-phosphate	61	0.295	0.1122	−22%
glucarate	50	0.3014	0.1144	−73%
Metabolite - 2055	61	0.303	0.1145	27%
Metabolite - 2368	61	0.3043	0.1145	−87%
pyridoxamine-phosphate	61	0.3047	0.1145	−24%
phosphoenolpyruvate	50	0.3051	0.1145	−43%
fructose	50	0.3065	0.1148	−44%
Metabolite - 5227	50	0.3077	0.1149	740%
Metabolite - 1088	61	0.3104	0.1155	−36%
2-deoxy-D-ribose	61	0.311	0.1155	17%
phytonadione	50	0.3221	0.1194	−11%
Metabolite - 1609	61	0.3244	0.1199	−33%
malic acid	50	0.3288	0.1212	17%
Metabolite - 4796	50	0.3315	0.1218	26%
6-phosphogluconic acid	61	0.3322	0.1218	16%
benzoic acid	50	0.333	0.1218	13%
Metabolite - 1211	61	0.3356	0.1224	10%
Metabolite - 4806	50	0.3385	0.1232	18%
2-deoxyuridine	61	0.3422	0.1237	31%
cholesterol	50	0.3424	0.1237	−9%
Metabolite - 3545	61	0.3426	0.1237	51%
Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose	61	0.3458	0.1246	−17%
Metabolite - 2056	61	0.3473	0.1248	18%
3-hydroxy-3-methylglutarate	50	0.3496	0.1253	22%
4-hydroxy-2-quinolinecarboxylic acid	61	0.3526	0.1261	−14%
Metabolite - 1653	61	0.3592	0.1277	−25%
xylitol	50	0.3596	0.1277	35%
Metabolite - 2348	61	0.3597	0.1277	48%
Metabolite - 3401	61	0.3637	0.1287	41%
Isobar-40-includes-Maltotetraose-stachyose	61	0.3704	0.1308	−36%
hippuric acid	61	0.3719	0.131	−29%
glutamic acid	50	0.3743	0.1315	17%
Metabolite - 2232	61	0.3753	0.1315	−36%
Metabolite - 4362	50	0.381	0.1332	−21%
Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	61	0.3854	0.1344	−23%
Metabolite - 3430	61	0.3874	0.1348	29%
Metabolite - 2313	61	0.3923	0.1361	14%
5-6-dihydrouracil	61	0.3941	0.1361	31%
Metabolite - 1104	61	0.3943	0.1361	−23%
Metabolite - 4355	50	0.3949	0.1361	−10%
Metabolite - 2074	61	0.4055	0.1394	45%
Metabolite - 2981	50	0.4071	0.1396	8%
Metabolite - 3094	50	0.4099	0.1402	−8%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 5189	61	0.4199	0.1433	−42%
Metabolite - 2194	61	0.4272	0.1454	43%
Metabolite - 2558	61	0.4305	0.146	35%
Metabolite - 4514	50	0.4309	0.146	17%
alpha-keto-glutarate	61	0.4325	0.1461	56%
Metabolite - 5211	50	0.4333	0.1461	−47%
cytidine	61	0.4411	0.1482	39%
Isobar-30-includes-maltotetraose-stachyose	61	0.4415	0.1482	−24%
Metabolite - 2198	61	0.4438	0.1486	−14%
Metabolite - 2389	61	0.447	0.1493	−10%
histamine	61	0.4668	0.1556	−12%
Metabolite - 3952	61	0.4773	0.1584	−19%
ascorbic acid	50	0.4775	0.1584	31%
Metabolite - 3694	61	0.4868	0.1611	−28%
Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	61	0.4925	0.1625	−15%
Metabolite - 1187	61	0.4931	0.1625	−24%
Metabolite - 4931	61	0.4969	0.1633	16%
Metabolite - 2319	61	0.5011	0.1643	−27%
Metabolite - 3189	61	0.5094	0.1667	39%
Metabolite - 3752	61	0.5167	0.1687	43%
Metabolite - 5215	50	0.5182	0.1688	−10%
Metabolite - 3484	61	0.5253	0.1707	32%
Metabolite - 3365	61	0.5283	0.171	−22%
Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	61	0.5285	0.171	−20%
Metabolite - 4272	50	0.5403	0.1742	−13%
Metabolite - 2185	61	0.5423	0.1742	19%
Metabolite - 3755	61	0.5431	0.1742	10%
Metabolite - 4497	50	0.5432	0.1742	−14%
orotidine-5-phosphate	61	0.5557	0.1777	−20%
Metabolite - 3051	61	0.5569	0.1777	26%
N-5-aminocarbonyl-L-ornithine	50	0.5705	0.1813	18%
Metabolite - 3317	61	0.5709	0.1813	19%
Metabolite - 2041	61	0.5719	0.1813	16%
Metabolite - 2846	61	0.5851	0.1844	−25%
cystine	50	0.5862	0.1844	−11%
Metabolite - 4032	50	0.5865	0.1844	26%
azelaic acid	61	0.5881	0.1844	16%
Metabolite - 3475	61	0.5881	0.1844	−17%
o-phosphoethanolamine	50	0.5905	0.1847	18%
cysteine	50	0.5935	0.1853	21%
Metabolite - 1911	61	0.5982	0.1861	22%
Metabolite - 4053	50	0.5988	0.1861	15%
galactose	50	0.6145	0.1906	−10%
Metabolite - 1183	61	0.6174	0.191	−22%
Metabolite - 2212	61	0.6301	0.1946	31%
hypotaurine	50	0.6325	0.1949	18%
Metabolite - 3957	61	0.6423	0.1975	11%
Metabolite - 1286	61	0.646	0.1982	−6%
Isobar-22-includes-glutamic acid-O-acetyl-L-serine	61	0.6499	0.199	6%
Metabolite - 4616	61	0.6537	0.1997	−16%
Isobar-32-includes-N-acetyl-D-glucosamine-N-acetyl-D-mannosamine	61	0.659	0.2009	−8%
Metabolite - 2407	61	0.6631	0.2017	−8%
N—N-dimethylarginine	61	0.6691	0.2031	13%
Metabolite - 4354	50	0.6766	0.2049	−8%
Metabolite - 4510	50	0.6881	0.2076	11%
tyramine	50	0.6893	0.2076	5%
Metabolite - 4632	50	0.6898	0.2076	6%
Metabolite - 4271	50	0.6928	0.2081	22%
Metabolite - 3994	61	0.6964	0.2087	−16%
Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	61	0.6977	0.2087	−8%
Metabolite - 4448	61	0.7093	0.2117	−6%

TABLE 3-continued

Prostate Cancer Biomarkers from subjects with Metastatic, High Grade Prostate Cancer compared to subjects with Lower Grade Prostate Cancer.

COMPOUND	Library	p-value	q-value	% Change in high grade PCA
Metabolite - 2064	61	0.7138	0.2126	7%
glutamine	50	0.7211	0.2143	12%
guanine	50	0.7322	0.2172	−14%
Metabolite - 2279	61	0.7424	0.2195	−10%
4-methyl-2-oxopentanoate	61	0.7432	0.2195	12%
Metabolite - 3040	50	0.7523	0.2217	−7%
Metabolite - 2691	61	0.7568	0.2226	11%
Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	61	0.7623	0.2233	−9%
Metabolite - 4523	50	0.7627	0.2233	6%
Metabolite - 3027	50	0.7639	0.2233	10%
Metabolite - 4043	50	0.7735	0.2254	4%
dulcitol	50	0.7743	0.2254	−6%
beta-D-lactose	50	0.7821	0.2272	11%
Metabolite - 1975	61	0.7859	0.2279	11%
5-oxoproline	50	0.7882	0.2281	5%
Metabolite - 3813	61	0.7998	0.2306	14%
3-nitro-L-tyrosine	50	0.8003	0.2306	8%
Metabolite - 4002	50	0.815	0.2344	5%
Metabolite - 4238	61	0.8303	0.2383	8%
Metabolite - 2388	61	0.8374	0.2399	−4%
Metabolite - 3783	61	0.8416	0.2406	−6%
Metabolite - 4084	50	0.849	0.2422	1%
Metabolite - 3778	61	0.8508	0.2423	−8%
Metabolite - 3476	61	0.8527	0.2423	−6%
Metabolite - 1979-Cl-adduct-of-C6H10O5	61	0.8564	0.2426	−5%
Metabolite - 1980	61	0.8571	0.2426	9%
Metabolite - 2005	61	0.8602	0.243	5%
alpha-amino-adipate	50	0.862	0.243	7%
Metabolite - 5213	50	0.8674	0.2441	−4%
glucose-6-phosphate	50	0.8781	0.2461	−4%
Metabolite - 2174	61	0.8781	0.2461	5%
Metabolite - 5147	61	0.881	0.2464	−14%
Metabolite - 4020	50	0.8947	0.2493	3%
adenine	50	0.8948	0.2493	−4%
Metabolite - 3176-possible-creatine	61	0.9158	0.2547	−1%
Metabolite - 2180	61	0.937	0.26	3%
Metabolite - 3576	61	0.9487	0.2624	2%
2-deoxyuridine-5-triphosphate	61	0.9491	0.2624	−2%
L-histidinol	61	0.9545	0.2629	1%
Metabolite - 4096-gamma-glu-gly-leu-	61	0.9545	0.2629	−1%
Metabolite - 2753	61	0.9699	0.2664	1%
Isobar-31-includes-maltotriose-melezitose	61	0.9712	0.2664	1%
glucono-gamma-lactone	50	0.9791	0.2681	1%
uridine-5-monophosphate	61	0.9814	0.2682	0%
asparagine	50	0.9893	0.2695	0%
mannose	50	0.9898	0.2695	0%
2-deoxy-D-glucose	50	0.9996	0.2716	0%

Example 2

Cancer vs. Non-Cancer

[0115] Biomarkers were discovered by (1) analyzing plasma and/or urine samples from different groups of human subjects to determine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0116] The plasma and/or urine samples used for the analysis were from 53 control individuals with negative biopsies for prostate cancer and 48 individuals with prostate cancer. After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0117] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Prostate cancer vs. Control plasma, Prostate cancer vs. Control urine).

Biomarkers:

[0118] As listed below in Table 4, biomarkers were discovered that were differentially present between plasma samples from subjects with prostate cancer and Control subjects with negative prostate biopsies (i.e. not diagnosed with prostate

cancer). Table 5 lists biomarkers that were discovered that were differentially present between urine samples from subjects with prostate cancer and Control subjects (i.e. not diagnosed with prostate cancer).

[0119] Tables 4 and 5 include, for each listed biomarker, the p-value and the q-value determined in the statistical analysis of the data concerning the biomarkers and an indication of the percentage difference in the lower grade prostate cancer mean level as compared to the control mean level (Table 4) and the metastatic/high grade prostate cancer mean level as compared to the control mean level (Table 5). The term "Isobar" as used in the tables indicates the compounds that could not be distinguished from each other on the analytical platform used in the analysis (i.e., the compounds in an isobar elute at nearly the same time and have similar (and sometimes exactly the same) quant ions, and thus cannot be distinguished). Library indicates the chemical library that was used to identify the compounds. The number 50 refers to the GC library and the number 35 refers to the LC library.

TABLE 4

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3377	35	0	0.0043	192%
Metabolite - 2329	35	1.00E-04	0.0144	73%
Metabolite - 3305	35	1.00E-04	0.0138	144%
palmitoleic acid	50	4.00E-04	0.0313	67%
Metabolite - 3327	35	5.00E-04	0.0313	111%
Metabolite - 1127	35	6.00E-04	0.0313	54%
DL-indole-3-lactic acid	50; 35	7.00E-04	0.0325	33%
Metabolite - 3322	35	8.00E-04	0.0325	84%
Metabolite - 1185	35	0.0012	0.045	-41%
elaidic acid	50	0.0021	0.0665	54%
Metabolite - 3603	35	0.0022	0.0665	-29%
lactate	50	0.0035	0.0882	17%
Metabolite - 2141	35	0.0036	0.0882	126%
Metabolite - 5349	50	0.0037	0.0882	-19%
Metabolite - 2711	35	0.0046	0.1028	27%
caffeine	35	0.0049	0.1041	104%
N-acetyl-L-valine	35	0.0061	0.1135	-18%
monosaccharide	50	0.0063	0.1135	-18%
Metabolite - 2108	35	0.0069	0.1135	65%
Metabolite - 3402	35	0.007	0.1135	59%
Metabolite - 2407	35	0.0071	0.1135	-34%
n-hexadecanoic acid	50	0.0078	0.1191	19%
Metabolite - 3030	50	0.0082	0.1196	-18%
Metabolite - 1988	35	0.01	0.1398	43%
alpha-keto-glutarate	35	0.0104	0.1398	81%
Metabolite - 1121	35	0.0123	0.1555	-24%
Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.0125	0.1555	-27%
Metabolite - 1104	35	0.0155	0.1863	20%
Metabolite - 1116	35	0.0183	0.2034	78%
Metabolite - 1286	35	0.0188	0.2034	-15%
Metabolite - 1713	35	0.0189	0.2034	54%
Metabolite - 3088	50	0.0199	0.2034	-30%
Metabolite - 3977	35	0.0207	0.2034	20%
theobromine-theophylline	35	0.0212	0.2034	74%
Metabolite - 1839	35	0.0223	0.2034	85%
valine	50	0.0224	0.2034	16%
tartaric acid	35	0.0225	0.2034	61%
Metabolite - 3033	50	0.0244	0.2034	-13%
Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	35	0.0247	0.2034	-17%
glycerol	50	0.0247	0.2034	16%
3-methylglutaric acid	35	0.0249	0.2034	22%
Metabolite - 1831-possible-Cl-adduct-of-citrulline	35	0.0253	0.2034	160%
Metabolite - 3303	35	0.0278	0.2179	19%
Metabolite - 3900	35	0.0294	0.2256	16%
octadecanoic acid	50	0.0337	0.2512	11%
Metabolite - 3843	35	0.0346	0.2512	22%
Metabolite - 2978	50	0.035	0.2512	-22%
Metabolite - 2005	35	0.0359	0.252	35%
aspartate	50	0.041	0.2818	34%
3-hydroxybutanoic acid	50	0.0434	0.2924	81%
Metabolite - 3832-possible-phenol-sulfate	35	0.0475	0.314	97%
phenylalanine	35	0.05	0.3241	7%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3040	50	0.0517	0.329	−21%
alpha-tocopherol	50	0.0529	0.3301	91%
Metabolite - 3002	50	0.0539	0.3305	27%
creatinine	35	0.0563	0.3392	11%
dethiobiotin	50; 35	0.0603	0.3565	30%
linoleic acid	50	0.0622	0.3598	17%
L-homoserine	50	0.063	0.3598	−16%
Metabolite - 3309	35	0.066	0.3707	37%
Metabolite - 4147	50	0.0676	0.3735	32%
3-chloro-L-tyrosine	50	0.0704	0.3747	23%
isoleucine	50	0.072	0.3747	15%
Metabolite - 1834	35	0.0729	0.3747	54%
Metabolite - 3781-possible-Na-adduct-of-Isobar-21	35	0.073	0.3747	−9%
Metabolite - 2390	35	0.0735	0.3747	38%
3-amino-isobutyrate	50	0.0756	0.3747	−13%
Metabolite - 3098	50	0.0761	0.3747	−24%
Metabolite - 2389	35	0.0767	0.3747	−65%
Metabolite - 3178-possible-NH3-adduct-of-isobar-42	35	0.0803	0.3786	16%
Metabolite - 4031-possible-norlevorphenol-isobutylphendienamide-amprolium	35	0.0804	0.3786	14%
alanine	50	0.0821	0.3786	18%
leucine	50	0.0833	0.3786	15%
Metabolite - 1817	35	0.084	0.3786	−20%
Metabolite - 3146	35	0.0842	0.3786	49%
Metabolite - 3830	35	0.0863	0.3791	31%
alpha-4-dihydroxybenzenepropanoic acid	50	0.0866	0.3791	36%
Metabolite - 1829	35	0.0881	0.3809	−13%
Metabolite - 3534	35	0.0918	0.3827	43%
Metabolite - 4511	50	0.0925	0.3827	37%
Metabolite - 2285	35	0.0932	0.3827	217%
D-quinic acid	50	0.094	0.3827	72%
Isobar-6-includes-valine-betaine	35	0.0949	0.3827	8%
Metabolite - 3707	35	0.0965	0.3827	−52%
Metabolite - 3837	35	0.0965	0.3827	30%
Metabolite - 3813	35	0.0991	0.3855	38%
Metabolite - 2130	35	0.1005	0.3855	−43%
Metabolite - 3014	50	0.1016	0.3855	19%
Metabolite - 1836	35	0.1036	0.3855	39%
tryptophan	50; 35	0.1049	0.3855	12%
Metabolite - 3772	35	0.1052	0.3855	16%
Metabolite - 3138	35	0.1056	0.3855	31%
4-methyl-2-oxopentanoate	50	0.1063	0.3855	20%
glycine	50	0.1082	0.386	19%
Metabolite - 3314	35	0.1088	0.386	28%
Metabolite - 2254	35	0.112	0.3897	70%
Metabolite - 2974	50	0.1132	0.3897	−13%
p-acetamidophenyl-beta-D-glucuronide	35	0.1133	0.3897	392%
Metabolite - 3489	35	0.1178	0.4011	54%
Metabolite - 4362	50	0.1232	0.4152	−19%
carnosine	35	0.1257	0.4163	24%
melatonin	50	0.1259	0.4163	−11%
Metabolite - 3758	35	0.1279	0.4163	62%
Metabolite - 1609	35	0.1285	0.4163	23%
Metabolite - 2698	35	0.1297	0.4163	42%
trans-4-hydroxyproline	35; 50	0.1352	0.4205	−22%
Metabolite - 2391	35	0.1363	0.4205	15%
Metabolite - 4769	50	0.1368	0.4205	−15%
Metabolite - 3074	50	0.1368	0.4205	70%
Metabolite - 3067	50	0.1372	0.4205	13%
adenosine-5-monophosphate	35	0.142	0.4314	22%
Metabolite - 2287	35	0.1436	0.4322	−78%
Metabolite - 2388	35	0.1466	0.4372	−10%
cholesterol	50	0.1481	0.4372	11%
Metabolite - 1975	35	0.15	0.4372	−35%
Metabolite - 3016	50	0.1504	0.4372	10%
heptanedioic acid	35	0.1522	0.4378	−33%
glyceric acid	50	0.1532	0.4378	−16%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 2506	35	0.1556	0.4395	63%
azelaic acid	35	0.1571	0.4395	12%
Metabolite - 3143	35	0.1583	0.4395	21%
Metabolite - 5419	50	0.159	0.4395	29%
Metabolite - 2867	35	0.1608	0.4408	100%
Metabolite - 2056	35	0.1623	0.4412	17%
Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid	35	0.1646	0.4439	24%
glutamic acid	50	0.1716	0.4557	22%
Metabolite - 2924	50	0.1732	0.4557	20%
Metabolite - 3073	50	0.1743	0.4557	−19%
Isobar-5-includes-asparagine-ornithine	35	0.1744	0.4557	−14%
benzoic acid	50; 35	0.176	0.4557	−19%
tyramine	50	0.1771	0.4557	14%
Metabolite - 2255	35	0.183	0.459	−58%
glucose-6-phosphate	50	0.1835	0.459	6%
Metabolite - 1977	35	0.1838	0.459	14%
Metabolite - 2316	35	0.1841	0.459	−36%
2-keto-L-gulonic acid	50	0.1863	0.459	5%
n-dodecanoate	50	0.187	0.459	14%
Metabolite - 3474	35	0.189	0.459	−19%
ornithine	50	0.1892	0.459	22%
L-beta-imidazolelactic acid	50; 35	0.1952	0.4677	10%
5-oxoproline	50	0.1956	0.4677	10%
carnitine	35	0.197	0.4678	−9%
glutamine	50	0.1993	0.4698	16%
Metabolite - 3216	35	0.2052	0.4785	21%
Metabolite - 2212	35	0.2067	0.4785	−17%
fructose	50	0.2072	0.4785	29%
Metabolite - 3091	50	0.2097	0.481	−32%
Metabolite - 3109	50	0.216	0.4901	−25%
Metabolite - 2507	35	0.2166	0.4901	54%
histidine	50	0.2197	0.4937	13%
Metabolite - 5403	50	0.2235	0.4991	−11%
Metabolite - 1113-possible-acetylcarnitine-or-isopentyl-adenine	35	0.2254	0.5	14%
catechol	35	0.2295	0.5058	53%
Metabolite - 3019	50	0.232	0.508	−10%
Metabolite - 4032	50	0.2399	0.5217	23%
Metabolite - 2898	35	0.2417	0.5223	57%
Metabolite - 3017	50	0.2449	0.5245	−13%
5-6-Dimethylbenzimidazole	50	0.2458	0.5245	25%
Metabolite - 1211	35	0.2482	0.5261	−67%
Metabolite - 2111	35	0.2497	0.5261	25%
Metabolite - 3160	35	0.2544	0.5298	18%
Metabolite - 4767	50	0.2546	0.5298	−19%
threonine	50	0.2588	0.5353	9%
Metabolite - 4042	50	0.2647	0.5433	8%
Metabolite - 2269-	35	0.2698	0.5433	−25%
Metabolite - 4078	35	0.2704	0.5433	23%
Metabolite - 3215	35	0.2706	0.5433	15%
Metabolite - 3624	35	0.2708	0.5433	23%
Metabolite - 3085	50	0.2758	0.5438	13%
Metabolite - 2914	50	0.2774	0.5438	−2%
Metabolite - 1110	35	0.2792	0.5438	−31%
Metabolite - 4167	35	0.2792	0.5438	20%
Metabolite - 3752	35	0.282	0.5438	−60%
Metabolite - 3877	35	0.2832	0.5438	28%
Metabolite - 3165	35	0.2842	0.5438	7%
glucono-gamma-lactone	50	0.2848	0.5438	7%
Metabolite - 3578	35	0.2855	0.5438	−24%
Metabolite - 3102	50	0.2897	0.5449	9%
Metabolite - 3131	35	0.2901	0.5449	−23%
Metabolite - 2027	35	0.2909	0.5449	18%
Metabolite - 3972	35	0.2949	0.5488	−13%
Metabolite - 1188	35	0.3012	0.5488	−17%
Metabolite - 2279	35	0.3017	0.5488	36%
arachidonic acid	50	0.304	0.5488	16%
Metabolite - 3089	50	0.3056	0.5488	23%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
DL-cystathionine	35	0.3083	0.5488	−11%
trans-2-3-4-trimethoxycinnamic acid	35	0.3128	0.5488	−26%
p-hydroxybenzaldehyde	35	0.3129	0.5488	10%
Metabolite - 3576	35	0.3151	0.5488	−17%
Metabolite - 5489	50	0.3161	0.5488	−9%
Metabolite - 4795	50	0.3168	0.5488	−18%
Metabolite - 4504	50	0.3207	0.5488	16%
Metabolite - 3025	50	0.321	0.5488	−9%
fumaric acid	50	0.3213	0.5488	12%
Isobar-36-includes-D-sorbitol-6-phosphate-mannitol-1-phosphate	35	0.3219	0.5488	16%
Metabolite - 1203-possible-acetylbrowniine-tricornine-germine-or-veracevine	35	0.3221	0.5488	33%
Metabolite - 3023	50	0.3225	0.5488	−9%
xylitol	35; 50	0.3244	0.5488	−16%
Metabolite - 2592	35	0.3264	0.5488	71%
methyl-indole-3-acetate	35	0.3269	0.5488	14%
Metabolite - 3313	35	0.3272	0.5488	61%
Metabolite - 1498	35	0.3289	0.549	−13%
Metabolite - 3184	35	0.3345	0.5509	15%
serine	50	0.3365	0.5509	7%
succinate	50	0.3397	0.5509	−7%
GABA	50	0.3397	0.5509	12%
Metabolite - 3027	50	0.3399	0.5509	−8%
Metabolite - 1656	35	0.341	0.5509	−14%
Metabolite - 3086	50	0.3429	0.5509	−19%
malic acid	35	0.3478	0.5509	26%
Metabolite - 4196	50	0.3484	0.5509	26%
Metabolite - 5906	50	0.3494	0.5509	35%
allantoin	35	0.351	0.5509	9%
L-alpha-glycerophosphorylcholine	35	0.3514	0.5509	22%
L-allo-threonine	50	0.3516	0.5509	7%
Metabolite - 2347	35	0.3533	0.5509	−23%
3-methyl-L-histidine	35	0.3568	0.5509	6%
Metabolite - 1914	35	0.3578	0.5509	−25%
3-phospho-d-glycerate	35	0.3582	0.5509	16%
Isobar-20-includes-fumaric acid-3-methyl-2-oxobutanoate	35	0.3628	0.5509	−17%
urea	50	0.3643	0.5509	−6%
4-hydroxyphenylacetate	35; 50	0.3644	0.5509	5%
Metabolite - 4611	50	0.3655	0.5509	7%
Metabolite - 3807	35	0.366	0.5509	5%
pyridoxal-phosphate	35	0.3699	0.5528	−4%
Metabolite - 4361	50	0.3706	0.5528	−15%
adonitol	50	0.3737	0.5551	5%
N-N-dimethylarginine	35	0.3769	0.5553	9%
pantothenic acid	35	0.3772	0.5553	20%
Metabolite - 3012	50	0.384	0.5609	−7%
DL-pipecolic acid	35	0.3851	0.5609	11%
Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.3861	0.5609	−12%
Metabolite - 4355	50	0.389	0.5609	24%
DL-homocysteine	35	0.3893	0.5609	13%
25-hydroxycholesterol	50	0.3953	0.5642	4%
Metabolite - 4272	50	0.3955	0.5642	13%
Metabolite - 3130	35	0.3968	0.5642	18%
diaminopimelic acid	50; 35	0.3989	0.5642	−8%
Metabolite - 1835	35	0.4018	0.5642	−11%
Metabolite - 2281	35	0.403	0.5642	39%
Metabolite - 3498	35	0.4042	0.5642	−9%
Metabolite - 4084	50	0.405	0.5642	22%
proline	35; 50	0.4097	0.5684	8%
Metabolite - 3058	50	0.4147	0.573	−13%
Metabolite - 2888-possible-sulfated-Rosiglitazone	35	0.4195	0.5751	−11%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3078	50	0.4196	0.5751	−8%
Metabolite - 1911	35	0.4221	0.5761	−20%
inositol	50	0.4245	0.577	5%
citrulline	50	0.428	0.5795	−6%
Metabolite - 3055-possible-NH3-adduct-of-hippuric acid	35	0.4333	0.5828	−19%
Metabolite - 4134	50	0.4339	0.5828	−6%
Metabolite - 2546	35	0.4358	0.583	15%
mannose	50	0.4399	0.5862	4%
Metabolite - 4516	50	0.4457	0.5899	−6%
Metabolite - 5437	50	0.4462	0.5899	27%
Metabolite - 3955	35	0.4482	0.5902	−23%
phosphoenolpyruvate	35	0.453	0.5922	10%
Metabolite - 4234	35	0.4546	0.5922	9%
Metabolite - 5847	50	0.455	0.5922	20%
citric acid	50	0.4573	0.5922	4%
Metabolite - 2915	50	0.4585	0.5922	−6%
Metabolite - 3125	35	0.4693	0.6021	7%
Metabolite - 3081	50	0.4697	0.6021	9%
Metabolite - 3370	35	0.4719	0.6026	9%
Metabolite - 4096-possible-gamma-glu-gly-leu-	35	0.4808	0.6117	−16%
4-amino-5-methyl-2-1H-pyrimidinone	35	0.4852	0.6129	9%
Metabolite - 5427	50	0.4874	0.6129	4%
Metabolite - 4163	35	0.4882	0.6129	13%
Metabolite - 1216	35	0.489	0.6129	8%
nonanate	50	0.4925	0.6137	−3%
oxitryptan	35	0.4933	0.6137	10%
Metabolite - 2139	35	0.4964	0.6153	−8%
methionine	35	0.499	0.6163	4%
Metabolite - 3783	35	0.5036	0.6193	−11%
galactose	50	0.5059	0.6193	−6%
sn-Glycerol-3-phosphate	50	0.5069	0.6193	5%
Metabolite - 1208	35	0.5108	0.6218	19%
Metabolite - 2250	35	0.5155	0.6239	−15%
dulcitol	50	0.5164	0.6239	−6%
Metabolite - 4133	50	0.5194	0.6239	−7%
Metabolite - 2849-related-to-citric acid-dopamine	35	0.52	0.6239	−6%
Metabolite - 2386	50	0.5264	0.6251	13%
Metabolite - 4986	35	0.5265	0.6251	17%
Metabolite - 3044	50	0.5287	0.6251	−14%
Metabolite - 3094	35	0.5288	0.6251	9%
Metabolite - 2387	50	0.5302	0.6251	7%
gamma-L-glutamyl-L-tyrosine	35	0.5328	0.6256	49%
Isobar-2-includes-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.5344	0.6256	−4%
L-homoserine-lactone	35	0.5412	0.6289	18%
Isobar-19-includes-D-saccharic acid-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.5419	0.6289	−13%
gamma-L-glutamyl-L-glutamine	35	0.5463	0.6289	−10%
Metabolite - 2567	35	0.5465	0.6289	−11%
Metabolite - 1086	35	0.5492	0.6289	−6%
Metabolite - 4275	50	0.5505	0.6289	11%
Metabolite - 3077	50	0.5511	0.6289	−6%
gamma-glu-leu	35	0.5522	0.6289	−6%
Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.5551	0.6291	5%
Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.5561	0.6291	27%
Metabolite - 1389-possible-glucuronide-form-of-Metabolite - 1359	35	0.56	0.6314	−4%
Metabolite - 3020	50	0.5643	0.6335	14%
guanosine-5-diphosphate	35	0.5697	0.6335	−6%
Metabolite - 3426	35	0.5698	0.6335	9%
Metabolite - 2185	35	0.5712	0.6335	2%
orotidine-5-phosphate	35	0.5746	0.6335	−5%
	35	0.5748	0.6335	12%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3951	35	0.575	0.6335	5%
biliverdin	35	0.5834	0.6407	9%
Metabolite - 2313	35	0.5904	0.6449	7%
Metabolite - 3056	35	0.5918	0.6449	5%
normetanephrine	50	0.593	0.6449	−6%
Metabolite - 2100	35	0.6011	0.6511	−4%
tyrosine	50	0.6026	0.6511	4%
Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	35	0.611	0.6582	12%
Metabolite - 1597	35	0.6293	0.6744	−3%
Metabolite - 3441	35	0.6319	0.6744	6%
glycochenodeoxycholic acid/glycodeoxycholic acid	35	0.6334	0.6744	14%
Metabolite - 5346	50	0.6341	0.6744	5%
Metabolite - 3765	35	0.6389	0.6774	12%
Metabolite - 2249	35	0.6409	0.6774	7%
Metabolite - 4593	50	0.6542	0.6824	−2%
hippuric acid	35	0.6581	0.6824	10%
Metabolite - 3022	50	0.6591	0.6824	−5%
niacinamide	35	0.6593	0.6824	11%
phytonadione	50	0.6599	0.6824	4%
5-methoxytryptamine	50	0.6645	0.6824	−6%
Metabolite - 2486	35	0.6655	0.6824	9%
N-6-trimethyl-l-lysine	35	0.6657	0.6824	6%
Metabolite - 2753	35	0.6692	0.6824	5%
Metabolite - 3670	35	0.6697	0.6824	4%
Metabolite - 1465	35	0.67	0.6824	6%
Metabolite - 3604	35	0.6701	0.6824	−11%
Metabolite - 3075	50	0.6739	0.6824	−6%
Metabolite - 3879	35	0.6755	0.6824	−20%
Metabolite - 4148	50	0.6761	0.6824	−7%
Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	35	0.6781	0.6824	−7%
N-acetyl-L-leucine	35	0.6834	0.6858	13%
D-allose	50	0.6934	0.6906	−5%
Metabolite - 3181	35	0.6944	0.6906	5%
Metabolite - 3099	50	0.697	0.6906	8%
Metabolite - 2688	35	0.6986	0.6906	−8%
3-nitro-L-tyrosine	50; 35	0.7005	0.6906	8%
Metabolite - 3653-Possible-stachydrine-	35	0.7021	0.6906	−12%
Metabolite - 2392	35	0.7026	0.6906	18%
Metabolite - 3132	35	0.7104	0.695	3%
Isobar-25-includes-L-gulono-1-4-lactone-glucono-gamma-lactone-	35	0.7112	0.695	8%
Metabolite - 1323-possible-4-sulfobenzyl-alcohol	35	0.7154	0.6971	3%
heneicosanoic acid-methyl-ester	50	0.7198	0.6975	−4%
guanidineacetic acid	35	0.7202	0.6975	−5%
Metabolite - 1215	35	0.7223	0.6975	−11%
hypoxanthine	35	0.7241	0.6975	5%
Metabolite - 3134	35	0.7323	0.7008	13%
Isobar-30-includes-maltotetraose-stachyose	35	0.7345	0.7008	5%
Metabolite - 2853	35	0.7345	0.7008	7%
Metabolite - 1244	35	0.7359	0.7008	6%
Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.7405	0.7032	−7%
Metabolite - 3135	35	0.7437	0.7043	−11%
pyrophosphate	35; 50	0.7499	0.7082	9%
ethyl-3-indoleacetate	50	0.7704	0.7186	3%
Metabolite - 3476	35	0.7739	0.7186	7%
Metabolite - 1183	35	0.778	0.7186	−8%
Isobar-9-includes-sucrose-beta-D-lactose-D-trehalose-D-cellobiose-D-Maltose-palatinose-melibiose-alpha-D-lactose	35	0.7787	0.7186	5%
Metabolite - 4503	50	0.7819	0.7186	9%
L-kynurenine	35	0.7838	0.7186	3%
Metabolite - 3093	50	0.7844	0.7186	6%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 4365	50	0.7869	0.7186	5%
Metabolite - 3698	35	0.7885	0.7186	6%
oxalacetic acid	35	0.7896	0.7186	5%
inosine	35	0.7915	0.7186	−9%
Metabolite - 1573	35	0.7953	0.7186	5%
uric acid	35	0.7956	0.7186	1%
vitamin-B6	50	0.7962	0.7186	2%
Metabolite - 4020	50	0.7967	0.7186	1%
Metabolite - 1351	35	0.7988	0.7186	3%
alphahydroxybenzeneacetic acid	35	0.8012	0.7186	−3%
Metabolite - 1915	35	0.8026	0.7186	−13%
Metabolite - 3994	35	0.8031	0.7186	7%
Metabolite - 3218	35	0.8059	0.7186	4%
phenyl-beta-glucopyranoside	50	0.8076	0.7186	−4%
Metabolite - 1289	35	0.8079	0.7186	5%
histamine	35	0.81	0.7186	−5%
Metabolite - 2370	35	0.8174	0.7197	−4%
Metabolite - 2053	35	0.818	0.7197	4%
Metabolite - 5907	50	0.8229	0.7197	−2%
hydroxyacetic acid	50	0.8232	0.7197	−4%
maltose	50	0.8234	0.7197	−4%
Metabolite - 3761	35	0.824	0.7197	5%
tryptamine	50	0.8298	0.7229	−3%
Metabolite - 2809	35	0.8365	0.7257	5%
Metabolite - 4768	50	0.8383	0.7257	6%
Metabolite - 2256	35	0.8395	0.7257	4%
Metabolite - 2973	50	0.8416	0.7257	−1%
Metabolite - 3245	35	0.8492	0.7286	4%
Metabolite - 2129	35	0.8493	0.7286	5%
Metabolite - 4274	50	0.8535	0.7303	2%
Metabolite - 1974	35	0.8572	0.7316	−4%
Metabolite - 1220	35	0.8619	0.7331	−5%
pyridoxamine-phosphate	35	0.8654	0.7331	−2%
thyroxine	35	0.8659	0.7331	−2%
N-acetylserotonin	50	0.868	0.7331	1%
Metabolite - 3968	35	0.8698	0.7331	4%
Metabolite - 3108	50	0.8722	0.7333	−1%
Metabolite - 2055	35	0.8779	0.7362	−2%
D-alanyl-D-alanine	35	0.8819	0.7378	2%
Metabolite - 4791	50	0.8875	0.7401	5%
Metabolite - 3816	35	0.8926	0.7401	2%
Metabolite - 3167	35	0.8948	0.7401	3%
4-Guanidinobutanoic acid	35	0.895	0.7401	2%
glycocholic acid	35	0.8957	0.7401	5%
Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose	35	0.8978	0.7401	2%
3-hydroxyphenylacetate	35	0.9038	0.7415	1%
Metabolite - 3004	50	0.9114	0.7415	2%
noradrenaline	50	0.9121	0.7415	2%
Metabolite - 2074	35	0.9154	0.7415	−2%
Metabolite - 2686	35	0.9155	0.7415	−1%
Metabolite - 3436	35	0.916	0.7415	−2%
Metabolite - 4091-possible-gamma-glutamyl-glutamic acid	35	0.9173	0.7415	1%
3-methoxy-L-tyrosine	50	0.9174	0.7415	0%
7-8-dihydrofolic acid	35	0.9197	0.7415	−4%
Metabolite - 4238	35	0.9224	0.7415	−2%
glucarate	50	0.9243	0.7415	2%
phosphate	50	0.9259	0.7415	1%
Metabolite - 1979-Cl-adduct-of-C6H10O5	35	0.9351	0.7426	−1%
Metabolite - 1335	35	0.9375	0.7426	−1%
Metabolite - 3166	35	0.9387	0.7426	2%
xanthine	35	0.9416	0.7426	−2%
3-hydroxypropanoate	50	0.9424	0.7426	1%
Metabolite - 4015	50	0.9455	0.7426	0%
Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine-or-aspartame	35	0.946	0.7426	−1%

TABLE 4-continued

Prostate Cancer Biomarkers from Plasma from subjects with Prostate Cancer compared to Plasma from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	35	0.9467	0.7426	−1%
Metabolite - 1843	35	0.9471	0.7426	−1%
Metabolite - 3615	35	0.9529	0.7437	−1%
octopamine	50	0.9564	0.7447	1%
Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	35	0.9652	0.7498	0%
Metabolite - 3003	50	0.9736	0.7546	0%
Metabolite - 5366	50	0.983	0.757	0%
Metabolite - 4360	50	0.9831	0.757	−1%
Metabolite - 3097	50	0.9839	0.757	−1%
Metabolite - 1392	35	0.9857	0.757	1%
Metabolite - 3129	35	0.9973	0.7602	0%
Metabolite - 1133-possible-Na-adduct-of-EDTA	35	0.9981	0.7602	0%
Metabolite - 3243	35	0.9986	0.7602	0%
Metabolite - 1349	35	0.9989	0.7602	0%

TABLE 5

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 2974	50	0.0023	0.1555	−32%
2-amino-butyrate	50	0.0035	0.1555	−27%
guanidineacetic acid	35	0.0048	0.1555	−65%
citrulline	50	0.006	0.1555	−43%
Metabolite - 2752	35	0.0063	0.1555	−38%
adenosine	35	0.0067	0.1555	−46%
Metabolite - 2242	35	0.0068	0.1555	170%
3-methoxy-4-hydroxyphenylacetate	50	0.0096	0.1555	−41%
Metabolite - 4504	50	0.0118	0.1555	−36%
N-acetyl-D-glucosamine	50	0.012	0.1555	−53%
Metabolite - 2978	50	0.012	0.1555	−29%
Metabolite - 1573	35	0.013	0.1555	−28%
Metabolite - 2181	35	0.0134	0.1555	−34%
Metabolite - 4522	50	0.0149	0.1555	−35%
serine	50	0.016	0.1555	−38%
methionine	35	0.0162	0.1555	−32%
catechol	35	0.0163	0.1555	−60%
Metabolite - 3215	35	0.0164	0.1555	−31%
Metabolite - 4593	50	0.0167	0.1555	−36%
Isobar-9-includes-sucrose-beta-D-lactose-D-trehalose-D-cellobiose-D-Maltose-palatinose-melibiose-alpha-D-lactose	35	0.017	0.1555	−49%
Metabolite - 2567	35	0.0188	0.1611	−33%
uracil	50	0.0194	0.1611	−36%
Metabolite - 3020	50	0.0217	0.1611	−41%
Metabolite - 3807	35	0.0225	0.1611	−25%
arabinose	50	0.0227	0.1611	−47%
histamine	35	0.0249	0.1611	−37%
Metabolite - 3761	35	0.026	0.1611	−31%
Metabolite - 3443	35	0.0262	0.1611	100%
DL-homocysteine	35	0.0263	0.1611	−43%
Metabolite - 2271	35	0.0264	0.1611	−47%
Metabolite - 4503	50	0.0264	0.1611	−38%
glycine	50	0.0284	0.1641	−37%
Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.0297	0.1641	−33%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
adenosine-3-5-cyclic-monophosphate	35	0.0301	0.1641	−24%
citric acid	50	0.0304	0.1641	−38%
dopamine	50	0.0317	0.1641	−30%
Metabolite - 1974	35	0.0347	0.1641	−42%
N-acetylneuraminate	50	0.0348	0.1641	−32%
Metabolite - 3381	35	0.0352	0.1641	−35%
adenine	50	0.0359	0.1641	−37%
Metabolite - 2051	35	0.0361	0.1641	−22%
serotonin	35	0.0364	0.1641	−33%
Metabolite - 4636	50	0.0396	0.1641	−44%
Isobar-19-includes-D-saccharic acid-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.0416	0.1641	−58%
L-allo-threonine	50	0.0421	0.1641	−31%
Metabolite - 1349	35	0.0426	0.1641	−36%
N-6-trimethyl-l-lysine	35	0.0433	0.1641	−38%
Metabolite - 3370	35	0.0481	0.1641	−35%
Metabolite - 3056	35	0.0489	0.1641	−29%
Metabolite - 3803	35	0.049	0.1641	−41%
1-methyladenosine	35	0.0501	0.1641	−34%
N-tigloylglycine	35	0.0501	0.1641	−31%
tyrosine	50	0.0503	0.1641	−31%
threonine	50	0.0516	0.1641	−31%
Metabolite - 3951	35	0.0518	0.1641	−25%
carnosine	35	0.0542	0.1641	−37%
xylitol	35; 50	0.055	0.1641	−35%
caffeine	35	0.0555	0.1641	79%
Metabolite - 2277	35	0.0558	0.1641	−28%
Metabolite - 1979-Cl-adduct-of-C6H10O5	35	0.0565	0.1641	−45%
heptanedioic acid	35	0.0573	0.1641	−28%
orotic acid	50	0.0584	0.1641	−44%
Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.0596	0.1641	−29%
beta-hydroxyisovaleric acid	50	0.0598	0.1641	−34%
Metabolite - 1911	35	0.0613	0.1641	−50%
ornithine	50	0.0615	0.1641	−34%
Metabolite - 4499	50	0.0619	0.1641	−36%
Metabolite - 4519	50	0.0619	0.1641	−55%
Metabolite - 2390	35	0.0635	0.1641	−43%
Metabolite - 3329	35	0.064	0.1641	−59%
7-8-dihydrofolic acid	35	0.0648	0.1641	−26%
Metabolite - 4251	50	0.0652	0.1641	−40%
Metabolite - 1655	35	0.0659	0.1641	−51%
Metabolite - 3955	35	0.0663	0.1641	−43%
N-acetyl-L-valine	35	0.0669	0.1641	−51%
3-ureidopropionic acid	35	0.0672	0.1641	−49%
erythrose-4-phosphate	50	0.0681	0.1641	−45%
Metabolite - 3033	50	0.0691	0.1641	−35%
gluconic acid	50	0.0697	0.1641	−46%
succinate	50	0.0704	0.1641	−41%
2-acetamido-1-amino-1-2-dideoxy-beta-D-glucopyranose	50	0.0705	0.1641	−36%
fructose	50	0.072	0.1641	−43%
Metabolite - 3327	35	0.0729	0.1641	−46%
5-6-Dihydrothymine	35	0.0731	0.1641	−34%
Metabolite - 3908	35	0.0744	0.1641	−39%
Metabolite - 3305	35	0.0747	0.1641	−43%
Metabolite - 4502	50	0.0748	0.1641	−5%
phenylalanine	35	0.0753	0.1641	−25%
Metabolite - 3055-possible-NH3-adduct-of-hippuric acid	35	0.0765	0.1641	46%
pyrophosphate	35; 50	0.0783	0.1641	−53%
Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine-or-aspartame	35	0.079	0.1641	−37%
guanine	35	0.0803	0.1641	−30%
Metabolite - 3970	35	0.0804	0.1641	−31%
Metabolite - 3246-possible-Ala-GLy-glycyl-sarcosine-or-ureido-butyric acid	35	0.0816	0.1641	−38%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
5-6-Dimethylbenzimidazole	50	0.0818	0.1641	−47%
urocanic acid	35	0.0821	0.1641	−35%
Metabolite - 3813	35	0.083	0.1641	−32%
Metabolite - 4523	50	0.0831	0.1641	−30%
Metabolite - 2285	35	0.084	0.1641	−34%
5-hydroxyindoleacetate	50	0.0847	0.1641	−35%
Isobar-29-includes-R—S-hydroorotic acid-5-6-dihydroorotic acid	35	0.0847	0.1641	−81%
valine	50	0.0849	0.1641	−23%
leucine	50	0.0862	0.1651	−37%
Metabolite - 4639	50	0.0905	0.1703	−52%
4-hydroxy-3-methoxymandelate	50	0.0906	0.1703	−33%
Metabolite - 1656	35	0.0927	0.1726	−52%
Metabolite - 2781	35	0.0965	0.1752	−22%
3-phospho-d-glycerate	35	0.0989	0.1752	−33%
N-acetyl-L-leucine	35	0.099	0.1752	−33%
Metabolite - 4505	50	0.0997	0.1752	−49%
Metabolite - 4002	50	0.0999	0.1752	−35%
Metabolite - 4112	35	0.1002	0.1752	−33%
4-acetominophen-sulfate	35	0.1013	0.1755	−35%
cellobiose	50	0.1027	0.1765	−48%
Metabolite - 1829	35	0.1037	0.1767	−22%
Metabolite - 3489	35	0.1062	0.1794	102%
DL-beta-hydroxyphenylethylamine	35	0.1082	0.1813	−29%
Metabolite - 4628	50	0.1098	0.182	−57%
4-hydroxymandelate	50	0.1115	0.182	−39%
5-oxoproline	50	0.1124	0.182	−29%
4-acetamidobutyric acid	35	0.1142	0.182	−28%
4-Guanidinobutanoic acid	35	0.1143	0.182	−28%
Metabolite - 2546	35	0.1157	0.182	−23%
histidine	50	0.1191	0.182	−38%
cysteine	50	0.1196	0.182	−52%
Metabolite - 4516	50	0.1197	0.182	−53%
L-beta-imidazolelactic acid	50; 35	0.1201	0.182	−25%
Metabolite - 2293-possible-O-desmethylvenlafaxine-glucuronide	35	0.1215	0.182	−32%
Metabolite - 1383-possible-salicyluric-glucuronide	35	0.1218	0.182	−52%
Metabolite - 4027	50	0.1224	0.182	−28%
Metabolite - 2807	35	0.1228	0.182	−44%
Metabolite - 3576	35	0.1229	0.182	−44%
cis-aconitic acid	50	0.124	0.182	−43%
Metabolite - 3322	35	0.1266	0.182	−39%
N—N-dimethylarginine	35	0.1269	0.182	−23%
Metabolite - 3828	35	0.1273	0.182	−32%
noradrenaline	50	0.1276	0.182	−43%
Metabolite - 4638	50	0.1281	0.182	−49%
creatinine	35	0.1327	0.1866	−17%
Metabolite - 4618	50	0.1343	0.1868	−32%
Metabolite - 4629	50	0.1347	0.1868	−31%
Metabolite - 3800	35	0.1366	0.1881	−40%
3-hydroxybutanoic acid	50	0.1415	0.1926	92%
Metabolite - 3817	35	0.1418	0.1926	−30%
methylmalonic acid	50	0.143	0.193	−42%
Metabolite - 4595	50	0.1443	0.1932	−23%
Metabolite - 4637	50	0.1468	0.1932	−54%
Metabolite - 3830	35	0.1474	0.1932	−40%
Metabolite - 4624	50	0.1475	0.1932	−24%
xanthine	35	0.148	0.1932	−43%
Metabolite - 3805	35	0.1504	0.195	−26%
Metabolite - 4635	50	0.1599	0.1957	−56%
folic acid	35	0.1603	0.1957	−37%
diaminopimelic acid	50; 35	0.1608	0.1957	−26%
Metabolite - 2973	50	0.1618	0.1957	29%
Metabolite - 3973	35	0.1629	0.1957	−65%
Metabolite - 3605	35	0.163	0.1957	−44%
N-formyl-L-methionine	35	0.1643	0.1957	−35%
urea	50	0.1643	0.1957	−21%
riboflavine	35	0.1654	0.1957	−73%
Metabolite - 1289	35	0.1665	0.1957	−16%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3380	35	0.1674	0.1957	−29%
Metabolite - 4611	50	0.1674	0.1957	−26%
Metabolite - 4511	50	0.1685	0.1957	−38%
(1'R-1'S)_biopterin	35	0.1687	0.1957	−25%
1-methyladenine	50	0.1694	0.1957	−45%
4-hydroxy-2-quinolinecarboxylic acid	50	0.17	0.1957	−41%
Metabolite - 3994	35	0.1716	0.1957	−32%
Metabolite - 2550	35	0.1717	0.1957	−44%
Metabolite - 3898	35	0.1721	0.1957	−16%
Metabolite - 3103	50	0.1723	0.1957	43%
possible-L-homocysteine-thiolactone-identical-to-homocysteine	50	0.1735	0.1959	−30%
Metabolite - 1122	35	0.1757	0.1972	−23%
tryptophan	50; 35	0.1769	0.1972	−20%
Metabolite - 1335	35	0.1775	0.1972	−23%
Metabolite - 2557-possible-Pantoprazole-metabolite	35	0.1812	0.2002	−34%
asparagine	50	0.1833	0.2014	−32%
Metabolite - 3837	35	0.1862	0.2025	−33%
Metabolite - 3659	35	0.1878	0.2025	−26%
mannitol	50	0.1883	0.2025	−39%
D-alanyl-D-alanine	35	0.1885	0.2025	−23%
3-amino-isobutyrate	50	0.1894	0.2025	−39%
Metabolite - 4498	50	0.1936	0.2059	−27%
hypoxanthine	35	0.1978	0.2093	−36%
Isobar-24-includes-L-arabitol-adonitol	35	0.2001	0.2095	−8%
hydroxyacetic acid	50	0.2012	0.2095	−21%
Metabolite - 1843	35	0.2013	0.2095	−18%
Metabolite - 3216	35	0.2022	0.2095	−8%
Metabolite - 2175	35	0.2045	0.2108	−49%
alanine	50	0.2058	0.211	−27%
Metabolite - 2366	35	0.2076	0.2118	40%
Metabolite - 3873	35	0.2143	0.2124	−23%
Metabolite - 4046	50	0.2165	0.2124	−73%
Metabolite - 1455	35	0.2166	0.2124	−18%
Metabolite - 3708	35	0.2167	0.2124	−63%
Metabolite - 3843	35	0.217	0.2124	−30%
Metabolite - 3886	35	0.2177	0.2124	−21%
Metabolite - 2174	35	0.2178	0.2124	−23%
4-8-dihydroxyquinoline-2-carboxylic acid	50	0.2182	0.2124	−31%
Metabolite - 3387	35	0.2183	0.2124	−23%
Metabolite - 4271	50	0.2193	0.2124	−30%
tyramine	50	0.2204	0.2124	−42%
Metabolite - 4496	50	0.2215	0.2124	−15%
normetanephrine	50	0.2223	0.2124	−13%
Metabolite - 1679	35	0.2229	0.2124	−22%
trans-4-hydroxyproline	35; 50	0.2281	0.2163	−24%
Metabolite - 2703	35	0.2307	0.2174	−14%
Metabolite - 3169	35	0.2314	0.2174	−62%
Metabolite - 4634	50	0.2337	0.2185	−28%
Metabolite - 3221	35	0.2367	0.2196	−25%
alpha-4-dihydroxybenzenepropanoic acid	50	0.237	0.2196	−48%
uric acid	35	0.243	0.2227	−6%
Metabolite - 3841	35	0.2435	0.2227	−32%
Metabolite - 4500	50	0.2437	0.2227	−62%
Metabolite - 3667	35	0.2468	0.2245	−20%
Metabolite - 4495	50	0.2517	0.228	−22%
Metabolite - 3706	35	0.2536	0.2286	−17%
D-lyxose	50	0.2626	0.2336	−26%
glutamine	50	0.2629	0.2336	−28%
Metabolite - 3014	50	0.2637	0.2336	−21%
Metabolite - 3802	35	0.2638	0.2336	−34%
Metabolite - 2591	35	0.2717	0.2375	32%
Metabolite - 3178-possible-NH3-adduct-of-isobar-42	35	0.2724	0.2375	−28%
Metabolite - 2607	35	0.2727	0.2375	−38%
L-kynurenine	35	0.2729	0.2375	−76%
gamma-L-glutamyl-L-tyrosine	35	0.2752	0.2385	−23%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3832-possible-phenol-sulfate	35	0.2771	0.2391	66%
hippuric acid	35	0.2825	0.2427	−21%
4-hydroxyphenylacetate	35; 50	0.2898	0.2469	−24%
Metabolite - 3108	50	0.2898	0.2469	−34%
Metabolite - 3834	35	0.2916	0.2473	−33%
allantoin	35	0.2933	0.2478	−19%
Metabolite - 2118	35	0.2957	0.2488	−19%
Metabolite - 3440	35	0.2986	0.2501	192%
ascorbic acid	50	0.3011	0.2502	−70%
Metabolite - 1498	35	0.3011	0.2502	−40%
Metabolite - 4509	50	0.3032	0.2508	−38%
Isobar-6-includes-valine-betaine	35	0.3058	0.2519	−16%
Metabolite - 2150	35	0.312	0.2556	−24%
Metabolite - 3911	35	0.3148	0.2556	−14%
1-5-diaminopentane	50	0.3158	0.2556	−40%
proline	35; 50	0.3161	0.2556	−29%
salicyluric acid	35	0.3167	0.2556	−71%
Metabolite - 4494	50	0.3178	0.2556	14%
porphobilinogen	35	0.3208	0.2569	−20%
Metabolite - 3804	35	0.3263	0.2589	−21%
pantothenic acid	35	0.3273	0.2589	−36%
Metabolite - 3099	50	0.3281	0.2589	−25%
Metabolite - 3660	35	0.3284	0.2589	−39%
Metabolite - 3090	50	0.3345	0.2598	−11%
Metabolite - 4632	50	0.3356	0.2598	−45%
Isobar-2-includes-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.3373	0.2598	183%
Metabolite - 3309	35	0.3374	0.2598	−18%
Metabolite - 1110	35	0.3379	0.2598	−17%
Metabolite - 3493	35	0.3384	0.2598	−17%
Metabolite - 3163-possible-methylcytidine-benserazide-or-Pyr-Gln-OH	35	0.3387	0.2598	−15%
N-alpha-acetyl-L-ornithine-	50	0.345	0.2637	−16%
Metabolite - 1465	35	0.3552	0.2705	−14%
Metabolite - 1834	35	0.3614	0.2729	53%
3-methyl-L-histidine	35	0.3622	0.2729	−14%
carnitine	35	0.3625	0.2729	32%
Metabolite - 1338	35	0.3638	0.2729	25%
dulcitol	50	0.3732	0.2789	−36%
glutamic acid	50	0.3771	0.2808	−15%
Metabolite - 2259	35	0.3795	0.2815	−42%
S-adenosyl-l-homocysteine	35	0.3841	0.2839	−19%
D-allose	50	0.3895	0.2858	−21%
Metabolite - 4234	35	0.3895	0.2858	−51%
Metabolite - 3091	50	0.3975	0.2906	−27%
2-deoxy-D-glucose	50	0.4016	0.292	−26%
Metabolite - 3963	35	0.4038	0.292	−54%
Metabolite - 2292	35	0.4038	0.292	23%
isoleucine	50	0.4077	0.2936	−15%
Metabolite - 2893-possible-demethylated-Rosiglitazone	35	0.4115	0.2936	−21%
glucose-6-phosphate	50	0.4136	0.2936	189%
2-keto-L-gulonic acid	50	0.4138	0.2936	194%
Metabolite - 1496	35	0.4148	0.2936	−31%
theobromine-theophylline	35	0.418	0.2944	41%
Metabolite - 3131	35	0.42	0.2944	−19%
Metabolite - 3085	50	0.4202	0.2944	38%
Metabolite - 3893	35	0.4258	0.2971	−15%
Metabolite - 2686	35	0.4273	0.2971	−15%
Metabolite - 2386	35	0.4286	0.2971	−13%
Metabolite - 2108	35	0.432	0.2981	55%
Metabolite - 2249	35	0.4331	0.2981	−30%
Metabolite - 3604	35	0.4379	0.3004	−16%
Metabolite - 3543	35	0.4474	0.3041	−42%
Metabolite - 3878	35	0.4474	0.3041	25%
Metabolite - 4507	50	0.4492	0.3041	−21%
Metabolite - 3771	35	0.4493	0.3041	−28%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
3-nitro-L-tyrosine	50; 35	0.4548	0.3062	−20%
lactate	50	0.4554	0.3062	14%
Metabolite - 3668	35	0.4624	0.3084	12%
Metabolite - 2506	35	0.4645	0.3084	−18%
Metabolite - 2254	35	0.4659	0.3084	69%
Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid	35	0.4661	0.3084	−34%
Metabolite - 3909	35	0.4663	0.3084	55%
Metabolite - 1682	35	0.4794	0.3142	−16%
dethiobiotin	50; 35	0.4799	0.3142	−39%
alpha-L-sorbopyranose	50	0.482	0.3142	−29%
beta-D-lactose	50	0.4838	0.3142	−21%
Metabolite - 2329	35	0.4846	0.3142	−11%
Metabolite - 4520	50	0.4866	0.3145	32%
Metabolite - 1114	35	0.4884	0.3147	−21%
malic acid	35	0.49	0.3147	−15%
Metabolite - 4501	50	0.4979	0.3188	−19%
Metabolite - 3436	35	0.5088	0.3247	−11%
Metabolite - 1351	35	0.5117	0.3255	−21%
Metabolite - 3806	35	0.5173	0.3281	−24%
Metabolite - 2726	35	0.519	0.3281	−12%
Metabolite - 4518	50	0.5282	0.3329	−32%
Metabolite - 3409	35	0.5303	0.3331	−17%
Metabolite - 4133	50	0.5446	0.341	−21%
Metabolite - 3952	35	0.547	0.3415	−20%
Metabolite - 3879	35	0.5531	0.3442	−27%
Metabolite - 3113	50	0.5631	0.3488	17%
Metabolite - 3433	35	0.5639	0.3488	−9%
tartaric acid	35	0.5703	0.3517	−20%
Metabolite - 2698	35	0.5772	0.3549	38%
Metabolite - 2056	35	0.5849	0.3582	−8%
Metabolite - 3670	35	0.5873	0.3582	−9%
Metabolite - 3786	35	0.5899	0.3582	−14%
Metabolite - 2853	35	0.5908	0.3582	−16%
Metabolite - 3981	35	0.5931	0.3582	−21%
Metabolite - 3564	35	0.5948	0.3582	−23%
Metabolite - 3781-possible-Na-adduct-of-Isobar-21	35	0.5951	0.3582	−12%
Metabolite - 1186	35	0.5992	0.3585	−11%
2-isopropylmalic acid	50	0.5992	0.3585	37%
Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose	35	0.6073	0.3623	26%
Metabolite - 1101	35	0.6174	0.3672	−10%
Metabolite - 4167	35	0.6297	0.3734	−10%
Metabolite - 2005	35	0.6452	0.3814	−9%
sn-Glycerol-3-phosphate	50	0.65	0.3814	−13%
3-methylglutaric acid	35	0.6501	0.3814	9%
Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.6507	0.3814	−5%
mercaptopyruvate	35	0.6565	0.383	−12%
homogentisate	35	0.6586	0.383	−9%
azelaic acid	35	0.6592	0.383	18%
Metabolite - 4510	50	0.6672	0.3866	−13%
3-hydroxyphenylacetate	35	0.674	0.3883	−10%
Metabolite - 3127	35	0.6771	0.3883	−9%
phosphoenolpyruvate	35	0.6772	0.3883	−17%
Metabolite - 3138	35	0.6779	0.3883	−10%
agmatine	35	0.6825	0.3898	−15%
Metabolite - 3402	35	0.6861	0.3899	−6%
alpha-keto-glutarate	35	0.7074	0.4	−11%
Metabolite - 4512	50	0.7083	0.4	−17%
Metabolite - 2323	35	0.7136	0.4012	−9%
Metabolite - 3701	35	0.7145	0.4012	−10%
Metabolite - 3016	50	0.73	0.4068	4%
Metabolite - 2272	35	0.7302	0.4068	−17%
DL-pipecolic acid	35	0.7319	0.4068	−12%
Metabolite - 4633	50	0.7325	0.4068	−8%
niacinamide	35	0.7378	0.4086	8%

TABLE 5-continued

Prostate Cancer Biomarkers from Urine from subjects with Prostate Cancer compared to Urine from Control subjects.

COMPOUND	Library	p-value	q-value	% Change in PCA
Metabolite - 3123	35	0.7434	0.41	−8%
galactose	50	0.7512	0.41	−13%
pyridoxamine-phosphate	35	0.752	0.41	5%
Metabolite - 3101	50	0.7539	0.41	−7%
o-phosphoethanolamine	50	0.756	0.41	−8%
Metabolite - 3516	35	0.7584	0.41	−7%
DL-indole-3-lactic acid	50; 35	0.76	0.41	11%
Metabolite - 1126	35	0.7615	0.41	−9%
Metabolite - 1981	35	0.7617	0.41	−6%
Metabolite - 3986	35	0.7628	0.41	−8%
Metabolite - 4598	50	0.7687	0.4121	−7%
Metabolite - 4514	50	0.775	0.4127	9%
Metabolite - 3507	35	0.7759	0.4127	−7%
Metabolite - 1216	35	0.776	0.4127	4%
Metabolite - 3053	35	0.788	0.4172	−12%
L-rhamnose	50	0.7886	0.4172	5%
Metabolite - 2389	35	0.7912	0.4175	6%
Metabolite - 1368	35	0.7964	0.4191	−11%
alphahydroxybenzeneacetic acid	35	0.7995	0.4196	−4%
benzoic acid	50; 35	0.809	0.4235	6%
N-acetyl-L-alanine	35	0.8203	0.4259	−4%
Metabolite - 4517	50	0.8203	0.4259	−6%
Metabolite - 4092	35	0.8218	0.4259	−6%
Metabolite - 3977	35	0.8221	0.4259	−8%
Isobar-38-includes-N-acetyl-L-methionine-5-hydroxy-1H-indole-3-acetic acid	35	0.8281	0.428	4%
Metabolite - 2706	35	0.8316	0.4284	6%
Metabolite - 3311-possible-Zolpidem-in-humans-	35	0.8367	0.4284	7%
Metabolite - 4010	50	0.8374	0.4284	−6%
Metabolite - 3773	35	0.8375	0.4284	−5%
Metabolite - 2897	35	0.847	0.4322	5%
Metabolite - 3364	35	0.8537	0.434	5%
Metabolite - 3231	35	0.8549	0.434	−4%
Metabolite - 3957	35	0.8591	0.435	−3%
Metabolite - 2269-	35	0.8619	0.4353	−3%
Metabolite - 3754	35	0.873	0.4398	5%
Metabolite - 2387	35	0.8782	0.4414	−5%
Metabolite - 3377	35	0.8819	0.4421	−6%
Metabolite - 2319	35	0.8913	0.445	−3%
suberic acid	35	0.8921	0.445	3%
oxalacetic acid	35	0.8946	0.4451	−2%
Metabolite - 3876	35	0.8969	0.4451	−6%
Metabolite - 2348	35	0.8988	0.4451	−4%
Metabolite - 1839	35	0.9015	0.4453	5%
Metabolite - 1113-possible-acetylcarnitine-or-isopentyl-adenine	35	0.9057	0.4462	−4%
3-methyl-2-oxovaleric acid	35	0.9096	0.4469	−4%
melibiose	50	0.9114	0.4469	4%
Metabolite - 1364	35	0.9316	0.4557	3%
Metabolite - 4524	50	0.9364	0.4569	4%
thymidine	35	0.9412	0.4581	2%
Metabolite - 3755	35	0.9473	0.46	−1%
Metabolite - 3855	35	0.9504	0.4604	−1%
Metabolite - 3058	50	0.966	0.4638	2%
Metabolite - 1116	35	0.9663	0.4638	−1%
Metabolite - 3847	35	0.9693	0.4638	−1%
Metabolite - 3313	35	0.9709	0.4638	−1%
5-s-methyl-5-thioadenosine	35	0.9714	0.4638	1%
Metabolite - 3887	35	0.9799	0.4668	−1%
Metabolite - 3824	35	0.9839	0.4676	0%
Metabolite - 3457	35	0.9863	0.4676	−1%
Metabolite - 1283	35	0.9995	0.4728	0%

Example 3

Distinguish Lower Grade from Higher Grade/Metastatic Prostate Cancer in Subjects Using Plasma

[0120] Biomarkers were discovered by (1) analyzing plasma samples from different groups of human subjects to determine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0121] The plasma samples used for the analysis were from 53 control individuals with negative biopsies for prostate cancer, 43 individuals with lower grade prostate cancer (i.e. Gleason Score major=3) and 15 individuals with aggressive, higher grade prostate cancer (i.e. Gleason Score major=4+). After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0122] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Lower Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Control, Metastatic/Higher Grade Prostate cancer vs. Lower Grade Prostate cancer).

Biomarkers:

[0123] As listed below in Table 6, biomarkers were discovered that were differentially present between plasma samples from subjects with lower grade prostate cancer and plasma samples from Control subjects with negative prostate biopsies (i.e. not diagnosed with prostate cancer). Table 7 lists biomarkers that were discovered that were differentially present between plasma samples from subjects with metastatic/high grade prostate cancer and plasma samples from Control subjects with biopsy negative prostates (i.e. not diagnosed with prostate cancer). Table 8 lists biomarkers that were discovered that were differentially present between plasma samples from subjects with metastatic/high grade prostate cancer and plasma from subjects with lower grade prostate cancer.

[0124] Tables 6-8 include, for each listed biomarker, the p-value and the q-value determined in the statistical analysis of the data concerning the biomarkers and an indication of the percentage difference in the lower grade prostate cancer mean level as compared to the control mean level (Table 6), the metastatic/high grade prostate cancer mean level as compared to the control mean level (Table 7), and the metastatic/high grade prostate cancer mean level as compared to the lower grade prostate cancer mean level (Table 8). The term "Isobar" as used in the tables indicates the compounds that could not be distinguished from each other on the analytical platform used in the analysis (i.e., the compounds in an isobar elute at nearly the same time and have similar (and sometimes exactly the same) quant ions, and thus cannot be distinguished). Library indicates the chemical library that was used to identify the compounds. The number 50 refers to the GC library and the number 35 refers to the LC library.

[0125] Biomarkers were discovered by (1) analyzing plasma samples from different groups of human subjects to determine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0126] The plasma samples used for the analysis were from 53 control individuals with negative biopsies for prostate cancer, 43 individuals with lower grade prostate cancer (i.e. Gleason Score major=3) and 15 individuals with aggressive, high grade prostate cancer (i.e. Gleason Score major=4+). After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0127] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Lower Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Lower Grade Prostate cancer).

TABLE 6

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
53	glutamine	50	0.9855	0.9993	−1%
54	tryptophan	50	0.6455	0.9851	3%
57	glutamic acid	50	0.5953	0.9851	−6%
59	histidine	50	0.4258	0.9478	−9%
60	leucine	50	0.2512	0.9478	8%
63	cholesterol	50	0.8251	0.9851	−1%
64	phenylalanine	35	0.61	0.9851	−2%
513	creatinine	35	0.0047	0.5749	−10%
527	lactate	50	0.6496	0.9851	−1%
528	alpha - keto-glutarate	35	0.0081	0.5749	−40%
541	4-hydroxyphenylacetate	35	0.2553	0.9478	−5%
542	3-hydroxybutanoic acid	50	0.748	0.9851	11%
569	caffeine	35	0.0542	0.7407	61%
577	fructose	50	0.2415	0.9478	−26%
581	glucose	50	0.254	0.9478	−4%
584	mannose	50	0.9209	0.9993	1%
594	niacinamide	35	0.7471	0.9851	10%
597	phosphoenolpyruvate	35	0.5253	0.9851	−6%
1105	linoleic acid	50	0.6374	0.9851	3%
1107	allantoin	50	0.6861	0.9851	−8%
1110	arachidonic acid	50	0.4338	0.9478	−6%
1121	heptadecanoic acid	50	0.0432	0.7407	12%
1123	inosine	35	0.8138	0.9851	8%
1125	isoleucine	50	0.2856	0.9478	7%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
1126	alanine	50	0.8973	0.9993	−1%
1284	threonine	50	0.9044	0.9993	−1%
1299	tyrosine	50	0.2074	0.9478	8%
1302	methionine	35	0.9843	0.9993	0%
1303	malic acid	35	0.5347	0.9851	−9%
1336	n-hexadecanoic acid	50	0.4029	0.9478	5%
1358	octadecanoic acid	50	0.05	0.7407	7%
1365	tetradecanoic acid	50	0.4504	0.9478	6%
1366	trans-4-hydroxyproline	50	0.8095	0.9851	1%
1413	3-hydroxyphenylacetate	35	0.4804	0.9659	−3%
1414	3-phospho-d-glycerate	35	0.9448	0.9993	−1%
1415	4-amino-5-methyl-2-1H-pyrimidinone	35	0.6722	0.9851	3%
1431	(p-Hydroxyphenyl)lactic acid	50	0.598	0.9851	6%
1432	alphahydroxybenzeneacetic acid	35	0.8582	0.9851	−2%
1437	succinate	50	0.6649	0.9851	−2%
1444	DL-pipecolic acid	35	0.3051	0.9478	−10%
1480	guanidineacetic acid	35	0.3889	0.9478	7%
1493	ornithine	50	0.9114	0.9993	1%
1494	5-oxoproline	50	0.5882	0.9851	4%
1498	N-6-trimethyl-1-lysine	35	0.2178	0.9478	−11%
1507	palmitoleic acid	50	0.5998	0.9851	8%
1508	pantothenic acid	35	0.4151	0.9478	20%
1519	sucrose	50	0.6854	0.9851	6%
1557	3-methylglutaric acid	35	0.1656	0.9478	−9%
1561	alpha - tocopherol	50	0.0145	0.6753	−50%
1564	citric acid	50	0.6977	0.9851	2%
1570	oleic acid	50	0.8649	0.9851	−2%
1572	glyceric acid	50	0.7217	0.9851	2%
1574	histamine	35	0.5568	0.9851	8%
1584	methyl-indole-3-acetate	35	0.9677	0.9993	0%
1587	N-acetyl-L-leucine	35	0.3101	0.9478	31%
1591	N-acetyl-L-valine	35	0.0094	0.5749	20%
1604	uric acid	35	0.9975	0.9993	0%
1643	fumaric acid	50	0.5347	0.9851	−3%
1645	n-dodecanoate	50	0.7836	0.9851	3%
1648	serine	50	0.2503	0.9478	8%
1649	valine	50	0.3429	0.9478	7%
1670	urea	50	0.5816	0.9851	4%
1708	7-8-dihydrofolic acid	35	0.3763	0.9478	30%
1898	proline	50	0.6963	0.9851	−3%
2078	pyrophosphate	35	0.97	0.9993	0%
2092	catechol	35	0.9928	0.9993	0%
2132	citrulline	50	0.7476	0.9851	−3%
2730	gamma - L-glutamyl-L-glutamine	35	0.8715	0.9852	−3%
2734	gamma - L-glutamyl-L-tyrosine	35	0.2947	0.9478	6%
2832	adenosine-5-monophosphate	35	0.661	0.9851	−4%
2848	guanosine-5-diphosphate	35	0.9286	0.9993	1%
3127	hypoxanthine	35	0.6226	0.9851	−6%
3138	pyridoxamine-phosphate	35	0.1559	0.9478	16%
3147	xanthine	35	0.4283	0.9478	−10%
4966	xylitol	35	0.6274	0.9851	5%
5280	biliverdin	35	0.2685	0.9478	33%
5331	pyridoxal-phosphate	35	0.2348	0.9478	−5%
5618	Metabolite - 1085-possible-isolobinine-or-4-aminoestra - 1-3-5-10-triene-3-17beta - diol	35	0.4282	0.9478	4%
5628	Metabolite - 1086	35	0.8863	0.9931	−2%
5669	Metabolite - 1104	35	0.7565	0.9851	−1%
5687	Metabolite - 1110	35	0.8421	0.9851	5%
5689	Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	35	0.1327	0.9478	11%
5697	acetylcarnitine-	35	0.8273	0.9851	−2%
5717	Metabolite - 1121	35	0.2772	0.9478	10%
5733	Metabolite - 1127	35	0.0093	0.5749	−18%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
5765	Metabolite - 1142-possible-5-hydroxypentanoate-or-beta - hydroxyisovaleric acid	35	0.7839	0.9851	9%
5788	Metabolite - 1183	35	0.3488	0.9478	145%
5792	Metabolite - 1185	35	0.001	0.3826	35%
5800	Metabolite - 1188	35	0.0412	0.7407	36%
6112	Metabolite - 1203-HXGXX - in-MTRX	35	0.3191	0.9478	53%
6130	Metabolite - 1208	35	0.7504	0.9851	7%
6136	Metabolite - 1211-possible-IHWESASLLR-	35	0.0416	0.7407	287%
6144	Metabolite - 1215	35	0.9559	0.9993	2%
6147	Metabolite - 1216	35	0.6032	0.9851	8%
6155	Metabolite - 1220	35	0.8003	0.9851	3%
6171	Metabolite - 1244	35	0.3509	0.9478	11%
6266	Metabolite - 1286	35	0.3935	0.9478	5%
6278	Metabolite - 1289	35	0.1436	0.9478	−16%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.3987	0.9478	17%
6398	Metabolite - 1335	35	0.9275	0.9993	−1%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.3835	0.9478	16%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.9654	0.9993	1%
6443	Metabolite - 1351	35	0.9312	0.9993	−1%
6537	Metabolite - 1389-possible-gemfibrozil-glucuronide-	35	0.3189	0.9478	308%
6549	Metabolite - 1392	35	0.4102	0.9478	12%
6787	Metabolite - 1465	35	0.7835	0.9851	5%
6852	Metabolite - 1498	35	0.1492	0.9478	−14%
6987	Metabolite - 1573	35	0.8168	0.9851	−2%
7029	Metabolite - 1597	35	0.0206	0.7407	10%
7081	Metabolite - 1609	35	0.3186	0.9478	8%
7177	Metabolite - 1656	35	0.8442	0.9851	2%
7359	n-acetyl-L-aspartic acid	35	0.7069	0.9851	−2%
7446	p-hydroxybenzaldehyde	35	0.3568	0.9478	−6%
7595	Metabolite - 1817	35	0.6472	0.9851	3%
7639	oxalic acid	35	0.7835	0.9851	2%
7644	Metabolite - 1831-possible-Cl-adduct-of-citrulline	35	0.2483	0.9478	−29%
7650	Metabolite - 1834	35	0.6754	0.9851	−8%
7652	Metabolite - 1835	35	0.031	0.7407	25%
7654	Metabolite - 1836	35	0.7242	0.9851	−3%
7660	Metabolite - 1839	35	0.8404	0.9851	−4%
7672	Metabolite - 1843	35	0.7507	0.9851	3%
7933	Metabolite - 1911	35	0.0739	0.7639	48%
7935	paraxanthine	35	0.1117	0.9478	38%
7941	Metabolite - 1914	35	0.8081	0.9851	6%
7944	Metabolite - 1915	35	0.3455	0.9478	55%
7957	trans-2-3-4-trimethoxycinnamic acid	35	0.8125	0.9851	5%
8091	glycocholic acid	35	0.2546	0.9478	30%
8176	Metabolite - 1974	35	0.4143	0.9478	10%
8189	Metabolite - 1977	35	0.8558	0.9851	2%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.5336	0.9851	−5%
8217	Metabolite - 1983	35	0.1187	0.9478	410%
8300	Metabolite - 1988	35	0.1698	0.9478	−14%
8336	Metabolite - 2005	35	0.8806	0.9897	−2%
8404	Metabolite - 2027	35	0.6346	0.9851	−4%
8649	Metabolite - 2053	35	0.2084	0.9478	17%
8669	Metabolite - 2055	35	0.9233	0.9993	1%
8677	Metabolite - 2056	35	0.5835	0.9851	6%
8796	Metabolite - 2074	35	0.8013	0.9851	−2%
8959	Metabolite - 2100	35	0.4481	0.9478	5%
9007	Metabolite - 2108	35	0.9789	0.9993	0%
9024	Metabolite - 2111	35	0.6202	0.9851	−5%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
9092	Metabolite - 2129	35	0.5701	0.9851	−9%
9106	Metabolite - 2130	35	0.4394	0.9478	−12%
9130	Metabolite - 2139	35	0.7305	0.9851	3%
9137	Metabolite - 2141	35	0.5077	0.9851	12%
9491	Metabolite - 2185	35	0.0387	0.7407	18%
9748	Metabolite - 2212	35	0.3479	0.9478	−9%
10087	Metabolite - 2249	35	0.6712	0.9851	−4%
10092	Metabolite - 2250	35	0.0564	0.7407	63%
10122	Metabolite - 2254	35	0.4991	0.9851	−15%
10143	Metabolite - 2255-hydroxyproline-form-of-bradykinin	35	0.0474	0.7407	89%
10145	Metabolite - 2256	35	0.1134	0.9478	−18%
10245	Metabolite - 2269-	35	0.7452	0.9851	8%
10317	Metabolite - 2279	35	0.2635	0.9478	32%
10327	Metabolite - 2281	35	0.5771	0.9851	34%
10378	Metabolite - 2287	35	0.395	0.9478	59%
10438	gamma - glu-leu	35	0.4307	0.9478	4%
10461	Metabolite - 2313	35	0.71	0.9851	−4%
10476	Metabolite - 2316	35	0.456	0.9478	−13%
10544	Metabolite - 2329	35	0.8979	0.9993	1%
10551	Metabolite - 2347	35	0.6776	0.9851	8%
10604	Metabolite - 2370	35	0.6853	0.9851	4%
10629	Metabolite - 2386	35	0.8269	0.9851	−4%
10644	Metabolite - 2387	35	0.5459	0.9851	52%
10655	Metabolite - 2388	35	0.7697	0.9851	−1%
10667	Metabolite - 2389	35	0.318	0.9478	20%
10672	Metabolite - 2390	35	0.4169	0.9478	23%
10692	Metabolite - 2391	35	0.397	0.9478	−6%
10698	Metabolite - 2392	35	0.7279	0.9851	−9%
10737	Isobar-1-includes-mannose-fructose-glucose-galactose-alpha - L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone	35	0.7112	0.9851	4%
10739	Metabolite - 2407	35	0.9869	0.9993	0%
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.6711	0.9851	−10%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.8686	0.9851	−2%
10744	Isobar-5-includes-asparagine-ornithine-gly-gly	35	0.7225	0.9851	4%
10746	Isobar-6-includes-valine-betaine	35	0.1667	0.9478	5%
10753	Isobar-9-includes-galactinol-dihydrate-turanose-kojibiose-D-leucrose-lactulose-sophorose-sucrose-beta - D-lactose-D-trehalose-D-cellobiose-D-Maltose-palatinose-melibiose-alpha - D-lactose	35	0.6051	0.9851	−7%
10782	Metabolite - 2486	35	0.5968	0.9851	8%
10785	Metabolite - 2506	35	0.9224	0.9993	2%
10787	Metabolite - 2507	35	0.6105	0.9851	−13%
10825	Metabolite - 2546	35	0.9993	0.9993	0%
11053	Metabolite - 2567	35	0.1285	0.9478	9%
11111	Metabolite - 2592	35	0.4637	0.9582	54%
11219	Metabolite - 2686	35	0.5844	0.9851	3%
11222	Metabolite - 2688	35	0.163	0.9478	14%
11323	Metabolite - 2711	35	0.9889	0.9993	0%
11438	phosphate	50	0.8104	0.9851	0%
11499	Metabolite - 2753	35	0.4215	0.9478	7%
11777	glycine	50	0.3338	0.9478	−8%
11813	Metabolite - 2809	35	0.8323	0.9851	3%
12035	nonanate	50	0.7544	0.9851	1%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
12109	Metabolite - 2853	35	0.0277	0.7407	39%
12298	Metabolite - 2867	35	0.1237	0.9478	−45%
12478	Metabolite - 2898	35	0.0495	0.7407	−51%
12532	Metabolite - 2914	50	0.1166	0.9478	2%
12533	Metabolite - 2915	50	0.2615	0.9478	−7%
12543	2-hydroxy-butanoic acid	50	0.1956	0.9478	17%
12562	Metabolite - 2955	50	0.279	0.9478	3%
12593	Metabolite - 2973	50	0.9818	0.9993	0%
12594	Metabolite - 2974	50	0.9799	0.9993	0%
12601	Metabolite - 2978	50	0.6254	0.9851	3%
12625	Metabolite - 3002	50	0.9162	0.9993	−2%
12626	Metabolite - 3003	50	0.1382	0.9478	−9%
12627	Metabolite - 3004	50	0.5311	0.9851	−5%
12639	Metabolite - 3012	50	0.4723	0.9653	5%
12641	meso-erythritol	50	0.3847	0.9478	−7%
12644	Metabolite - 3016	50	0.1293	0.9478	−7%
12645	Metabolite - 3017	50	0.0303	0.7407	18%
12647	Metabolite - 3019	50	0.2488	0.9478	7%
12648	Metabolite - 3020	50	0.4953	0.9851	6%
12650	Metabolite - 3022	50	0.9679	0.9993	0%
12656	Metabolite - 3025	50	0.195	0.9478	8%
12658	Metabolite - 3026	50	0.3559	0.9478	7%
12663	Metabolite - 3030	50	0.0934	0.9247	9%
12666	Metabolite - 3033	50	0.8631	0.9851	−1%
12673	Metabolite - 3040	50	0.3373	0.9478	10%
12682	Metabolite - 3044	35	0.1918	0.9478	12%
12719	Metabolite - 3055	35	0.741	0.9851	5%
12720	Metabolite - 3056	35	0.5288	0.9851	−4%
12726	Metabolite - 3058	50	0.727	0.9851	3%
12739	1-5-anhydro-D-glucitol	50	0.2751	0.9478	−8%
12751	Metabolite - 3073	50	0.921	0.9993	1%
12753	Metabolite - 3074	50	0.3835	0.9478	−22%
12754	Metabolite - 3075	50	0.2497	0.9478	−7%
12756	Metabolite - 3077	50	0.9463	0.9993	1%
12757	Metabolite - 3078	50	0.8351	0.9851	−2%
12761	Metabolite - 3081	50	0.0685	0.7493	−9%
12765	inositol	50	0.4516	0.9478	−5%
12768	Metabolite - 3088	50	0.1228	0.9478	−15%
12769	Metabolite - 3089	50	0.0654	0.7493	16%
12771	Metabolite - 3091	50	0.25	0.9478	21%
12773	Metabolite - 3093	50	0.4676	0.961	9%
12774	Metabolite - 3094	50	0.9437	0.9993	0%
12777	Metabolite - 3097	50	0.2879	0.9478	16%
12780	Metabolite - 3098	50	0.1558	0.9478	12%
12781	Metabolite - 3099	50	0.0718	0.7631	26%
12784	Metabolite - 3102	50	0.8378	0.9851	−1%
12790	Metabolite - 3108	50	0.6368	0.9851	2%
12876	Metabolite - 3125	35	0.4896	0.9793	−4%
12912	Metabolite - 3129	35	0.4506	0.9478	9%
12924	Metabolite - 3131	35	0.6823	0.9851	5%
12931	DL-hexanoyl-carnitine	35	0.6978	0.9851	3%
12960	Metabolite - 3134	35	0.9924	0.9993	0%
12969	Metabolite - 3135	35	0.5304	0.9851	13%
13018	Metabolite - 3138	35	0.0971	0.9247	−16%
13038	Metabolite - 3143	35	0.9259	0.9993	1%
13065	Metabolite - 3146	35	0.8545	0.9851	4%
13104	Metabolite - 3160	35	0.2622	0.9478	−10%
13142	Metabolite - 3165	35	0.3363	0.9478	−5%
13146	Metabolite - 3166	35	0.8043	0.9851	4%
13148	Metabolite - 3167	35	0.044	0.7407	21%
13179	possible-Metabolite - 3176-possible-creatine	35	0.7152	0.9851	5%
13208	Metabolite - 3181	35	0.354	0.9478	−9%
13211	Metabolite - 3182	35	0.9963	0.9993	0%
13214	Metabolite - 3183-possible-gamma - L-glutamyl-L-phenylalanine	35	0.7525	0.9851	2%
13217	Metabolite - 3184	35	0.1642	0.9478	−11%
13249	Metabolite - 3215	35	0.6878	0.9851	−4%
13251	Metabolite - 3216	35	0.2268	0.9478	−13%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
13257	Metabolite - 3218	35	0.5081	0.9851	5%
13342	Metabolite - 3243	35	0.5847	0.9851	10%
13448	Metabolite - 3303	35	0.0978	0.9247	−9%
13459	Metabolite - 3305	35	0.3143	0.9478	−19%
13484	Metabolite - 3309	35	0.0626	0.7493	−25%
13505	Metabolite - 3313	35	0.5629	0.9851	−23%
13509	Metabolite - 3314	35	0.2956	0.9478	−8%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.7791	0.9851	10%
13545	Metabolite - 3322	35	0.2266	0.9478	16%
13589	Metabolite - 3327	35	0.831	0.9851	−4%
13775	Metabolite - 3370	35	0.8025	0.9851	1%
13803	Metabolite - 3377	35	0.2963	0.9478	−17%
13904	Metabolite - 3402	35	0.3454	0.9478	−15%
14027	Metabolite - 3426	35	0.1435	0.9478	−3%
14084	Metabolite - 3436	35	0.2313	0.9478	13%
14117	Metabolite - 3441	35	0.2102	0.9478	−10%
14239	Metabolite - 3474	35	0.3092	0.9478	−9%
14249	Metabolite - 3476	35	0.3874	0.9478	−16%
14368	Metabolite - 3489	35	0.383	0.9478	−19%
14439	Metabolite - 3498	35	0.7901	0.9851	3%
14495	Metabolite - 3534	35	0.2653	0.9478	13%
14595	Metabolite - 3576	35	0.6382	0.9851	−5%
14608	Metabolite - 3578	35	0.243	0.9478	13%
14639	Metabolite - 3603	35	0.04	0.7407	19%
14640	Metabolite - 3604	35	0.2069	0.9478	30%
14672	Metabolite - 3615	35	0.275	0.9478	15%
14715	Metabolite - 3653-possible-stachydrine-	35	0.6884	0.9851	−12%
14766	Metabolite - 3670	35	0.1501	0.9478	8%
14785	isobar-glycochenodeoxycholic acid-glycodeoxycholic acid	35	0.3915	0.9478	18%
14787	Metabolite - 3698	35	0.3714	0.9478	−11%
14837	Metabolite - 3707	35	0.4795	0.9659	18%
14961	Metabolite - 3752	35	0.0597	0.7407	228%
15000	Metabolite - 3758	35	0.3269	0.9478	−23%
15017	Metabolite - 3761	35	0.6023	0.9851	−5%
15032	Metabolite - 3765	35	0.0289	0.7407	43%
15063	Metabolite - 3772	35	0.573	0.9851	−4%
15113	Metabolite - 3783	35	0.983	0.9993	0%
15122	glycerol	50	0.7135	0.9851	−2%
15128	DL-homocysteine	35	0.1339	0.9478	−14%
15129	D-alanyl-D-alanine	35	0.0165	0.6833	23%
15211	Metabolite - 3807	35	0.3174	0.9478	−5%
15220	Metabolite - 3813	35	0.6421	0.9851	−5%
15227	Metabolite - 3816	35	0.9802	0.9993	0%
15251	Metabolite - 3830	35	0.262	0.9478	20%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.0596	0.7407	−45%
15278	Metabolite - 3843	35	0.0092	0.5749	−16%
15319	DL-phenyllactic acid	35	0.2331	0.9478	32%
15326	Metabolite - 3879	35	0.5692	0.9851	13%
15328	azelaic acid	35	0.7398	0.9851	−2%
15336	tartaric acid	35	0.9993	0.9993	0%
15365	sn-Glycerol-3-phosphate	50	0.4116	0.9478	3%
15389	Metabolite - 3900	35	0.5829	0.9851	3%
15500	carnitine	35	0.528	0.9851	3%
15529	Metabolite - 3951	35	0.0399	0.7407	−11%
15535	Metabolite - 3955	35	0.5955	0.9851	−7%
15606	Metabolite - 3968	35	0.761	0.9851	−5%
15612	Metabolite - 3972	35	0.2908	0.9478	8%
15626	Metabolite - 3977	35	0.2184	0.9478	−7%
15677	3-methyl-L-histidine	35	0.1203	0.9478	−8%
15681	4-Guanidinobutanoic acid	35	0.2211	0.9478	−14%
15683	4-methyl-2-oxopentanoate	50	0.4541	0.9478	5%
15704	heptanedioic acid	35	0.8664	0.9851	−2%
15744	N-N-dimethylarginine	35	0.6586	0.9851	3%
15753	hippuric acid	35	0.6181	0.9851	10%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
15991	L-alpha - glycerophosphorylcholine	35	0.8467	0.9851	−3%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.874	0.9852	−1%
16016	Metabolite - 3994	35	0.7041	0.9851	−8%
16071	Metabolite - 4020	50	0.3935	0.9478	5%
16091	Metabolite - 4031-possible-norlevorphenol-isobutylphendienamide-amprolium	35	0.94	0.9993	−1%
16107	lysine	50	0.8238	0.9851	2%
16137	Metabolite - 4078	35	0.5038	0.9851	−12%
16161	gamma - glutamyl-glutamic acid	35	0.5112	0.9851	8%
16186	Metabolite - 4096-possible-gamma - glu-gly-leu-	35	0.2257	0.9478	18%
16226	Isobar-28-includes-L-threonine-L-allothreonine-L-homoserine-S-4-amino-2-hydroxybutyric acid	35	0.6861	0.9851	3%
16231	Isobar-20-includes-fumaric acid-3-methyl-2-oxobutanoate	35	0.2502	0.9478	18%
16232	Isobar-17-includes-arginine-N-alpha - acetyl-ornithine	35	0.9455	0.9993	−1%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.799	0.9851	3%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.8329	0.9851	3%
16237	Isobar-25-includes-L-gulono-1-4-lactone-glucono-gamma - lactone-	35	0.8393	0.9851	−3%
16241	Isobar-30-includes-maltotetraose-stachyose	35	0.282	0.9478	11%
16243	L-kynurenine	35	0.6848	0.9851	2%
16244	Isobar-21-includes-gamma - aminobutyryl-L-histidine-L-anserine	35	0.0676	0.7493	−21%
16246	Isobar-18-includes-D-fructose-1-phosphate-beta - D-fructose-6-phosphate	35	0.6754	0.9851	5%
16279	Isobar-36-includes-D-sorbitol-6-phosphate-mannitol-1-phosphate	35	0.0432	0.7407	18%
16290	Metabolite - 4133	50	0.1746	0.9478	−9%
16308	Metabolite - 4147	50	0.6922	0.9851	−4%
16330	Metabolite - 4163	35	0.4304	0.9478	−10%
16337	Metabolite - 4167	35	0.7076	0.9851	−3%
16462	Metabolite - 4234	35	0.4466	0.9478	−5%
16471	Metabolite - 4238	35	0.5384	0.9851	10%
16508	Metabolite - 4272	50	0.1526	0.9478	−11%
16621	Metabolite - 4355	50	0.3937	0.9478	−17%
16653	Metabolite - 4361	50	0.0994	0.9247	21%
16666	Metabolite - 4365	50	0.2946	0.9478	−10%
16824	iminodiacetic acid	50	0.7755	0.9851	−3%
16829	Metabolite - 4503	50	0.9392	0.9993	−1%
16848	Metabolite - 4511	50	0.8497	0.9851	−2%
16952	Metabolite - 4593	50	0.3035	0.9478	4%
17028	Metabolite - 4611	50	0.3813	0.9478	−5%
17328	Metabolite - 4768	50	0.4803	0.9659	13%
17330	Metabolite - 4769	50	0.2485	0.9478	14%
17359	Metabolite - 4791	50	0.8127	0.9851	−5%
17388	Metabolite - 4795	50	0.2822	0.9478	11%
17614	Metabolite - 4966	50	0.33	0.9478	9%
17627	Metabolite - 4986	50	0.0582	0.7407	28%
18118	Metabolite - 5346	50	0.4123	0.9478	6%
18146	Metabolite - 5366	50	0.0108	0.5749	40%

TABLE 6-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	pvalue	qvalue	% Change in PCA
18232	Metabolite - 5403	50	0.3291	0.9478	6%
18316	Metabolite - 5437	50	0.1177	0.9478	30%
18335	D-quinic acid	50	0.6344	0.9851	10%
18349	DL-indole-3-lactic acid	50	0.6042	0.9851	−4%
18868	Metabolite - 5847	50	0.8544	0.9851	3%
18926	Metabolite - 5906	50	0.9154	0.9993	4%
18929	Metabolite - 5907	50	0.2112	0.9478	8%

TABLE 7

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
53	glutamine	50	0.1993	0.3977	−14%
54	tryptophan	50	0.1049	0.3151	−10%
57	glutamic acid	50	0.1716	0.3828	−18%
59	histidine	50	0.2197	0.4209	−11%
60	leucine	50	0.0833	0.2916	−13%
63	cholesterol	50	0.1481	0.3699	−10%
64	phenylalanine	35	0.05	0.245	−7%
513	creatinine	35	0.0563	0.2564	−10%
527	lactate	50	0.0035	0.0655	−15%
528	alpha-keto-glutarate	35	0.0099	0.0976	−45%
541	4-hydroxyphenylacetate	35	0.3644	0.481	−5%
542	3-hydroxybutanoic acid	50	0.0434	0.221	−45%
569	caffeine	35	0.0049	0.0777	−51%
577	fructose	50	0.0544	0.2523	−41%
581	glucose	50	0.1835	0.3851	−6%
584	mannose	50	0.9521	0.6641	0%
594	niacinamide	35	0.6135	0.59	−11%
597	phosphoenolpyruvate	35	0.4146	0.5151	−9%
1105	linoleic acid	50	0.0622	0.2681	−14%
1107	allantoin	50	0.4785	0.5344	−14%
1110	arachidonic acid	50	0.3429	0.481	−12%
1121	heptadecanoic acid	50	0.0029	0.0624	−19%
1123	inosine	35	0.7999	0.6385	10%
1125	isoleucine	50	0.072	0.2829	−13%
1126	alanine	50	0.0821	0.2916	−16%
1284	threonine	50	0.2588	0.4682	−9%
1299	tyrosine	50	0.6026	0.5883	−4%
1302	methionine	35	0.499	0.5413	−4%
1303	malic acid	35	0.343	0.481	−21%
1336	n-hexadecanoic acid	50	0.0078	0.0976	−16%
1358	octadecanoic acid	50	0.0337	0.1829	−10%
1365	tetradecanoic acid	50	0.0076	0.0976	−17%
1366	trans-4-hydroxyproline	50	0.0164	0.1319	−14%
1413	3-hydroxyphenylacetate	35	0.9038	0.6568	−1%
1414	3-phospho-d-glycerate	35	0.3849	0.4882	−13%
1415	4-amino-5-methyl-2-1H-pyrimidinone	35	0.4688	0.5282	−8%
1431	(p-Hydroxyphenyl)lactic acid	50	0.0618	0.2681	−22%
1432	alphahydroxybenzeneacetic acid	35	0.9337	0.6641	1%
1437	succinate	50	0.3397	0.481	7%
1444	DL-pipecolic acid	35	0.3851	0.4882	−10%
1480	guanidineacetic acid	35	0.7214	0.6178	5%
1493	ornithine	50	0.1892	0.3889	−18%
1494	5-oxoproline	50	0.1956	0.3977	−9%
1498	N-6-trimethyl-l-lysine	35	0.6864	0.6107	−6%
1507	palmitoleic acid	50	4.00E−04	0.0178	−40%
1508	pantothenic acid	35	0.3718	0.481	−17%
1519	sucrose	50	0.8433	0.6512	4%
1557	3-methylglutaric acid	35	0.0249	0.1479	−18%
1561	alpha-tocopherol	50	0.0158	0.1319	−53%
1564	citric acid	50	0.4573	0.5239	−4%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
1570	oleic acid	50	0.0021	0.0503	−35%
1572	glyceric acid	50	0.1532	0.3719	20%
1574	histamine	35	0.8493	0.6519	4%
1584	methyl-indole-3-acetate	35	0.28	0.4695	−13%
1587	N-acetyl-L-leucine	35	0.71	0.6136	−10%
1591	N-acetyl-L-valine	35	0.0093	0.0976	21%
1604	uric acid	35	0.7956	0.6385	−1%
1643	fumaric acid	50	0.4015	0.5016	−9%
1645	n-dodecanoate	50	0.187	0.3875	−12%
1648	serine	50	0.3365	0.481	−7%
1649	valine	50	0.0224	0.1466	−14%
1670	urea	50	0.3643	0.481	7%
1708	7-8-dihydrofolic acid	35	0.9239	0.6628	4%
1898	proline	50	0.1339	0.3538	−19%
2078	pyrophosphate	35	0.7732	0.6377	−7%
2092	catechol	35	0.259	0.4682	−31%
2132	citrulline	50	0.4546	0.5239	6%
2730	gamma-L-glutamyl-L-glutamine	35	0.552	0.5628	12%
2734	gamma-L-glutamyl-L-tyrosine	35	0.5344	0.5577	4%
2832	adenosine-5-monophosphate	35	0.1631	0.3779	−17%
2848	guanosine-5-diphosphate	35	0.5329	0.5577	−8%
3127	hypoxanthine	35	0.7241	0.6178	−5%
3138	pyridoxamine-phosphate	35	0.8654	0.6522	2%
3147	xanthine	35	0.9538	0.6641	2%
4966	xylitol	35	0.3179	0.481	18%
5280	biliverdin	35	0.4282	0.5189	−11%
5331	pyridoxal-phosphate	35	0.3699	0.481	4%
5618	Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	35	0.0247	0.1479	21%
5628	Metabolite - 1086	35	0.5566	0.5628	−10%
5669	Metabolite - 1104	35	0.0086	0.0976	−15%
5687	Metabolite - 1110	35	0.2792	0.4695	45%
5689	Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	35	0.9467	0.6641	1%
5697	acetylcarnitine-	35	0.2254	0.4256	−12%
5717	Metabolite - 1121	35	0.0166	0.1319	29%
5733	Metabolite - 1127	35	6.00E−04	0.0178	−35%
5765	Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	35	0.611	0.59	−11%
5788	Metabolite - 1183	35	0.7587	0.6319	10%
5792	Metabolite - 1185	35	0.0012	0.034	68%
5800	Metabolite - 1188	35	0.2872	0.4722	18%
6112	Metabolite - 1203-HXGXX-in-MTRX	35	0.3875	0.4889	−20%
6130	Metabolite - 1208	35	0.5109	0.547	−15%
6136	Metabolite - 1211-possible-IHWESASLLR-	35	0.2482	0.4551	204%
6144	Metabolite - 1215	35	0.7273	0.6178	12%
6147	Metabolite - 1216	35	0.4342	0.5189	−8%
6155	Metabolite - 1220	35	0.8726	0.6522	3%
6171	Metabolite - 1244	35	0.7307	0.6186	−6%
6266	Metabolite - 1286	35	0.021	0.1462	16%
6278	Metabolite - 1289	35	0.8015	0.6385	−4%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.5645	0.5664	17%
6398	Metabolite - 1335	35	0.9375	0.6641	1%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.7405	0.6228	7%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.9989	0.6849	0%
6443	Metabolite - 1351	35	0.7988	0.6385	−3%
6537	Metabolite - 1389-possible-gemfibrozil-glucuronide-	35	0.5683	0.5664	−11%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
6549	Metabolite - 1392	35	0.8385	0.6512	−5%
6787	Metabolite - 1465	35	0.7433	0.6231	−4%
6852	Metabolite - 1498	35	0.3324	0.481	15%
6987	Metabolite - 1573	35	0.8266	0.6482	−4%
7029	Metabolite - 1597	35	0.6293	0.6006	3%
7081	Metabolite - 1609	35	0.118	0.327	−16%
7177	Metabolite - 1656	35	0.3641	0.481	15%
7359	n-acetyl-L-aspartic acid	35	0.0139	0.1266	−23%
7446	p-hydroxybenzaldehyde	35	0.3129	0.481	−9%
7595	Metabolite - 1817	35	0.0951	0.3035	24%
7639	oxalic acid	35	0.0942	0.3035	14%
7644	Metabolite - 1831-possible-Cl-adduct-of-citrulline	35	0.026	0.1507	−61%
7650	Metabolite - 1834	35	0.0722	0.2829	−35%
7652	Metabolite - 1835	35	0.4205	0.5151	11%
7654	Metabolite - 1836	35	0.0891	0.295	−28%
7660	Metabolite - 1839	35	0.0218	0.1462	−45%
7672	Metabolite - 1843	35	0.9787	0.6778	−1%
7933	Metabolite - 1911	35	0.4204	0.5151	25%
7935	paraxanthine	35	0.0203	0.1462	−41%
7941	Metabolite - 1914	35	0.3503	0.481	32%
7944	Metabolite - 1915	35	0.8018	0.6385	15%
7957	trans-2-3-4-trimethoxycinnamic acid	35	0.3149	0.481	35%
8091	glycocholic acid	35	0.9047	0.6568	−5%
8176	Metabolite - 1974	35	0.8572	0.6522	4%
8189	Metabolite - 1977	35	0.1838	0.3851	−12%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.9459	0.6641	1%
8217	Metabolite - 1983	35	0.3016	0.481	246%
8300	Metabolite - 1988	35	0.01	0.0976	−30%
8336	Metabolite - 2005	35	0.0359	0.1905	−26%
8404	Metabolite - 2027	35	0.1676	0.3788	−14%
8649	Metabolite - 2053	35	0.7092	0.6136	−5%
8669	Metabolite - 2055	35	0.8342	0.6512	4%
8677	Metabolite - 2056	35	0.1623	0.3779	−15%
8796	Metabolite - 2074	35	0.9322	0.6641	2%
8959	Metabolite - 2100	35	0.6011	0.5883	4%
9007	Metabolite - 2108	35	0.0055	0.0777	−29%
9024	Metabolite - 2111	35	0.3265	0.481	−15%
9092	Metabolite - 2129	35	0.8607	0.6522	−4%
9106	Metabolite - 2130	35	0.0964	0.3035	72%
9130	Metabolite - 2139	35	0.5099	0.547	7%
9137	Metabolite - 2141	35	0.0052	0.0777	−43%
9491	Metabolite - 2185	35	0.6878	0.6107	4%
9748	Metabolite - 2212	35	0.2255	0.4256	19%
10087	Metabolite - 2249	35	0.6409	0.6006	−6%
10092	Metabolite - 2250	35	0.4987	0.5413	18%
10122	Metabolite - 2254	35	0.1171	0.327	−39%
10143	Metabolite - 2255-hydroxyproline-form-of-bradykinin	35	0.1844	0.3851	139%
10145	Metabolite - 2256	35	0.862	0.6522	−3%
10245	Metabolite - 2269-	35	0.2698	0.4695	34%
10317	Metabolite - 2279	35	0.3109	0.481	−24%
10327	Metabolite - 2281	35	0.4355	0.5189	−24%
10378	Metabolite - 2287	35	0.1438	0.3664	346%
10438	gamma-glu-leu	35	0.4822	0.5344	−6%
10461	Metabolite - 2313	35	0.5649	0.5664	−6%
10476	Metabolite - 2316	35	0.2043	0.4036	51%
10544	Metabolite - 2329	35	1.00E−04	0.0086	−42%
10551	Metabolite - 2347	35	0.3563	0.481	30%
10604	Metabolite - 2370	35	0.8174	0.6449	4%
10629	Metabolite - 2386	35	0.516	0.5502	−14%
10644	Metabolite - 2387	35	0.5362	0.5577	−32%
10655	Metabolite - 2388	35	0.1466	0.3699	11%
10667	Metabolite - 2389	35	0.0776	0.291	186%
10672	Metabolite - 2390	35	0.0718	0.2829	−27%
10692	Metabolite - 2391	35	0.0982	0.3052	−12%
10698	Metabolite - 2392	35	0.6996	0.6131	−15%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
10737	Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone	35	0.8978	0.6568	−2%
10739	Metabolite - 2407	35	0.0093	0.0976	48%
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.5412	0.5606	−15%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.3542	0.481	14%
10744	Isobar-5-includes-asparagine-ornithine-gly-gly	35	0.1653	0.3788	17%
10746	Isobar-6-includes-valine-betaine	35	0.0606	0.2681	−8%
10753	Isobar-9-includes-galactinol-dihydrate-turanose-kojibiose-D-leucrose-lactulose-sophorose-sucrose-beta-D-lactose-D-trehalose-D-cellobiose-D-Maltose-palatinose-melibiose-alpha-D-lactose	35	0.7716	0.6377	−6%
10782	Metabolite - 2486	35	0.6665	0.6048	−8%
10785	Metabolite - 2506	35	0.1515	0.3712	−39%
10787	Metabolite - 2507	35	0.2156	0.4171	−34%
10825	Metabolite - 2546	35	0.4358	0.5189	−13%
11053	Metabolite - 2567	35	0.5492	0.5628	6%
11111	Metabolite - 2592	35	0.3309	0.481	−41%
11219	Metabolite - 2686	35	0.9155	0.6628	1%
11222	Metabolite - 2688	35	0.6923	0.6112	6%
11323	Metabolite - 2711	35	0.0036	0.0655	−21%
11438	phosphate	50	0.9259	0.6628	−1%
11499	Metabolite - 2753	35	0.6692	0.6048	−5%
11777	glycine	50	0.1082	0.3168	−16%
11813	Metabolite - 2809	35	0.7365	0.6215	−7%
12035	nonanate	50	0.4925	0.5413	3%
12109	Metabolite - 2853	35	0.6348	0.6006	−8%
12298	Metabolite - 2867	35	0.1809	0.3851	−47%
12444	Metabolite - 2888-possible-sulfated-Rosiglitazone	35	0.3955	0.4965	13%
12478	Metabolite - 2898	35	0.2404	0.4472	−36%
12532	Metabolite - 2914	50	0.2774	0.4695	2%
12533	Metabolite - 2915	50	0.4585	0.5239	7%
12543	2-hydroxy-butanoic acid	50	0.1732	0.3828	−17%
12562	Metabolite - 2955	50	0.8848	0.6555	1%
12593	Metabolite - 2973	50	0.8416	0.6512	1%
12594	Metabolite - 2974	50	0.1138	0.3224	11%
12601	Metabolite - 2978	50	0.0765	0.291	23%
12625	Metabolite - 3002	50	0.0539	0.2523	−21%
12626	Metabolite - 3003	50	0.9736	0.6761	0%
12627	Metabolite - 3004	50	0.9538	0.6641	−1%
12639	Metabolite - 3012	50	0.384	0.4882	7%
12641	meso-erythritol	50	0.1016	0.3119	−16%
12644	Metabolite - 3016	50	0.1504	0.3712	−9%
12645	Metabolite - 3017	50	0.2449	0.4523	15%
12647	Metabolite - 3019	50	0.232	0.4348	11%
12648	Metabolite - 3020	50	0.5697	0.5664	7%
12650	Metabolite - 3022	50	0.6591	0.6042	5%
12656	Metabolite - 3025	50	0.3225	0.481	9%
12658	Metabolite - 3026	50	0.321	0.481	10%
12663	Metabolite - 3030	50	0.0082	0.0976	22%
12666	Metabolite - 3033	50	0.0244	0.1479	14%
12673	Metabolite - 3040	50	0.0517	0.2487	27%
12682	Metabolite - 3044	35	0.5288	0.5577	−8%
12719	Metabolite - 3055	35	0.4505	0.5239	21%
12720	Metabolite - 3056	35	0.7025	0.6131	−3%
12726	Metabolite - 3058	50	0.4992	0.5413	12%
12739	1-5-anhydro-D-glucitol	50	0.3236	0.481	−12%
12751	Metabolite - 3073	50	0.1743	0.3828	23%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
12753	Metabolite - 3074	50	0.136	0.3538	−39%
12754	Metabolite - 3075	50	0.6421	0.6006	6%
12756	Metabolite - 3077	50	0.5522	0.5628	6%
12757	Metabolite - 3078	50	0.4196	0.5151	9%
12761	Metabolite - 3081	50	0.4686	0.5282	−8%
12765	inositol	50	0.2758	0.4695	−12%
12768	Metabolite - 3088	50	0.0202	0.1462	38%
12769	Metabolite - 3089	50	0.2713	0.4695	−14%
12771	Metabolite - 3091	50	0.2132	0.4171	48%
12773	Metabolite - 3093	50	0.7501	0.6267	−5%
12774	Metabolite - 3094	50	0.5302	0.5577	−7%
12777	Metabolite - 3097	50	0.9998	0.6849	0%
12780	Metabolite - 3098	50	0.0769	0.291	31%
12781	Metabolite - 3099	50	0.8957	0.6568	2%
12784	Metabolite - 3102	50	0.3579	0.481	−7%
12790	Metabolite - 3108	50	0.8722	0.6522	1%
12876	Metabolite - 3125	35	0.4287	0.5189	−6%
12912	Metabolite - 3129	35	0.9973	0.6849	0%
12924	Metabolite - 3131	35	0.2901	0.4739	29%
12931	DL-hexanoyl-carnitine	35	0.7104	0.6136	−3%
12960	Metabolite - 3134	35	0.6932	0.6112	−11%
12969	Metabolite - 3135	35	0.7666	0.6364	10%
13018	Metabolite - 3138	35	0.1116	0.3215	−20%
13038	Metabolite - 3143	35	0.1583	0.3769	−17%
13065	Metabolite - 3146	35	0.0835	0.2916	−33%
13104	Metabolite - 3160	35	0.1779	0.3843	−15%
13142	Metabolite - 3165	35	0.2842	0.4702	−7%
13146	Metabolite - 3166	35	0.9041	0.6568	−3%
13148	Metabolite - 3167	35	0.9239	0.6628	1%
13179	possible-Metabolite - 3176-possible-creatine	35	0.1352	0.3538	28%
13208	Metabolite - 3181	35	0.5937	0.5841	−6%
13211	Metabolite - 3182	35	0.649	0.6015	11%
13214	Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine	35	0.946	0.6641	1%
13217	Metabolite - 3184	35	0.3141	0.481	−13%
13249	Metabolite - 3215	35	0.2706	0.4695	−13%
13251	Metabolite - 3216	35	0.2161	0.4171	−16%
13257	Metabolite - 3218	35	0.8158	0.6449	−4%
13342	Metabolite - 3243	35	0.9895	0.6834	0%
13448	Metabolite - 3303	35	0.0146	0.128	−17%
13459	Metabolite - 3305	35	1.00E−04	0.0086	−59%
13484	Metabolite - 3309	35	0.0639	0.2681	−27%
13505	Metabolite - 3313	35	0.3298	0.481	−38%
13509	Metabolite - 3314	35	0.1312	0.3519	−19%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.556	0.5628	−21%
13545	Metabolite - 3322	35	5.00E−04	0.0178	−39%
13589	Metabolite - 3327	35	5.00E−04	0.0178	−52%
13775	Metabolite - 3370	35	0.4705	0.5282	−7%
13803	Metabolite - 3377	35	0	0.0026	−64%
13904	Metabolite - 3402	35	0.0047	0.0777	−38%
14027	Metabolite - 3426	35	0.5712	0.5664	−2%
14084	Metabolite - 3436	35	0.8882	0.6558	2%
14117	Metabolite - 3441	35	0.4955	0.5413	−6%
14239	Metabolite - 3474	35	0.168	0.3788	20%
14249	Metabolite - 3476	35	0.7254	0.6178	−8%
14368	Metabolite - 3489	35	0.1059	0.3151	−35%
14439	Metabolite - 3498	35	0.4571	0.5239	9%
14495	Metabolite - 3534	35	0.1123	0.3215	−23%
14595	Metabolite - 3576	35	0.3216	0.481	19%
14608	Metabolite - 3578	35	0.3148	0.481	23%
14639	Metabolite - 3603	35	0.0022	0.0503	40%
14640	Metabolite - 3604	35	0.6656	0.6048	12%
14672	Metabolite - 3615	35	0.8695	0.6522	3%
14715	Metabolite - 3653-possible-stachydrine-	35	0.7021	0.6131	13%
14766	Metabolite - 3670	35	0.5739	0.5668	−5%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
14785	isobar-glycochenodeoxycholic acid-glycodeoxycholic acid	35	0.6413	0.6006	−12%
14787	Metabolite - 3698	35	0.798	0.6385	−4%
14837	Metabolite - 3707	35	0.0965	0.3035	108%
14961	Metabolite - 3752	35	0.2823	0.4701	145%
15000	Metabolite - 3758	35	0.123	0.3334	−38%
15017	Metabolite - 3761	35	0.8844	0.6555	−2%
15032	Metabolite - 3765	35	0.6458	0.6006	−11%
15063	Metabolite - 3772	35	0.0788	0.291	−15%
15113	Metabolite - 3783	35	0.4349	0.5189	12%
15122	glycerol	50	0.0247	0.1479	−14%
15128	DL-homocysteine	35	0.3684	0.481	−11%
15129	D-alanyl-D-alanine	35	0.8683	0.6522	−2%
15211	Metabolite - 3807	35	0.2961	0.4806	−6%
15220	Metabolite - 3813	35	0.0871	0.295	−23%
15227	Metabolite - 3816	35	0.8378	0.6512	−3%
15251	Metabolite - 3830	35	0.0863	0.295	−24%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.0475	0.2374	−49%
15278	Metabolite - 3843	35	0.0309	0.1711	−17%
15319	DL-phenyllactic acid	35	0.2786	0.4695	−22%
15326	Metabolite - 3879	35	0.6363	0.6006	28%
15328	azelaic acid	35	0.1571	0.3769	−10%
15336	tartaric acid	35	0.0214	0.1462	−38%
15365	sn-Glycerol-3-phosphate	50	0.5069	0.547	−5%
15389	Metabolite - 3900	35	0.0294	0.1667	−14%
15500	carnitine	35	0.197	0.3977	10%
15529	Metabolite - 3951	35	0.6687	0.6048	−3%
15535	Metabolite - 3955	35	0.4421	0.5216	27%
15606	Metabolite - 3968	35	0.8468	0.6519	−4%
15612	Metabolite - 3972	35	0.3503	0.481	11%
15626	Metabolite - 3977	35	0.0207	0.1462	−17%
15677	3-methyl-L-histidine	35	0.3568	0.481	−6%
15681	4-Guanidinobutanoic acid	35	0.8904	0.6558	−2%
15683	4-methyl-2-oxopentanoate	50	0.1063	0.3151	−16%
15704	heptanedioic acid	35	0.1218	0.3334	47%
15744	N-N-dimethylarginine	35	0.3455	0.481	−8%
15753	hippuric acid	35	0.6581	0.6042	−9%
15991	L-alpha-glycerophosphorylcholine	35	0.3514	0.481	−18%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.643	0.6006	3%
16016	Metabolite - 3994	35	0.7835	0.6385	−8%
16071	Metabolite - 4020	50	0.7967	0.6385	−1%
16091	Metabolite - 4031-possible-norlevorphenol-isobutylphendienamide-amprolium	35	0.0804	0.2916	−12%
16107	lysine	50	0.1771	0.3843	−12%
16137	Metabolite - 4078	35	0.2647	0.4695	−19%
16161	gamma-glutamyl-glutamic acid	35	0.9512	0.6641	0%
16186	Metabolite - 4096-possible-gamma-glu-gly-leu-	35	0.4824	0.5344	19%
16226	Isobar-28-includes-L-threonine-L-allothreonine-L-homoserine-S-4-amino-2-hydroxybutyric acid	35	0.1998	0.3977	14%
16231	Isobar-20-includes-fumaric acid-3-methyl-2-oxobutanoate	35	0.5237	0.5561	12%
16232	Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.0125	0.1175	36%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.1598	0.3771	−19%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.5502	0.5628	11%

TABLE 7-continued

Plasma Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
16237	Isobar-25-includes-L-gulono-1-4-lactone-glucono-gamma-lactone-	35	0.7148	0.6154	−8%
16241	Isobar-30-includes-maltotetraose-stachyose	35	0.6804	0.6106	−6%
16243	L-kynurenine	35	0.7838	0.6385	−3%
16244	Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	35	0.6805	0.6106	7%
16246	Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	35	0.8566	0.6522	4%
16279	Isobar-36-includes-D-sorbitol-6-phosphate-mannitol-1-phosphate	35	0.3438	0.481	−13%
16290	Metabolite - 4133	50	0.6833	0.6107	5%
16308	Metabolite - 4147	50	0.0642	0.2681	−24%
16330	Metabolite - 4163	35	0.4532	0.5239	−12%
16337	Metabolite - 4167	35	0.2792	0.4695	−17%
16462	Metabolite - 4234	35	0.4546	0.5239	−8%
16471	Metabolite - 4238	35	0.9246	0.6628	2%
16508	Metabolite - 4272	50	0.3504	0.481	−12%
16621	Metabolite - 4355	50	0.3773	0.4856	−17%
16653	Metabolite - 4361	50	0.3706	0.481	17%
16666	Metabolite - 4365	50	0.7897	0.6385	−4%
16824	iminodiacetic acid	50	0.041	0.213	−26%
16829	Metabolite - 4503	50	0.8049	0.639	−7%
16848	Metabolite - 4511	50	0.0692	0.2829	−25%
16952	Metabolite - 4593	50	0.6542	0.604	2%
17028	Metabolite - 4611	50	0.3655	0.481	−6%
17328	Metabolite - 4768	50	0.7791	0.6385	−7%
17330	Metabolite - 4769	50	0.1385	0.3566	17%
17359	Metabolite - 4791	50	0.8812	0.6555	−5%
17388	Metabolite - 4795	50	0.3033	0.481	22%
17614	Metabolite - 4966	50	0.3248	0.481	11%
17627	Metabolite - 4986	50	0.6096	0.59	12%
18118	Metabolite - 5346	50	0.6124	0.59	−6%
18146	Metabolite - 5366	50	0.6449	0.6006	7%
18232	Metabolite - 5403	50	0.2718	0.4695	10%
18316	Metabolite - 5437	50	0.4383	0.5195	−19%
18335	D-quinic acid	50	0.0891	0.295	−42%
18349	DL-indole-3-lactic acid	50	5.00E−04	0.0178	−25%
18868	Metabolite - 5847	50	0.4666	0.5282	−15%
18926	Metabolite - 5906	50	0.3425	0.481	−27%
18929	Metabolite - 5907	50	0.8229	0.6473	2%

TABLE 8

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
53	glutamine	50	0.2081	0.4944	−13%
54	tryptophan	50	0.0734	0.3431	−13%
57	glutamic acid	50	0.3386	0.6063	−13%
59	histidine	50	0.742	0.7437	−3%
60	leucine	50	0.015	0.154	−19%
63	cholesterol	50	0.19	0.4682	−9%
64	phenylalanine	35	0.1602	0.4579	−5%
513	creatinine	35	0.9764	0.7893	0%
527	lactate	50	0.0062	0.0915	−14%
528	alpha-keto-glutarate	35	0.6988	0.7368	−9%
541	4-hydroxyphenylacetate	35	0.9884	0.7893	0%
542	3-hydroxybutanoic acid	50	0.1111	0.4081	−50%
569	caffeine	35	6.00E−04	0.0433	−70%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
577	fructose	50	0.0966	0.3887	−20%
581	glucose	50	0.6171	0.7298	−2%
584	mannose	50	0.9074	0.7713	−1%
594	niacinamide	35	0.4972	0.666	−18%
597	phosphoenolpyruvate	35	0.7347	0.7434	−4%
1105	linoleic acid	50	0.0404	0.2538	−17%
1107	allantoin	50	0.7673	0.7448	−6%
1110	arachidonic acid	50	0.6643	0.7368	−6%
1121	heptadecanoic acid	50	0	0.0036	−27%
1123	inosine	35	0.972	0.7891	1%
1125	isoleucine	50	0.0129	0.1407	−19%
1126	alanine	50	0.0951	0.3887	−15%
1284	threonine	50	0.3138	0.5918	−8%
1299	tyrosine	50	0.1559	0.4579	−11%
1302	methionine	35	0.5223	0.687	−4%
1303	malic acid	35	0.5527	0.712	−13%
1336	n-hexadecanoic acid	50	0.0024	0.0649	−20%
1358	octadecanoic acid	50	9.00E−04	0.0464	−16%
1365	tetradecanoic acid	50	0.0017	0.0613	−22%
1366	trans-4-hydroxyproline	50	0.0035	0.0738	−15%
1413	3-hydroxyphenylacetate	35	0.6788	0.7368	2%
1414	3-phospho-d-glycerate	35	0.4156	0.6338	−12%
1415	4-amino-5-methyl-2-1H-pyrimidinone	35	0.3	0.5825	−10%
1431	(p-Hydroxyphenyl)lactic acid	50	0.0035	0.0738	−27%
1432	alphahydroxybenzeneacetic acid	35	0.8113	0.751	3%
1437	succinate	50	0.2184	0.5028	9%
1444	DL-pipecolic acid	35	0.9642	0.7862	0%
1480	guanidineacetic acid	35	0.8726	0.7585	−2%
1493	ornithine	50	0.1811	0.4682	−19%
1494	5-oxoproline	50	0.0231	0.2124	−12%
1498	N-6-trimethyl-l-lysine	35	0.7026	0.7368	5%
1507	palmitoleic acid	50	7.00E−04	0.0433	−44%
1508	pantothenic acid	35	0.182	0.4682	−31%
1519	sucrose	50	0.9548	0.7862	−2%
1557	3-methylglutaric acid	35	0.19	0.4682	−10%
1561	alpha-tocopherol	50	0.8757	0.759	−6%
1564	citric acid	50	0.2758	0.5606	−6%
1570	oleic acid	50	0.0045	0.0866	−34%
1572	glyceric acid	50	0.2114	0.4945	17%
1574	histamine	35	0.8416	0.7585	−4%
1584	methyl-indole-3-acetate	35	0.2877	0.569	−13%
1587	N-acetyl-L-leucine	35	0.2729	0.5593	−31%
1591	N-acetyl-L-valine	35	0.9102	0.7713	1%
1604	uric acid	35	0.813	0.751	−1%
1643	fumaric acid	50	0.5872	0.7241	−6%
1645	n-dodecanoate	50	0.1214	0.4111	−15%
1648	serine	50	0.0574	0.3133	−14%
1649	valine	50	0.0074	0.1041	−19%
1670	urea	50	0.6012	0.7257	3%
1708	7-8-dihydrofolic acid	35	0.5075	0.673	−20%
1898	proline	50	0.221	0.5048	−16%
2078	pyrophosphate	35	0.7583	0.7448	−7%
2092	catechol	35	0.2733	0.5593	−31%
2132	citrulline	50	0.3254	0.5955	9%
2730	gamma-L-glutamyl-L-glutamine	35	0.4725	0.6556	16%
2734	gamma-L-glutamyl-L-tyrosine	35	0.7177	0.7423	−2%
2832	adenosine-5-monophosphate	35	0.3158	0.5918	−14%
2848	guanosine-5-diphosphate	35	0.445	0.6491	−9%
3127	hypoxanthine	35	0.948	0.7855	1%
3138	pyridoxamine-phosphate	35	0.4558	0.6552	−12%
3147	xanthine	35	0.6472	0.73	13%
4966	xylitol	35	0.463	0.6556	13%
5280	biliverdin	35	0.1482	0.4503	−33%
5331	pyridoxal-phosphate	35	0.0379	0.2538	9%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
5618	Metabolite - 1085-possible-isolobinine-or-4-aminoestra-1-3-5-10-triene-3-17beta-diol	35	0.0709	0.3425	16%
5628	Metabolite - 1086	35	0.6001	0.7257	−8%
5669	Metabolite - 1104	35	0.0196	0.1865	−14%
5687	Metabolite - 1110	35	0.3645	0.6113	37%
5689	Metabolite - 1111-possible-methylnitronitrosoguanidine-or-ethyl-thiocarbamoylacetate	35	0.4217	0.6338	−9%
5697	acetylcarnitine-	35	0.262	0.559	−11%
5717	Metabolite - 1121	35	0.1136	0.4081	17%
5733	Metabolite - 1127	35	0.0695	0.3413	−20%
5765	Metabolite - 1142-possible-5-hydroxypentanoate-or-beta-hydroxyisovaleric acid	35	0.5859	0.7241	−18%
5788	Metabolite - 1183	35	0.3872	0.6303	−55%
5792	Metabolite - 1185	35	0.0919	0.3869	24%
5800	Metabolite - 1188	35	0.4258	0.6338	−13%
6112	Metabolite - 1203-HXGXA in-MTRX	35	0.1905	0.4682	−48%
6130	Metabolite - 1208	35	0.3544	0.6113	−20%
6136	Metabolite - 1211-possible-IHWESASLLR-	35	0.6994	0.7368	−22%
6144	Metabolite - 1215	35	0.7751	0.7448	10%
6147	Metabolite - 1216	35	0.3347	0.6063	−15%
6155	Metabolite - 1220	35	0.9929	0.7893	0%
6171	Metabolite - 1244	35	0.3205	0.5918	−15%
6266	Metabolite - 1286	35	0.1856	0.4682	11%
6278	Metabolite - 1289	35	0.4585	0.6556	14%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.9961	0.7893	0%
6398	Metabolite - 1335	35	0.8918	0.766	2%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.7003	0.7368	−8%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.9819	0.7893	−1%
6443	Metabolite - 1351	35	0.871	0.7585	−2%
6537	Metabolite - 1389-possible-gemfibrozil-glucuronide-	35	0.302	0.5825	−78%
6549	Metabolite - 1392	35	0.4157	0.6338	−15%
6787	Metabolite - 1465	35	0.649	0.73	−8%
6852	Metabolite - 1498	35	0.0777	0.3524	33%
6987	Metabolite - 1573	35	0.9489	0.7855	−1%
7029	Metabolite - 1597	35	0.4038	0.6338	−6%
7081	Metabolite - 1609	35	0.0305	0.2368	−23%
7177	Metabolite - 1656	35	0.4157	0.6338	13%
7359	n-acetyl-L-aspartic acid	35	0.0437	0.2628	−21%
7446	p-hydroxybenzaldehyde	35	0.6766	0.7368	−4%
7595	Metabolite - 1817	35	0.153	0.4554	21%
7639	oxalic acid	35	0.2078	0.4944	11%
7644	Metabolite - 1831-possible-Cl-adduct-of-citrulline	35	0.0691	0.3413	−44%
7650	Metabolite - 1834	35	0.1156	0.4081	−30%
7652	Metabolite - 1835	35	0.4281	0.6338	−11%
7654	Metabolite - 1836	35	0.147	0.4503	−25%
7660	Metabolite - 1839	35	0.0387	0.2538	−42%
7672	Metabolite - 1843	35	0.7808	0.7448	−3%
7933	Metabolite - 1911	35	0.5335	0.6956	−16%
7935	paraxanthine	35	0.0019	0.0613	−58%
7941	Metabolite - 1914	35	0.4757	0.6556	25%
7944	Metabolite - 1915	35	0.6141	0.7297	−26%
7957	trans-2-3-4-trimethoxycinnamic acid	35	0.4257	0.6338	28%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
8091	glycocholic acid	35	0.4181	0.6338	−27%
8176	Metabolite - 1974	35	0.7599	0.7448	−5%
8189	Metabolite - 1977	35	0.0864	0.3689	−14%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.6427	0.73	6%
8217	Metabolite - 1983	35	0.6235	0.73	−32%
8300	Metabolite - 1988	35	0.0635	0.3225	−19%
8336	Metabolite - 2005	35	0.0395	0.2538	−25%
8404	Metabolite - 2027	35	0.3196	0.5918	−10%
8649	Metabolite - 2053	35	0.1695	0.4624	−19%
8669	Metabolite - 2055	35	0.9053	0.7713	3%
8677	Metabolite - 2056	35	0.0608	0.3144	−20%
8796	Metabolite - 2074	35	0.7798	0.7448	4%
8959	Metabolite - 2100	35	0.9464	0.7855	−1%
9007	Metabolite - 2108	35	0.0164	0.1608	−29%
9024	Metabolite - 2111	35	0.5873	0.7241	−10%
9092	Metabolite - 2129	35	0.8698	0.7585	5%
9106	Metabolite - 2130	35	0.0606	0.3144	95%
9130	Metabolite - 2139	35	0.6874	0.7368	5%
9137	Metabolite - 2141	35	0.0058	0.0915	−49%
9491	Metabolite - 2185	35	0.1596	0.4579	−12%
9748	Metabolite - 2212	35	0.0811	0.355	31%
10087	Metabolite - 2249	35	0.8331	0.7585	−3%
10092	Metabolite - 2250	35	0.2327	0.5235	−27%
10122	Metabolite - 2254	35	0.3765	0.6227	−29%
10143	Metabolite - 2255-hydroxyproline-form-of-bradykinin	35	0.6393	0.73	27%
10145	Metabolite - 2256	35	0.4476	0.6495	18%
10245	Metabolite - 2269-	35	0.4123	0.6338	24%
10317	Metabolite - 2279	35	0.0505	0.2916	−42%
10327	Metabolite - 2281	35	0.3395	0.6063	−44%
10378	Metabolite - 2287	35	0.2325	0.5235	180%
10438	gamma-glu-leu	35	0.245	0.5351	−10%
10461	Metabolite - 2313	35	0.7899	0.7448	−3%
10476	Metabolite - 2316	35	0.1189	0.4081	74%
10544	Metabolite - 2329	35	0	0.0014	−42%
10551	Metabolite - 2347	35	0.5251	0.6877	20%
10604	Metabolite - 2370	35	0.9852	0.7893	0%
10629	Metabolite - 2386	35	0.5977	0.7257	−11%
10644	Metabolite - 2387	35	0.3024	0.5825	−55%
10655	Metabolite - 2388	35	0.1144	0.4081	12%
10667	Metabolite - 2389	35	0.1156	0.4081	138%
10672	Metabolite - 2390	35	0.0817	0.355	−41%
10692	Metabolite - 2391	35	0.3467	0.6113	−7%
10698	Metabolite - 2392	35	0.8622	0.7585	−7%
10737	Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone	35	0.6822	0.7368	−6%
10739	Metabolite - 2407	35	0.0119	0.1402	48%
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.6689	0.7368	−7%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.3076	0.5847	16%
10744	Isobar-5-includes-asparagine-ornithine-gly-gly	35	0.2642	0.559	13%
10746	Isobar-6-includes-valine-betaine	35	0.0032	0.0738	−12%
10753	Isobar-9-includes-galactinol-dihydrate-turanose-kojibiose-D-	35	0.9571	0.7862	1%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
	leucrose-lactulose-sophorose-sucrose-beta-D-lactose-D-trehalose-D-cellobiose-D-Maltose-palatinose-melibiose-alpha-D-lactose				
10782	Metabolite - 2486	35	0.427	0.6338	−15%
10785	Metabolite - 2506	35	0.1333	0.4318	−41%
10787	Metabolite - 2507	35	0.354	0.6113	−25%
10825	Metabolite - 2546	35	0.4672	0.6556	−13%
11053	Metabolite - 2567	35	0.7367	0.7434	−3%
11111	Metabolite - 2592	35	0.1638	0.4579	−62%
11219	Metabolite - 2686	35	0.7815	0.7448	−2%
11222	Metabolite - 2688	35	0.6332	0.73	−7%
11323	Metabolite - 2711	35	0.0047	0.0866	−21%
11438	phosphate	50	0.7922	0.7448	−1%
11499	Metabolite - 2753	35	0.3071	0.5847	−11%
11777	glycine	50	0.355	0.6113	−9%
11813	Metabolite - 2809	35	0.5982	0.7257	−10%
12035	nonanate	50	0.6366	0.73	2%
12109	Metabolite - 2853	35	0.0251	0.2202	−34%
12298	Metabolite - 2867	35	0.9249	0.7787	−4%
12478	Metabolite - 2898	35	0.4273	0.6338	30%
12532	Metabolite - 2914	50	0.8816	0.7596	0%
12533	Metabolite - 2915	50	0.1622	0.4579	14%
12543	2-hydroxy-butanoic acid	50	0.0286	0.2334	−29%
12562	Metabolite - 2955	50	0.5565	0.7129	−2%
12593	Metabolite - 2973	50	0.8623	0.7585	1%
12594	Metabolite - 2974	50	0.1248	0.4179	11%
12601	Metabolite - 2978	50	0.1299	0.4252	19%
12625	Metabolite - 3002	50	0.0819	0.355	−20%
12626	Metabolite - 3003	50	0.4436	0.6491	9%
12627	Metabolite - 3004	50	0.6919	0.7368	5%
12639	Metabolite - 3012	50	0.8549	0.7585	2%
12641	meso-erythritol	50	0.163	0.4579	−9%
12644	Metabolite - 3016	50	0.6845	0.7368	−3%
12645	Metabolite - 3017	50	0.7813	0.7448	−3%
12647	Metabolite - 3019	50	0.6788	0.7368	4%
12648	Metabolite - 3020	50	0.9322	0.7826	1%
12650	Metabolite - 3022	50	0.6859	0.7368	5%
12656	Metabolite - 3025	50	0.9228	0.7787	1%
12658	Metabolite - 3026	50	0.7257	0.7423	3%
12663	Metabolite - 3030	50	0.114	0.4081	12%
12666	Metabolite - 3033	50	0.0152	0.154	15%
12673	Metabolite - 3040	50	0.2695	0.5593	15%
12682	Metabolite - 3044	35	0.1443	0.4503	−18%
12719	Metabolite - 3055	35	0.5731	0.7241	15%
12720	Metabolite - 3056	35	0.9358	0.7834	1%
12726	Metabolite - 3058	50	0.6191	0.7298	9%
12739	1-5-anhydro-D-glucitol	50	0.7986	0.7448	−4%
12751	Metabolite - 3073	50	0.1953	0.4717	22%
12753	Metabolite - 3074	50	0.3904	0.6321	−22%
12754	Metabolite - 3075	50	0.2559	0.5505	15%
12756	Metabolite - 3077	50	0.5804	0.7241	5%
12757	Metabolite - 3078	50	0.2799	0.5648	11%
12761	Metabolite - 3081	50	0.8489	0.7585	1%
12765	inositol	50	0.5387	0.6992	−7%
12768	Metabolite - 3088	50	0.0017	0.0613	63%
12769	Metabolite - 3089	50	0.0293	0.2334	−26%
12771	Metabolite - 3091	50	0.4809	0.6576	22%
12773	Metabolite - 3093	50	0.4029	0.6338	−13%
12774	Metabolite - 3094	50	0.4972	0.666	−7%
12777	Metabolite - 3097	50	0.3855	0.6303	−14%
12780	Metabolite - 3098	50	0.2867	0.569	17%
12781	Metabolite - 3099	50	0.1762	0.4679	−19%
12784	Metabolite - 3102	50	0.3989	0.6338	−6%
12790	Metabolite - 3108	50	0.8644	0.7585	−1%
12876	Metabolite - 3125	35	0.7646	0.7448	−2%
12912	Metabolite - 3129	35	0.4822	0.6576	−8%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
12924	Metabolite - 3131	35	0.3961	0.6338	23%
12931	DL-hexanoyl-carnitine	35	0.487	0.6583	−6%
12960	Metabolite - 3134	35	0.6922	0.7368	−11%
12969	Metabolite - 3135	35	0.9108	0.7713	−3%
13018	Metabolite - 3138	35	0.7404	0.7437	−4%
13038	Metabolite - 3143	35	0.1276	0.4226	−18%
13065	Metabolite - 3146	35	0.0976	0.3887	−35%
13104	Metabolite - 3160	35	0.6297	0.73	−6%
13142	Metabolite - 3165	35	0.7536	0.7448	−2%
13146	Metabolite - 3166	35	0.7532	0.7448	−7%
13148	Metabolite - 3167	35	0.217	0.5028	−16%
13179	possible-Metabolite - 3176-possible-creatine	35	0.1906	0.4682	22%
13208	Metabolite - 3181	35	0.7725	0.7448	3%
13211	Metabolite - 3182	35	0.6544	0.7332	11%
13214	Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine	35	0.8943	0.766	−1%
13217	Metabolite - 3184	35	0.8706	0.7585	−2%
13249	Metabolite - 3215	35	0.4668	0.6556	−9%
13251	Metabolite - 3216	35	0.7987	0.7448	−4%
13257	Metabolite - 3218	35	0.5009	0.6678	−8%
13342	Metabolite - 3243	35	0.6378	0.73	−9%
13448	Metabolite - 3303	35	0.2433	0.5351	−9%
13459	Metabolite - 3305	35	0.0084	0.1083	−50%
13484	Metabolite - 3309	35	0.8307	0.7585	−4%
13505	Metabolite - 3313	35	0.3577	0.6113	−20%
13509	Metabolite - 3314	35	0.3672	0.6113	−12%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.4843	0.6576	−28%
13545	Metabolite - 3322	35	0	0.0014	−47%
13589	Metabolite - 3327	35	0.0057	0.0915	−50%
13775	Metabolite - 3370	35	0.3669	0.6113	−8%
13803	Metabolite - 3377	35	0.006	0.0915	−57%
13904	Metabolite - 3402	35	0.0721	0.3428	−26%
14027	Metabolite - 3426	35	0.7318	0.7434	1%
14084	Metabolite - 3436	35	0.6058	0.7257	−10%
14117	Metabolite - 3441	35	0.7013	0.7368	5%
14239	Metabolite - 3474	35	0.0599	0.3144	31%
14249	Metabolite - 3476	35	0.7249	0.7423	9%
14368	Metabolite - 3489	35	0.3626	0.6113	−20%
14439	Metabolite - 3498	35	0.5688	0.7241	6%
14495	Metabolite - 3534	35	0.0262	0.2202	−32%
14595	Metabolite - 3576	35	0.2107	0.4945	26%
14608	Metabolite - 3578	35	0.6691	0.7368	9%
14639	Metabolite - 3603	35	0.1163	0.4081	18%
14640	Metabolite - 3604	35	0.5838	0.7241	−13%
14672	Metabolite - 3615	35	0.6102	0.728	−10%
14715	Metabolite - 3653-possible-stachydrine-	35	0.473	0.6556	28%
14766	Metabolite - 3670	35	0.147	0.4503	−13%
14785	isobar-glycochenodeoxycholic acid-glycodeoxycholic acid	35	0.3213	0.5918	−25%
14787	Metabolite - 3698	35	0.7067	0.7385	8%
14837	Metabolite - 3707	35	0.1711	0.4624	76%
14961	Metabolite - 3752	35	0.639	0.73	−25%
15000	Metabolite - 3758	35	0.1668	0.4593	−19%
15017	Metabolite - 3761	35	0.8791	0.7596	3%
15032	Metabolite - 3765	35	0.0335	0.2531	−38%
15063	Metabolite - 3772	35	0.1466	0.4503	−11%
15113	Metabolite - 3783	35	0.4353	0.6413	12%
15122	glycerol	50	0.056	0.3133	−13%
15128	DL-homocysteine	35	0.728	0.7423	3%
15129	D-alanyl-D-alanine	35	0.0754	0.3472	−21%
15211	Metabolite - 3807	35	0.8721	0.7585	−1%
15220	Metabolite - 3813	35	0.1744	0.4672	−20%
15227	Metabolite - 3816	35	0.8542	0.7585	−3%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
15251	Metabolite - 3830	35	0.0126	0.1407	−36%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.7773	0.7448	−8%
15278	Metabolite - 3843	35	0.8645	0.7585	−1%
15319	DL-phenyllactic acid	35	0.0478	0.2816	−41%
15326	Metabolite - 3879	35	0.7977	0.7448	13%
15328	azelaic acid	35	0.2378	0.5309	−9%
15336	tartaric acid	35	0.0388	0.2538	−38%
15365	sn-Glycerol-3-phosphate	50	0.2692	0.5593	−8%
15389	Metabolite - 3900	35	0.0079	0.1061	−16%
15500	carnitine	35	0.344	0.6106	7%
15529	Metabolite - 3951	35	0.2451	0.5351	9%
15535	Metabolite - 3955	35	0.3382	0.6063	37%
15606	Metabolite - 3968	35	0.9659	0.7862	1%
15612	Metabolite - 3972	35	0.7724	0.7448	2%
15626	Metabolite - 3977	35	0.1527	0.4554	−10%
15677	3-methyl-L-histidine	35	0.5533	0.712	3%
15681	4-Guanidinobutanoic acid	35	0.3014	0.5825	15%
15683	4-methyl-2-oxopentanoate	50	0.0405	0.2538	−20%
15704	heptanedioic acid	35	0.1181	0.4081	51%
15744	N—N-dimethylarginine	35	0.1838	0.4682	−11%
15753	hippuric acid	35	0.3545	0.6113	−17%
15991	L-alpha-glycerophosphorylcholine	35	0.4761	0.6556	−16%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.586	0.7241	4%
16016	Metabolite - 3994	35	0.9895	0.7893	0%
16071	Metabolite - 4020	50	0.3655	0.6113	−6%
16091	Metabolite - 4031-possible-norlevorphenol-isobutylphendienamide-amprolium	35	0.1019	0.4004	−11%
16107	lysine	50	0.1647	0.4579	−14%
16137	Metabolite - 4078	35	0.7185	0.7423	−8%
16161	gamma-glutamyl-glutamic acid	35	0.5784	0.7241	−8%
16186	Metabolite - 4096-possible-gamma-glu-gly-leu-	35	0.9805	0.7893	1%
16226	Isobar-28-includes-L-threonine-L-allothreonine-L-homoserine-S-4-amino-2-hydroxybutyric acid	35	0.2869	0.569	11%
16231	Isobar-20-includes-fumaric acid-3-methyl-2-oxobutanoate	35	0.7914	0.7448	−5%
16232	Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.01	0.1225	38%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.1191	0.4081	−21%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.6445	0.73	8%
16237	Isobar-25-includes-L-gulono-1-4-lactone-glucono-gamma-lactone-	35	0.821	0.756	−5%
16241	Isobar-30-includes-maltotetraose-stachyose	35	0.2512	0.5443	−15%
16243	L-kynurenine	35	0.6009	0.7257	−5%
16244	Isobar-21-includes-gamma-aminobutyryl-L-histidine-L-anserine	35	0.1351	0.4326	36%
16246	Isobar-18-includes-D-fructose-1-phosphate-beta-D-fructose-6-phosphate	35	0.9657	0.7862	−1%

TABLE 8-continued

Plasma Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
16279	Isobar-36-includes-D-sorbitol-6-phosphate-mannitol-1-phosphate	35	0.0397	0.2538	−26%
16290	Metabolite - 4133	50	0.1945	0.4717	16%
16308	Metabolite - 4147	50	0.1066	0.4081	−21%
16330	Metabolite - 4163	35	0.866	0.7585	−3%
16337	Metabolite - 4167	35	0.4046	0.6338	−14%
16462	Metabolite - 4234	35	0.7831	0.7448	−4%
16471	Metabolite - 4238	35	0.7117	0.741	−8%
16508	Metabolite - 4272	50	0.939	0.7839	−1%
16621	Metabolite - 4355	50	0.9609	0.7862	−1%
16653	Metabolite - 4361	50	0.8571	0.7585	−3%
16666	Metabolite - 4365	50	0.6891	0.7368	7%
16824	iminodiacetic acid	50	0.0261	0.2202	−23%
16829	Metabolite - 4503	50	0.839	0.7585	−7%
16848	Metabolite - 4511	50	0.0959	0.3887	−23%
16952	Metabolite - 4593	50	0.7253	0.7423	−2%
17028	Metabolite - 4611	50	0.7939	0.7448	−2%
17328	Metabolite - 4768	50	0.414	0.6338	−17%
17330	Metabolite - 4769	50	0.8061	0.7493	3%
17359	Metabolite - 4791	50	0.9964	0.7893	0%
17388	Metabolite - 4795	50	0.6053	0.7257	10%
17614	Metabolite - 4966	50	0.866	0.7585	2%
17627	Metabolite - 4986	50	0.4496	0.6495	−13%
18118	Metabolite - 5346	50	0.2656	0.559	−11%
18146	Metabolite - 5366	50	0.0574	0.3133	−23%
18232	Metabolite - 5403	50	0.6472	0.73	4%
18316	Metabolite - 5437	50	0.0382	0.2538	−38%
18335	D-quinic acid	50	0.0437	0.2628	−48%
18349	DL-indole-3-lactic acid	50	0.0021	0.0633	−22%
18868	Metabolite - 5847	50	0.3783	0.6227	−18%
18926	Metabolite - 5906	50	0.4724	0.6556	−29%
18929	Metabolite - 5907	50	0.5093	0.673	−6%

Example 4

Distinguish Lower Grade from Higher Grade, Urine

[0128] Biomarkers were discovered by (1) analyzing urine samples from different groups of human subjects to determine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0129] The urine samples used for the analysis were from 53 control individuals with negative biopsies for prostate cancer, 43 individuals with lower grade prostate cancer (i.e. Gleason Score major=3) and 15 individuals with aggressive, high grade prostate cancer (i.e. Gleason Score major=4+). After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0130] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Lower Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Lower Grade Prostate cancer).

Biomarkers:

[0131] As listed below in Table 9, biomarkers were discovered that were differentially present between urine samples from subjects with lower grade prostate cancer and urine samples from Control subjects with negative prostate biopsies (i.e. not diagnosed with prostate cancer). Table 10 lists biomarkers that were discovered that were differentially present between urine samples from subjects with metastatic/high grade prostate cancer and urine samples from Control subjects with biopsy negative prostates (i.e. not diagnosed with prostate cancer). Table 11 lists biomarkers that were discovered that were differentially present between urine samples from subjects with metastatic/high grade prostate cancer and urine from subjects with lower grade prostate cancer.

[0132] Tables 9-11 include, for each listed biomarker, the p-value and q-value determined in the statistical analysis of the data concerning the biomarkers and an indication of the percentage difference in the lower grade prostate cancer mean level as compared to the control mean level (Table 9), the metastatic/high grade prostate cancer mean level as compared to the control mean level (Table 10), and the metastatic/high grade prostate cancer mean level as compared to the lower grade prostate cancer mean level (Table 11). The term "Isobar" as used in the tables indicates the compounds that could not be distinguished from each other on the analytical platform used in the analysis (i.e., the compounds in an isobar elute at nearly the same time and have similar (and sometimes exactly the same) quant ions, and thus cannot be distinguished). Library indicates the chemical library that was used to identify the compounds. The number 50 refers to the GC library and the number 35 refers to the LC library.

[0133] Biomarkers were discovered by (1) analyzing urine samples from different groups of human subjects to deter-

mine the levels of metabolites in the samples and then (2) statistically analyzing the results to determine those metabolites that were differentially present in the two groups.

[0134] The urine samples used for the analysis were from 53 control individuals with negative biopsies for prostate cancer, 43 individuals with lower grade prostate cancer (i.e. Gleason Score major=3) and 15 individuals with aggressive, high grade prostate cancer (i.e. Gleason Score major=4+). After the levels of metabolites were determined, the data was analyzed using univariate T-tests (i.e., Welch's T-test).

[0135] T-tests were used to determine differences in the mean levels of metabolites between two populations (i.e., Lower Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Control, Metastatic/High Grade Prostate cancer vs. Lower Grade Prostate cancer).

TABLE 9

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
53	glutamine	50	0.796	0.9846	5%
54	tryptophan	35	0.1502	0.9846	−15%
57	glutamic acid	50	0.855	0.9846	−3%
59	histidine	50	0.4545	0.9846	17%
60	leucine	50	0.7145	0.9846	8%
64	phenylalanine	35	0.6419	0.9846	−6%
418	guanine	50	0.9595	0.9875	1%
512	asparagine	50	0.4606	0.9846	−9%
513	creatinine	35	0.1826	0.9846	−10%
521	homogentisate	50	0.8571	0.9846	−5%
527	lactate	50	0.3716	0.9846	−9%
528	alpha-keto-glutarate	35	0.1009	0.9846	35%
531	3-hydroxy-3-methylglutarate	50	0.9687	0.9875	0%
541	4-hydroxyphenylacetate	50	0.4362	0.9846	25%
542	3-hydroxybutanoic acid	50	0.6851	0.9846	27%
554	adenine	50	0.2417	0.9846	23%
555	adenosine	35	0.9098	0.9875	2%
563	alpha-L-sorbopyranose	50	0.9777	0.9875	−1%
569	caffeine	35	0.4377	0.9846	21%
575	arabinose	50	0.5366	0.9846	10%
577	fructose	50	0.4858	0.9846	31%
581	glucose	50	0.3339	0.9846	−77%
587	gluconic acid	50	0.5172	0.9846	14%
594	niacinamide	35	0.8901	0.9875	1%
597	phosphoenolpyruvate	35	0.4537	0.9846	−20%
605	uracil	50	0.4138	0.9846	15%
607	urocanic acid	35	0.2858	0.9846	39%
608	vitamin-B6	35	0.1525	0.9846	112%
1101	3-methoxy-4-hydroxyphenylacetate	50	0.9705	0.9875	1%
1107	allantoin	50	0.6965	0.9846	6%
1125	isoleucine	50	0.4588	0.9846	−12%
1126	alanine	50	0.9256	0.9875	1%
1284	threonine	50	0.7919	0.9846	5%
1299	tyrosine	50	0.8374	0.9846	4%
1302	methionine	35	0.6757	0.9846	−6%
1303	malic acid	35	0.81	0.9846	6%
1366	trans-4-hydroxyproline	50	0.2618	0.9846	22%
1413	3-hydroxyphenylacetate	35	0.8047	0.9846	−4%
1417	kynurenic acid	50	0.9471	0.9875	−1%
1418	5-6-Dihydrothymine	35	0.9664	0.9875	−1%
1419	5-s-methyl-5-thioadenosine	35	0.2486	0.9846	−15%
1431	(p-Hydroxyphenyl)lactic acid	50	0.1211	0.9846	32%
1432	alphahydroxybenzeneacetic acid	35	0.8358	0.9846	−2%
1437	succinate	50	0.0633	0.9846	42%
1444	DL-pipecolic acid	35	0.9345	0.9875	−4%
1480	guanidineacetic acid	35	0.0371	0.9846	42%
1493	ornithine	50	0.2975	0.9846	54%
1494	5-oxoproline	50	0.4228	0.9846	14%
1498	N-6-trimethyl-l-lysine	35	0.2734	0.9846	18%
1505	orotic acid	50	0.2172	0.9846	26%
1508	pantothenic acid	35	0.9729	0.9875	−1%
1519	sucrose	50	0.3449	0.9846	95%
1557	3-methylglutaric acid	35	0.8338	0.9846	3%
1558	4-acetamidobutyric acid	35	0.3994	0.9846	−13%
1559	5-6-dihydrouracil	50	0.2764	0.9846	14%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
1560	L-methyldopa	35	0.3931	0.9846	19%
1564	citric acid	50	0.4898	0.9846	13%
1566	3-amino-isobutyrate	50	0.3393	0.9846	41%
1567	4-hydroxy-3-methoxymandelate	50	0.8926	0.9875	−3%
1568	4-hydroxymandelate	50	0.6452	0.9846	11%
1569	DL-beta-hydroxyphenylethylamine	35	0.4562	0.9846	16%
1574	histamine	35	0.892	0.9875	−3%
1580	noradrenaline	50	0.6485	0.9846	11%
1585	N-acetyl-L-alanine	35	0.5936	0.9846	−8%
1587	N-acetyl-L-leucine	35	0.7574	0.9846	5%
1591	N-acetyl-L-valine	35	0.2762	0.9846	34%
1592	N-acetylneuraminic acid	50	0.9603	0.9875	−1%
1598	N-tigloylglycine	35	0.434	0.9846	13%
1604	uric acid	35	0.8166	0.9846	1%
1640	ascorbic acid	50	0.5353	0.9846	113%
1648	serine	50	0.448	0.9846	10%
1649	valine	50	0.8355	0.9846	4%
1708	7-8-dihydrofolic acid	35	0.3057	0.9846	10%
1778	gamma-glu-cys	35	0.9805	0.9875	−1%
1827	riboflavine	35	0.3791	0.9846	29%
1860	3-nitro-L-tyrosine	35	0.3596	0.9846	26%
1868	cysteine	50	0.3622	0.9846	69%
1898	proline	50	0.806	0.9846	−5%
1899	quinolinic acid	50	0.8475	0.9846	3%
2078	pyrophosphate	50	0.3881	0.9846	44%
2092	catechol	35	0.9299	0.9875	3%
2132	citrulline	50	0.1077	0.9846	29%
2183	thymidine	35	0.6528	0.9846	−7%
2245	Metabolite - 294	35	0.1857	0.9846	32%
2342	serotonin	35	0.631	0.9846	6%
2734	gamma-L-glutamyl-L-tyrosine	35	0.1668	0.9846	−24%
2829	N-formyl-L-methionine	35	0.3164	0.9846	19%
2831	adenosine-3-5-cyclic-monophosphate	35	0.4814	0.9846	−8%
3127	hypoxanthine	35	0.8698	0.9875	3%
3138	pyridoxamine-phosphate	35	0.3482	0.9846	−9%
3147	xanthine	35	0.3736	0.9846	10%
3155	3-ureidopropionic acid	35	0.3809	0.9846	17%
4966	xylitol	50	0.3043	0.9846	38%
5493	Metabolite - 1059	35	0.7607	0.9846	4%
5495	Metabolite - 1060	35	0.0016	0.6911	−17%
5514	Metabolite - 1081	35	0.904	0.9875	0%
5538	Metabolite - 1101	35	0.5358	0.9846	−21%
5664	Metabolite - 1101	35	0.506	0.9846	25%
5687	Metabolite - 1110	35	0.7134	0.9846	−6%
5697	acetylcarnitine-	35	0.6634	0.9846	12%
5702	Metabolite - 1114	35	0.4207	0.9846	−23%
5711	2-hydroxybutyric acid	35	0.7116	0.9846	7%
5719	Metabolite - 1122	35	0.5481	0.9846	11%
5727	Metabolite - 1126	35	0.541	0.9846	10%
5797	Metabolite - 1186	35	0.3318	0.9846	−14%
6137	Metabolite - 1212	35	0.2597	0.9846	−50%
6147	Metabolite - 1216	35	0.5806	0.9846	4%
6238	normetanephrine	50	0.8045	0.9846	−3%
6253	Metabolite - 1283	35	0.0674	0.9846	−25%
6278	Metabolite - 1289	35	0.7974	0.9846	4%
6329	urea	50	0.903	0.9875	2%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.4176	0.9846	18%
6398	Metabolite - 1335	35	0.4128	0.9846	12%
6405	Metabolite - 1338	35	0.741	0.9846	−6%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.4637	0.9846	10%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
6421	Metabolite - 1345	35	0.5336	0.9846	20%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.5691	0.9846	10%
6443	Metabolite - 1351	35	0.3894	0.9846	23%
6477	Metabolite - 1364	35	0.3757	0.9846	167%
6486	Metabolite - 1368	35	0.5104	0.9846	−22%
6493	salicyluric acid	35	0.2953	0.9846	888%
6528	Metabolite - 1383-possible-salicyluric-glucuronide	35	0.2172	0.9846	287%
6760	Metabolite - 1455	35	0.0407	0.9846	−22%
6764	Metabolite - 1459	35	0.1583	0.9846	36%
6777	Metabolite - 1463	35	0.172	0.9846	161%
6787	Metabolite - 1465	35	0.848	0.9846	−3%
6847	Metabolite - 1496	35	0.2291	0.9846	24%
6852	Metabolite - 1498	35	0.6978	0.9846	13%
6987	Metabolite - 1573	35	0.1323	0.9846	18%
7132	Metabolite - 1667	35	0.3324	0.9846	256%
7175	Metabolite - 1655	35	0.3706	0.9846	14%
7177	Metabolite - 1656	35	0.0404	0.9846	68%
7272	Metabolite - 1679	35	0.4554	0.9846	−10%
7286	Metabolite - 1682	35	0.363	0.9846	15%
7359	n-acetyl-L-aspartic acid	35	0.7265	0.9846	−6%
7639	oxalic acid	35	0.842	0.9846	2%
7650	Metabolite - 1834	35	0.6964	0.9846	−16%
7660	Metabolite - 1839	35	0.9696	0.9875	−1%
7672	Metabolite - 1843	35	0.5216	0.9846	−6%
7933	Metabolite - 1911	35	0.219	0.9846	41%
8176	Metabolite - 1974	35	0.4332	0.9846	20%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.0901	0.9846	96%
8210	Metabolite - 1981	35	0.7764	0.9846	5%
8336	Metabolite - 2005	35	0.3343	0.9846	23%
8644	Metabolite - 2051	35	0.0878	0.9846	18%
8677	Metabolite - 2056	35	0.3734	0.9846	−12%
9007	Metabolite - 2108	35	0.2858	0.9846	−44%
9038	Metabolite - 2118	35	0.5665	0.9846	−7%
9113	Metabolite - 2133	35	0.1426	0.9846	−18%
9165	Metabolite - 2150	35	0.9275	0.9875	1%
9333	Metabolite - 2174	35	0.4734	0.9846	13%
9334	Metabolite - 2175	35	0.8327	0.9846	13%
9458	Metabolite - 2181	35	0.8365	0.9846	−3%
10058	Metabolite - 2242	35	0.3634	0.9846	427%
10087	Metabolite - 2249	35	0.3102	0.9846	−22%
10122	Metabolite - 2254	35	0.4777	0.9846	−40%
10136	Metabolite - 2034	35	0.8375	0.9846	−5%
10156	Metabolite - 2259	35	0.836	0.9846	−7%
10240	4-acetominophen-sulfate	35	0.2026	0.9846	34%
10245	Metabolite - 2269-	35	0.8222	0.9846	−2%
10247	Metabolite - 2270	35	0.6261	0.9846	15%
10252	Metabolite - 2271	35	0.2147	0.9846	30%
10286	Metabolite - 2272	35	0.4099	0.9846	−34%
10309	Metabolite - 2277	35	0.3674	0.9846	−12%
10347	Metabolite - 2285	35	0.8582	0.9846	4%
10407	Metabolite - 2059	35	0.663	0.9846	−6%
10424	Metabolite - 2292	35	0.1432	0.9846	30%
10433	Metabolite - 2293-possible-O-desmethylvenlafaxine-glucuronide	35	0.3141	0.9846	1403%
10490	Metabolite - 2319	35	0.83	0.9846	−4%
10526	Metabolite - 2323	35	0.8463	0.9846	4%
10544	Metabolite - 2329	35	0.9805	0.9875	1%
10555	Metabolite - 2348	35	0.2902	0.9846	65%
10570	Metabolite - 2366	35	0.1258	0.9846	−37%
10629	Metabolite - 2386	35	0.7455	0.9846	−4%
10644	Metabolite - 2387	35	0.3475	0.9846	−24%
10667	Metabolite - 2389	35	0.2017	0.9846	22%
10672	Metabolite - 2390	35	0.9346	0.9875	1%
10737	Isobar-1-includes-mannose-fructose-glucose-	35	0.4849	0.9846	−26%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
	galactose-alpha-L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone				
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.356	0.9846	−61%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.986	0.9883	0%
10746	Isobar-6-includes-valine-betaine	35	0.8873	0.9875	4%
10785	Metabolite - 2506	35	0.6703	0.9846	7%
10825	Metabolite - 2546	35	0.3625	0.9846	13%
10872	Metabolite - 2550	35	0.5812	0.9846	−11%
10906	Metabolite - 2557-possible-Pantoprazole-metabolite	35	0.0411	0.9846	64%
11053	Metabolite - 2567	35	0.7296	0.9846	5%
11085	Metabolite - 2588	35	0.2272	0.9846	25%
11110	Metabolite - 2591	35	0.4451	0.9846	17%
11173	Metabolite - 2607	35	0.2724	0.9846	42%
11219	Metabolite - 2686	35	0.4501	0.9846	13%
11264	Metabolite - 2698	35	0.6617	0.9846	27%
11271	Metabolite - 2700	35	0.1367	0.9846	48%
11292	Metabolite - 2703	35	0.6289	0.9846	−6%
11299	Metabolite - 2706	35	0.2913	0.9846	−22%
11390	Metabolite - 2726	35	0.3521	0.9846	−14%
11411	Metabolite - 2746	35	0.2543	0.9846	−21%
11438	phosphate	50	0.5453	0.9846	11%
11484	Metabolite - 2752	35	0.245	0.9846	18%
11661	Metabolite - 2781	35	0.7701	0.9846	−4%
11777	glycine	50	0.5674	0.9846	10%
11808	Metabolite - 2807	35	0.0487	0.9846	62%
11851	Metabolite - 2811	35	0.0085	0.9846	161%
12025	cis-aconitic acid	50	0.3727	0.9846	58%
12055	galactose	50	0.6975	0.9846	11%
12102	o-phosphoethanolamine	50	0.6267	0.9846	−13%
12104	Metabolite - 2852	35	0.5159	0.9846	29%
12109	Metabolite - 2853	35	0.9627	0.9875	1%
12129	beta-hydroxyisovaleric acid	50	0.8271	0.9846	4%
12300	Metabolite - 2868	35	0.7519	0.9846	−16%
12358	(1'R,1'S)_biopterin	35	0.2306	0.9846	26%
12426	Metabolite - 2416	35	0.4534	0.9846	20%
12463	Metabolite - 2893-possible-demethylated-Rosiglitazone	35	0.4566	0.9846	18%
12474	Metabolite - 2897	35	0.2372	0.9846	−17%
12593	Metabolite - 2973	50	0.0377	0.9846	−25%
12641	meso-erythritol	50	0.9483	0.9875	−2%
12644	Metabolite - 3016	50	0.3011	0.9846	−8%
12648	Metabolite - 3020	50	0.8127	0.9846	5%
12666	Metabolite - 3033	50	0.8413	0.9846	3%
12711	Metabolite - 3053	35	0.5017	0.9846	24%
12720	Metabolite - 3056	35	0.5412	0.9846	8%
12765	inositol	50	0.4102	0.9846	−27%
12770	Metabolite - 3090	50	0.1121	0.9846	−11%
12771	Metabolite - 3091	50	0.2399	0.9846	−25%
12795	Metabolite - 3113	50	0.3928	0.9846	−14%
12856	Metabolite - 3123	35	0.4327	0.9846	17%
12902	Metabolite - 3127	35	0.765	0.9846	−4%
12904	Metabolite - 2457	35	0.0497	0.9846	66%
12924	Metabolite - 3131	35	0.7354	0.9846	−7%
12938	Metabolite - 2459	35	0.9267	0.9875	−1%
13018	Metabolite - 3138	35	0.9748	0.9875	0%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
13136	Metabolite - 3163-possible-methylcytidine-benserazide-Pyr-Gln-OH-or-glycerophosphocholine-	35	0.9502	0.9875	1%
13153	Metabolite - 3169	35	0.6836	0.9846	13%
13179	Metabolite - 3176	35	0.8382	0.9846	−13%
13214	Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine	35	0.6928	0.9846	8%
13217	Metabolite - 3184	35	0.3549	0.9846	10%
13249	Metabolite - 3215	35	0.8582	0.9846	3%
13251	Metabolite - 3216	35	0.3024	0.9846	−7%
13265	Metabolite - 3221	35	0.9343	0.9875	−2%
13297	Metabolite - 3231	35	0.9212	0.9875	−2%
13318	DL-indole-3-lactic acid	35	0.4237	0.9846	−19%
13356	Metabolite - 3246-possible-Ala-GLy-glycyl-sarcosine-or-ureido-butyric acid	35	0.5345	0.9846	−8%
13459	Metabolite - 3305	35	0.483	0.9846	16%
13484	Metabolite - 3309	35	0.8589	0.9846	3%
13493	Metabolite - 3311-	35	0.1888	0.9846	56%
13505	Metabolite - 3313	35	0.5469	0.9846	−13%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.6718	0.9846	13%
13545	Metabolite - 3322	35	0.393	0.9846	−14%
13589	Metabolite - 3327	35	0.2554	0.9846	26%
13594	Metabolite - 3329	35	0.9464	0.9875	−2%
13704	Metabolite - 3355	35	0.2556	0.9846	20%
13744	Metabolite - 3364	35	0.2659	0.9846	19%
13775	Metabolite - 3370	35	0.5874	0.9846	12%
13791	Metabolite - 3373	35	0.985	0.9883	0%
13803	Metabolite - 3377	35	0.5535	0.9846	−22%
13817	Metabolite - 3380	35	0.3112	0.9846	−11%
13820	beta-nicotinamide-mononucleotide	35	0.8355	0.9846	4%
13847	Metabolite - 3387	35	0.7957	0.9846	4%
13904	Metabolite - 3402	35	0.3187	0.9846	71%
13968	Metabolite - 3409	35	0.3858	0.9846	18%
14036	Metabolite - 3427	35	0.7015	0.9846	8%
14066	Metabolite - 3433	35	0.7142	0.9846	−4%
14084	Metabolite - 3436	35	0.5508	0.9846	10%
14115	Metabolite - 3440	35	0.3104	0.9846	−64%
14125	Metabolite - 3443	35	0.5809	0.9846	11%
14170	Metabolite - 3457	35	0.6752	0.9846	12%
14220	Metabolite - 3470	35	0.8918	0.9875	4%
14249	Metabolite - 3476	35	0.0695	0.9846	82%
14368	Metabolite - 3489	35	0.3569	0.9846	−27%
14406	Metabolite - 3493	35	0.818	0.9846	3%
14453	Metabolite - 3507	35	0.5637	0.9846	14%
14471	Metabolite - 3516	35	0.2008	0.9846	34%
14506	Metabolite - 3543	35	0.5679	0.9846	−18%
14539	Metabolite - 3564	35	0.1262	0.9846	−38%
14595	Metabolite - 3576	35	0.4931	0.9846	9%
14640	Metabolite - 3604	35	0.1561	0.9846	20%
14641	Metabolite - 3605	35	0.1604	0.9846	44%
14731	Metabolite - 3659	35	0.4077	0.9846	18%
14732	Metabolite - 3660	35	0.2255	0.9846	31%
14733	Metabolite - 3661	35	0.7777	0.9846	−9%
14759	Metabolite - 3667	35	0.2647	0.9846	19%
14762	Metabolite - 3668	35	0.57	0.9846	−5%
14766	Metabolite - 3670	35	0.5103	0.9846	12%
14769	Metabolite - 3691	35	0.6776	0.9846	−8%
14808	Metabolite - 3701	35	0.0336	0.9846	−31%
14835	Metabolite - 3706	35	0.9101	0.9875	2%
14840	Metabolite - 3708	35	0.8511	0.9846	−6%
14907	Metabolite - 3734	35	0.3113	0.9846	16%
14983	Metabolite - 3754	35	0.9005	0.9875	−2%
14984	Metabolite - 3755	35	0.3521	0.9846	154%
15017	Metabolite - 3761	35	0.1689	0.9846	21%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
15057	Metabolite - 3771	35	0.1457	0.9846	52%
15064	Metabolite - 3773	35	0.4225	0.9846	−10%
15096	N-acetyl-D-glucosamine	50	0.612	0.9846	10%
15121	Metabolite - 3786	35	0.3986	0.9846	20%
15124	porphobilinogen	35	0.8882	0.9875	2%
15125	(2-Aminoethyl)phosphonate	35	0.1453	0.9846	14%
15128	DL-homocysteine	35	0.0781	0.9846	46%
15129	D-alanyl-D-alanine	35	0.9606	0.9875	1%
15130	diaminopimelic acid	35	0.4317	0.9846	−9%
15131	dethiobiotin	35	0.7544	0.9846	−6%
15187	Metabolite - 3800	35	0.7143	0.9846	−8%
15197	Metabolite - 3802	35	0.701	0.9846	8%
15201	Metabolite - 3803	35	0.3018	0.9846	16%
15202	Metabolite - 3804	35	0.213	0.9846	−22%
15203	Metabolite - 3805	35	0.9354	0.9875	−2%
15207	Metabolite - 3806	35	0.1744	0.9846	−33%
15211	Metabolite - 3807	35	0.8708	0.9875	2%
15220	Metabolite - 3813	35	0.3635	0.9846	17%
15228	Metabolite - 3817	35	0.5239	0.9846	−12%
15240	Metabolite - 3824	35	0.8028	0.9846	−7%
15249	Metabolite - 3828	35	0.8756	0.9875	3%
15251	Metabolite - 3830	35	0.0975	0.9846	39%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.2712	0.9846	−41%
15258	Metabolite - 3834-Peptide	35	0.4949	0.9846	18%
15275	Metabolite - 3840	35	0.6594	0.9846	5%
15276	Metabolite - 3841	35	0.3623	0.9846	58%
15278	Metabolite - 3843	35	0.8581	0.9846	−4%
15284	Metabolite - 3847	35	0.9705	0.9875	0%
15294	Metabolite - 3855	35	0.8089	0.9846	5%
15312	Metabolite - 3873	35	0.609	0.9846	−8%
15315	Metabolite - 3876	35	0.379	0.9846	29%
15324	Metabolite - 3878	35	0.3307	0.9846	−18%
15326	Metabolite - 3879	35	0.9133	0.9875	−3%
15328	azelaic acid	35	0.1572	0.9846	−33%
15335	mannitol	50	0.123	0.9846	50%
15336	tartaric acid	35	0.2935	0.9846	−26%
15356	Metabolite - 3886	35	0.5807	0.9846	8%
15359	Metabolite - 3887	35	0.7867	0.9846	−5%
15365	sn-Glycerol-3-phosphate	50	0.8503	0.9846	−7%
15374	Metabolite - 3893	35	0.8837	0.9875	2%
15382	Metabolite - 3898	35	0.6325	0.9846	4%
15410	Metabolite - 3908	35	0.5194	0.9846	10%
15411	Metabolite - 3909	35	0.6385	0.9846	−23%
15418	Metabolite - 3911	35	0.4593	0.9846	8%
15496	agmatine	35	0.0364	0.9846	34%
15500	carnitine	35	0.7459	0.9846	10%
15529	Metabolite - 3951	35	0.9957	0.9957	0%
15532	Metabolite - 3952	35	0.4244	0.9846	−16%
15535	Metabolite - 3955	35	0.9603	0.9875	1%
15541	Metabolite - 3957	35	0.8287	0.9846	−3%
15599	Metabolite - 3963	35	0.3146	0.9846	24%
15610	Metabolite - 3970	35	0.4461	0.9846	17%
15620	Metabolite - 3973	35	0.3553	0.9846	44%
15626	Metabolite - 3977	35	0.1456	0.9846	−35%
15636	Metabolite - 3981	35	0.5962	0.9846	−16%
15641	Metabolite - 3986	35	0.6453	0.9846	−6%
15650	1-methyladenosine	35	0.8651	0.9875	−2%
15667	2-isopropylmalic acid	50	0.6338	0.9846	−24%
15676	3-methyl-2-oxovaleric acid	35	0.4947	0.9846	16%
15677	3-methyl-L-histidine	35	0.046	0.9846	−23%
15679	xanthurenic acid	50	0.5776	0.9846	14%
15681	4-Guanidinobutanoic acid	35	0.8135	0.9846	4%
15704	heptanedioic acid	35	0.7689	0.9846	−3%
15716	L-beta-imidazolelactic acid	50	0.5938	0.9846	18%
15730	suberic acid	35	0.2788	0.9846	−13%
15737	hydroxyacetic acid	50	0.5729	0.9846	−9%
15743	N-N-dimethylarginine	35	0.7457	0.9846	4%
15753	hippuric acid	35	0.4325	0.9846	14%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
15778	benzoic acid	35	0.1887	0.9846	63%
15804	maltose	50	0.428	0.9846	64%
15835	L-xylose	50	0.7767	0.9846	10%
15948	S-adenosyl-l-homocysteine	35	0.6109	0.9846	−11%
15964	D-arabitol	50	0.9713	0.9875	1%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.1682	0.9846	16%
16016	Metabolite - 3994	35	0.1703	0.9846	−24%
16034	Metabolite - 4002	50	0.1968	0.9846	30%
16071	Metabolite - 4020	50	0.6192	0.9846	8%
16082	Metabolite - 4027	50	0.7798	0.9846	5%
16107	lysine	50	0.2773	0.9846	145%
16175	Metabolite - 4092	35	0.4841	0.9846	−13%
16197	Metabolite - 4112	35	0.8282	0.9846	4%
16217	Metabolite - 4116	35	0.8574	0.9846	−6%
16230	Isobar-29-includes-R-S-hydroorotic acid-5-6-dihydroorotic acid	35	0.0326	0.9846	114%
16232	Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.7984	0.9846	5%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.7037	0.9846	−8%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.1465	0.9846	66%
16243	L-kynurenine	35	0.5787	0.9846	−8%
16276	Isobar-38-includes-N-acetyl-L-methionine-5-hydroxy-1H-indole-3-acetic acid	35	0.4495	0.9846	19%
16278	Isobar-35-includes-D-arabinose-5-phosphate-D-ribulose-5-phosphate-alpha-D-ribose-5-phosphate	35	0.1346	0.9846	20%
16290	Metabolite - 4133	50	0.4411	0.9846	35%
16337	Metabolite - 4167	35	0.633	0.9846	12%
16338	Metabolite - 4168	35	0.6584	0.9846	20%
16457	Metabolite - 4233	35	0.4705	0.9846	21%
16462	Metabolite - 4234	35	0.1194	0.9846	57%
16496	Metabolite - 4251	50	0.1706	0.9846	−16%
16506	Metabolite - 4271	50	0.2282	0.9846	31%
16816	Metabolite - 4494	50	0.938	0.9875	−1%
16818	Metabolite - 4495	50	0.3478	0.9846	18%
16819	Metabolite - 4496	50	0.4825	0.9846	6%
16821	Metabolite - 4498	50	0.2269	0.9846	34%
16822	Metabolite - 4499	50	0.5555	0.9846	11%
16823	Metabolite - 4500	50	0.3974	0.9846	63%
16824	iminodiacetic acid	50	0.1445	0.9846	−23%
16827	Metabolite - 4502	50	0.6363	0.9846	−1%
16829	Metabolite - 4503	50	0.2869	0.9846	23%
16831	Metabolite - 4504	50	0.7348	0.9846	6%
16834	Metabolite - 4505	50	0.6099	0.9846	15%
16837	Metabolite - 4507	50	0.2767	0.9846	26%
16848	Metabolite - 4511	50	0.3715	0.9846	33%
16851	Metabolite - 4512	50	0.1504	0.9846	59%
16859	Metabolite - 4516	50	0.6517	0.9846	8%
16860	Metabolite - 4517	50	0.7046	0.9846	10%
16861	Metabolite - 4518	50	0.9422	0.9875	1%
16862	Metabolite - 4519	50	0.7079	0.9846	−11%
16863	Metabolite - 4520	50	0.9455	0.9875	−2%
16864	Metabolite - 4521	50	0.8773	0.9875	−5%
16865	Metabolite - 4522	50	0.6761	0.9846	7%

TABLE 9-continued

Urine Metabolite Biomarkers to distinguish Non-cancer vs. Lower Grade PCA

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
16866	Metabolite - 4523	50	0.7153	0.9846	6%
16867	Metabolite - 4524	50	0.2787	0.9846	−31%
16952	Metabolite - 4593	50	0.2049	0.9846	18%
16959	Metabolite - 4595	50	0.7468	0.9846	3%
17028	Metabolite - 4611	50	0.872	0.9875	3%
17050	Metabolite - 4618	50	0.2699	0.9846	72%
17064	Metabolite - 4624	50	0.3903	0.9846	13%
17072	Metabolite - 4628	50	0.2516	0.9846	81%
17074	Metabolite - 4629	50	0.6487	0.9846	9%
17080	Metabolite - 4632	50	0.8257	0.9846	7%
17083	Metabolite - 4634	50	0.7731	0.9846	6%
17084	Metabolite - 4635	50	0.3361	0.9846	134%
17085	Metabolite - 4636	50	0.5178	0.9846	18%
17086	Metabolite - 4637	50	0.834	0.9846	7%
17087	Metabolite - 4638	50	0.2699	0.9846	44%
17088	Metabolite - 4639	50	0.3228	0.9846	32%

TABLE 10

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
53	glutamine	50	0.2634	0.2182	39%
54	tryptophan	35	0.1769	0.1876	25%
57	glutamic acid	50	0.3771	0.2666	18%
59	histidine	50	0.1191	0.1705	61%
60	leucine	50	0.0862	0.1546	58%
64	phenylalanine	35	0.0753	0.1546	33%
418	guanine	50	0.0722	0.1546	56%
512	asparagine	50	0.1886	0.1931	45%
513	creatinine	35	0.1327	0.1736	21%
521	homogentisate	50	0.1389	0.1744	59%
527	lactate	50	0.4598	0.2867	−11%
528	alpha-keto-glutarate	35	0.7074	0.3708	12%
531	3-hydroxy-3-methylglutarate	50	0.378	0.2666	24%
541	4-hydroxyphenylacetate	50	0.2908	0.2279	32%
542	3-hydroxybutanoic acid	50	0.1308	0.1723	−48%
554	adenine	50	0.0464	0.1546	55%
555	adenosine	35	0.0068	0.1546	84%
563	alpha-L-sorbopyranose	50	0.2249	0.2026	92%
569	caffeine	35	0.0527	0.1546	−43%
575	arabinose	50	0.0227	0.1546	88%
577	fructose	50	0.4822	0.2929	41%
581	glucose	50	0.4136	0.2782	−65%
587	gluconic acid	50	0.0697	0.1546	86%
594	niacinamide	35	0.6385	0.3496	−8%
597	phosphoenolpyruvate	35	0.6788	0.3622	20%
605	uracil	50	0.0194	0.1546	55%
607	urocanic acid	35	0.0836	0.1546	54%
608	vitamin-B6	35	0.0887	0.1575	79%
1101	3-methoxy-4-hydroxyphenylacetate	50	0.0139	0.1546	57%
1107	allantoin	50	0.0457	0.1546	83%
1125	isoleucine	50	0.3971	0.272	16%
1126	alanine	50	0.2068	0.1964	36%
1284	threonine	50	0.0516	0.1546	45%
1299	tyrosine	50	0.0503	0.1546	45%
1302	methionine	35	0.0169	0.1546	45%
1303	malic acid	35	0.5118	0.3041	18%
1366	trans-4-hydroxyproline	50	0.229	0.2026	32%
1413	3-hydroxyphenylacetate	35	0.671	0.36	12%
1417	kynurenic acid	50	0.172	0.1874	66%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
1418	5-6-Dihydrothymine	35	0.0782	0.1546	44%
1419	5-s-methyl-5-thioadenosine	35	0.9786	0.4388	0%
1431	(p-Hydroxyphenyl)lactic acid	50	0.2483	0.2111	87%
1432	alphahydroxybenzeneacetic acid	35	0.7995	0.3952	4%
1437	succinate	50	0.0769	0.1546	62%
1444	DL-pipecolic acid	35	0.728	0.3756	13%
1480	guanidineacetic acid	35	0.0049	0.1546	184%
1493	ornithine	50	0.062	0.1546	52%
1494	5-oxoproline	50	0.1124	0.1698	42%
1498	N-6-trimethyl-1-lysine	35	0.0433	0.1546	62%
1505	orotic acid	50	0.0559	0.1546	74%
1508	pantothenic acid	35	0.3273	0.2426	56%
1519	sucrose	50	0.102	0.1641	95%
1557	3-methylglutaric acid	35	0.6501	0.3538	−9%
1558	4-acetamidobutyric acid	35	0.1142	0.1698	39%
1559	5-6-dihydrouracil	50	0.0325	0.1546	44%
1560	L-methyldopa	35	0.2445	0.2093	36%
1564	citric acid	50	0.0304	0.1546	62%
1566	3-amino-isobutyrate	50	0.1884	0.1931	64%
1567	4-hydroxy-3-methoxymandelate	50	0.0913	0.1595	48%
1568	4-hydroxymandelate	50	0.1129	0.1698	62%
1569	DL-beta-hydroxyphenylethylamine	35	0.1404	0.1744	36%
1574	histamine	35	0.0267	0.1546	57%
1580	noradrenaline	50	0.1426	0.1744	67%
1585	N-acetyl-L-alanine	35	0.8018	0.3953	5%
1587	N-acetyl-L-leucine	35	0.1032	0.1641	49%
1591	N-acetyl-L-valine	35	0.0682	0.1546	101%
1592	N-acetylneuraminic acid	50	0.035	0.1546	46%
1598	N-tigloylglycine	35	0.0515	0.1546	46%
1604	uric acid	35	0.243	0.2093	6%
1640	ascorbic acid	50	0.3011	0.2324	228%
1648	serine	50	0.016	0.1546	60%
1649	valine	50	0.0849	0.1546	31%
1708	7-8-dihydrofolic acid	35	0.0656	0.1546	36%
1778	gamma-glu-cys	35	0.4751	0.2914	45%
1827	riboflavine	35	0.1656	0.1865	264%
1860	3-nitro-L-tyrosine	35	0.4409	0.2848	25%
1868	cysteine	50	0.1193	0.1705	108%
1898	proline	50	0.3203	0.2413	39%
1899	quinolinic acid	50	0.0925	0.1595	44%
2078	pyrophosphate	50	0.0839	0.1546	107%
2092	catechol	35	0.0165	0.1546	151%
2132	citrulline	50	0.0064	0.1546	73%
2183	thymidine	35	0.8414	0.4032	−4%
2245	Metabolite - 294	35	0.1285	0.1705	89%
2342	serotonin	35	0.0389	0.1546	41%
2734	gamma-L-glutamyl-L-tyrosine	35	0.3139	0.2394	26%
2829	N-formyl-L-methionine	35	0.1969	0.195	46%
2831	adenosine-3-5-cyclic-monophosphate	35	0.0306	0.1546	32%
3127	hypoxanthine	35	0.1978	0.195	56%
3138	pyridoxamine-phosphate	35	0.752	0.3841	−5%
3147	xanthine	35	0.148	0.1787	77%
3155	3-ureidopropionic acid	35	0.069	0.1546	96%
4966	xylitol	50	0.7869	0.3926	−5%
5493	Metabolite - 1059	35	0.9512	0.4306	1%
5495	Metabolite - 1060	35	0.1027	0.1641	−19%
5514	Metabolite - 1081	35	0.008	0.1546	11%
5538	Metabolite - 1101	35	0.6862	0.363	26%
5664	Metabolite - 1101	35	0.7561	0.3849	6%
5687	Metabolite - 1110	35	0.4575	0.2863	16%
5697	acetylcarnitine-	35	0.9057	0.4171	4%
5702	Metabolite - 1114	35	0.477	0.2917	27%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
5711	2-hydroxybutyric acid	35	0.9468	0.4297	2%
5719	Metabolite - 1122	35	0.1964	0.195	24%
5727	Metabolite - 1126	35	0.7746	0.3891	8%
5797	Metabolite - 1186	35	0.6024	0.3354	12%
6137	Metabolite - 1212	35	0.479	0.2919	−32%
6147	Metabolite - 1216	35	0.7457	0.3827	−5%
6238	normetanephrine	50	0.2267	0.2026	13%
6253	Metabolite - 1283	35	0.9728	0.4373	1%
6278	Metabolite - 1289	35	0.1762	0.1876	17%
6329	urea	50	0.1643	0.1865	27%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.0787	0.1546	84%
6398	Metabolite - 1335	35	0.1991	0.195	25%
6405	Metabolite - 1338	35	0.3289	0.2426	−21%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.0596	0.1546	40%
6421	Metabolite - 1345	35	0.1218	0.1705	105%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.0435	0.1546	54%
6443	Metabolite - 1351	35	0.5184	0.3061	26%
6477	Metabolite - 1364	35	0.8749	0.413	−6%
6486	Metabolite - 1368	35	0.7964	0.3952	13%
6493	salicyluric acid	35	0.3168	0.2401	243%
6528	Metabolite - 1383-possible-salicyluric-glucuronide	35	0.1243	0.1705	97%
6760	Metabolite - 1455	35	0.1951	0.195	23%
6764	Metabolite - 1459	35	0.386	0.2688	54%
6777	Metabolite - 1463	35	0.3817	0.2674	79%
6787	Metabolite - 1465	35	0.3552	0.2553	16%
6847	Metabolite - 1496	35	0.4314	0.2831	43%
6852	Metabolite - 1498	35	0.2973	0.2314	67%
6987	Metabolite - 1573	35	0.0136	0.1546	38%
7132	Metabolite - 1667	35	0.9013	0.4171	−3%
7175	Metabolite - 1655	35	0.0662	0.1546	103%
7177	Metabolite - 1656	35	0.0932	0.1595	106%
7272	Metabolite - 1679	35	0.2252	0.2026	28%
7286	Metabolite - 1682	35	0.4881	0.2937	19%
7359	n-acetyl-L-aspartic acid	35	0.0973	0.1641	56%
7639	oxalic acid	35	0.1037	0.1641	28%
7650	Metabolite - 1834	35	0.3481	0.2512	−34%
7660	Metabolite - 1839	35	0.9015	0.4171	−4%
7672	Metabolite - 1843	35	0.2013	0.1955	21%
7933	Metabolite - 1911	35	0.0604	0.1546	100%
8176	Metabolite - 1974	35	0.0348	0.1546	71%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.0609	0.1546	77%
8210	Metabolite - 1981	35	0.7647	0.3861	6%
8336	Metabolite - 2005	35	0.6452	0.3522	10%
8644	Metabolite - 2051	35	0.041	0.1546	27%
8677	Metabolite - 2056	35	0.5849	0.3294	9%
9007	Metabolite - 2108	35	0.4471	0.2848	−34%
9038	Metabolite - 2118	35	0.3323	0.2426	20%
9113	Metabolite - 2133	35	0.6941	0.3651	8%
9165	Metabolite - 2150	35	0.3174	0.2401	30%
9333	Metabolite - 2174	35	0.2248	0.2026	29%
9334	Metabolite - 2175	35	0.2046	0.1961	95%
9458	Metabolite - 2181	35	0.0134	0.1546	52%
10058	Metabolite - 2242	35	0.0104	0.1546	−55%
10087	Metabolite - 2249	35	0.4419	0.2848	39%
10122	Metabolite - 2254	35	0.4675	0.2896	−41%
10136	Metabolite - 2034	35	0.4115	0.2778	35%
10156	Metabolite - 2259	35	0.3889	0.2693	71%
10240	4-acetominophen-sulfate	35	0.1068	0.1675	54%
10245	Metabolite - 2269-	35	0.8384	0.4028	3%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
10247	Metabolite - 2270	35	0.2488	0.2111	−42%
10252	Metabolite - 2271	35	0.0323	0.1546	79%
10286	Metabolite - 2272	35	0.7248	0.375	19%
10309	Metabolite - 2277	35	0.0567	0.1546	39%
10347	Metabolite - 2285	35	0.0852	0.1546	50%
10407	Metabolite - 2059	35	0.4659	0.2896	14%
10424	Metabolite - 2292	35	0.3819	0.2674	−17%
10433	Metabolite - 2293-possible-O-desmethylvenlafaxine-glucuronide	35	0.1642	0.1865	35%
10490	Metabolite - 2319	35	0.8212	0.3991	4%
10526	Metabolite - 2323	35	0.713	0.372	11%
10544	Metabolite - 2329	35	0.4846	0.2934	12%
10555	Metabolite - 2348	35	0.8929	0.4163	5%
10570	Metabolite - 2366	35	0.2076	0.1964	−29%
10629	Metabolite - 2386	35	0.4286	0.2831	14%
10644	Metabolite - 2387	35	0.8787	0.4132	6%
10667	Metabolite - 2389	35	0.7983	0.3952	−5%
10672	Metabolite - 2390	35	0.0662	0.1546	70%
10737	Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone	35	0.4454	0.2848	−28%
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.3313	0.2426	−65%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-xylose-DL-lyxose-D-xylulose	35	0.0302	0.1546	48%
10746	Isobar-6-includes-valine-betaine	35	0.3058	0.2341	19%
10785	Metabolite - 2506	35	0.6343	0.3485	11%
10825	Metabolite - 2546	35	0.119	0.1705	29%
10872	Metabolite - 2550	35	0.1693	0.1865	77%
10906	Metabolite - 2557-possible-Pantoprazole-metabolite	35	0.1732	0.1874	51%
11053	Metabolite - 2567	35	0.0188	0.1546	49%
11085	Metabolite - 2588	35	0.2532	0.2129	105%
11110	Metabolite - 2591	35	0.2696	0.2198	−24%
11173	Metabolite - 2607	35	0.2777	0.2216	59%
11219	Metabolite - 2686	35	0.4301	0.2831	18%
11264	Metabolite - 2698	35	0.5771	0.3274	−27%
11271	Metabolite - 2700	35	0.116	0.1705	91%
11292	Metabolite - 2703	35	0.2307	0.2026	17%
11299	Metabolite - 2706	35	0.8211	0.3991	−6%
11390	Metabolite - 2726	35	0.5251	0.308	13%
11411	Metabolite - 2746	35	0.1037	0.1641	−29%
11438	phosphate	50	0.0685	0.1546	42%
11484	Metabolite - 2752	35	0.0063	0.1546	60%
11661	Metabolite - 2781	35	0.1145	0.1698	25%
11777	glycine	50	0.0284	0.1546	58%
11808	Metabolite - 2807	35	0.1406	0.1744	64%
11851	Metabolite - 2811	35	0.026	0.1546	235%
12025	cis-aconitic acid	50	0.1274	0.1705	76%
12055	galactose	50	0.7432	0.3824	14%
12102	o-phosphoethanolamine	50	0.7644	0.3861	8%
12104	Metabolite - 2852	35	0.1765	0.1876	285%
12109	Metabolite - 2853	35	0.6347	0.3485	15%
12129	beta-hydroxyisovaleric acid	50	0.066	0.1546	49%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
12300	Metabolite - 2868	35	0.4388	0.2848	76%
12358	(1'R,1'S)_biopterin	35	0.1576	0.1865	30%
12426	Metabolite - 2416	35	0.1652	0.1865	72%
12463	Metabolite - 2893-possible-demethylated-Rosiglitazone	35	0.4067	0.2755	27%
12474	Metabolite - 2897	35	0.8628	0.4093	−4%
12593	Metabolite - 2973	50	0.1595	0.1865	−22%
12641	meso-erythritol	50	0.3364	0.2437	28%
12644	Metabolite - 3016	50	0.72	0.3736	−4%
12648	Metabolite - 3020	50	0.0217	0.1546	69%
12666	Metabolite - 3033	50	0.0719	0.1546	51%
12711	Metabolite - 3053	35	0.788	0.3926	14%
12720	Metabolite - 3056	35	0.0489	0.1546	41%
12765	inositol	50	0.4194	0.2789	−27%
12770	Metabolite - 3090	50	0.3345	0.2432	12%
12771	Metabolite - 3091	50	0.3988	0.2721	37%
12795	Metabolite - 3113	50	0.5631	0.3223	−15%
12856	Metabolite - 3123	35	0.7525	0.3841	8%
12902	Metabolite - 3127	35	0.6832	0.363	10%
12904	Metabolite - 2457	35	0.169	0.1865	83%
12924	Metabolite - 3131	35	0.4335	0.2834	22%
12938	Metabolite - 2459	35	0.6893	0.3637	10%
13018	Metabolite - 3138	35	0.669	0.36	12%
13136	Metabolite - 3163-possible-methylcytidine-benserazide-Pyr-Gln-OH-or-glycerophosphocholine-	35	0.2764	0.2216	19%
13153	Metabolite - 3169	35	0.2308	0.2026	162%
13179	Metabolite - 3176	35	0.8221	0.3991	14%
13214	Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine	35	0.0768	0.1546	57%
13217	Metabolite - 3184	35	0.0416	0.1546	51%
13249	Metabolite - 3215	35	0.0164	0.1546	45%
13251	Metabolite - 3216	35	0.2086	0.1964	9%
13265	Metabolite - 3221	35	0.2654	0.2182	31%
13297	Metabolite - 3231	35	0.8602	0.4091	4%
13318	DL-indole-3-lactic acid	35	0.7643	0.3861	−9%
13356	Metabolite - 3246-possible-Ala-GLy-glycyl-sarcosine-or-ureido-butyric acid	35	0.0822	0.1546	62%
13459	Metabolite - 3305	35	0.0755	0.1546	71%
13484	Metabolite - 3309	35	0.3911	0.2698	17%
13493	Metabolite - 3311-	35	0.837	0.4028	−6%
13505	Metabolite - 3313	35	0.9682	0.4363	1%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.4164	0.2789	51%
13545	Metabolite - 3322	35	0.1275	0.1705	63%
13589	Metabolite - 3327	35	0.085	0.1546	74%
13594	Metabolite - 3329	35	0.0641	0.1546	145%
13704	Metabolite - 3355	35	0.1883	0.1931	33%
13744	Metabolite - 3364	35	0.8656	0.4096	−3%
13775	Metabolite - 3370	35	0.0505	0.1546	51%
13791	Metabolite - 3373	35	0.3231	0.2424	1137%
13803	Metabolite - 3377	35	0.882	0.4132	7%
13817	Metabolite - 3380	35	0.1975	0.195	36%
13820	beta-nicotinamide-mononucleotide	35	0.0287	0.1546	51%
13847	Metabolite - 3387	35	0.2135	0.2001	28%
13904	Metabolite - 3402	35	0.6861	0.363	6%
13968	Metabolite - 3409	35	0.5164	0.3059	22%
14036	Metabolite - 3427	35	0.0743	0.1546	72%
14066	Metabolite - 3433	35	0.5622	0.3223	7%
14084	Metabolite - 3436	35	0.5088	0.3032	13%
14115	Metabolite - 3440	35	0.2994	0.232	−66%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
14125	Metabolite - 3443	35	0.0258	0.1546	−49%
14170	Metabolite - 3457	35	0.9959	0.4445	0%
14220	Metabolite - 3470	35	0.0581	0.1546	91%
14249	Metabolite - 3476	35	0.0267	0.1546	66%
14368	Metabolite - 3489	35	0.1102	0.1698	−48%
14406	Metabolite - 3493	35	0.3257	0.2426	21%
14453	Metabolite - 3507	35	0.774	0.3891	8%
14471	Metabolite - 3516	35	0.7774	0.3894	6%
14506	Metabolite - 3543	35	0.4448	0.2848	73%
14539	Metabolite - 3564	35	0.5935	0.3317	29%
14595	Metabolite - 3576	35	0.1252	0.1705	78%
14640	Metabolite - 3604	35	0.4348	0.2834	20%
14641	Metabolite - 3605	35	0.1679	0.1865	78%
14731	Metabolite - 3659	35	0.182	0.1904	34%
14732	Metabolite - 3660	35	0.3269	0.2426	64%
14733	Metabolite - 3661	35	0.5283	0.308	17%
14759	Metabolite - 3667	35	0.2604	0.217	24%
14762	Metabolite - 3668	35	0.473	0.2914	−11%
14766	Metabolite - 3670	35	0.6732	0.3602	8%
14769	Metabolite - 3691	35	0.0229	0.1546	116%
14808	Metabolite - 3701	35	0.716	0.3725	11%
14835	Metabolite - 3706	35	0.2566	0.2148	21%
14840	Metabolite - 3708	35	0.2166	0.2008	166%
14907	Metabolite - 3734	35	0.0383	0.1546	73%
14983	Metabolite - 3754	35	0.9142	0.4199	−3%
14984	Metabolite - 3755	35	0.9378	0.4275	1%
15017	Metabolite - 3761	35	0.029	0.1546	40%
15057	Metabolite - 3771	35	0.4518	0.2856	38%
15064	Metabolite - 3773	35	0.8169	0.3991	5%
15096	N-acetyl-D-glucosamine	50	0.016	0.1546	100%
15121	Metabolite - 3786	35	0.5899	0.3306	17%
15124	porphobilinogen	35	0.2695	0.2198	25%
15125	(2-Aminoethyl)phosphonate	35	0.0023	0.1546	42%
15128	DL-homocysteine	35	0.0263	0.1546	76%
15129	D-alanyl-D-alanine	35	0.1999	0.195	28%
15130	diaminopimelic acid	35	0.1669	0.1865	36%
15131	dethiobiotin	35	0.4736	0.2914	64%
15187	Metabolite - 3800	35	0.1387	0.1744	68%
15197	Metabolite - 3802	35	0.2646	0.2182	50%
15201	Metabolite - 3803	35	0.049	0.1546	69%
15202	Metabolite - 3804	35	0.3305	0.2426	26%
15203	Metabolite - 3805	35	0.18	0.1894	29%
15207	Metabolite - 3806	35	0.5382	0.3128	31%
15211	Metabolite - 3807	35	0.0225	0.1546	33%
15220	Metabolite - 3813	35	0.083	0.1546	48%
15228	Metabolite - 3817	35	0.14	0.1744	43%
15240	Metabolite - 3824	35	0.9991	0.4448	1%
15249	Metabolite - 3828	35	0.1281	0.1705	48%
15251	Metabolite - 3830	35	0.1474	0.1787	67%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.2771	0.2216	−40%
15258	Metabolite - 3834-Peptide	35	0.2916	0.2279	50%
15275	Metabolite - 3840	35	0.419	0.2789	17%
15276	Metabolite - 3841	35	0.2765	0.2216	39%
15278	Metabolite - 3843	35	0.2183	0.2008	42%
15284	Metabolite - 3847	35	0.9603	0.4337	2%
15294	Metabolite - 3855	35	0.9398	0.4275	2%
15312	Metabolite - 3873	35	0.2025	0.1956	30%
15315	Metabolite - 3876	35	0.8981	0.4171	7%
15324	Metabolite - 3878	35	0.4489	0.2848	−19%
15326	Metabolite - 3879	35	0.5546	0.3194	36%
15328	azelaic acid	35	0.6594	0.3573	−15%
15335	mannitol	50	0.1881	0.1931	65%
15336	tartaric acid	35	0.5703	0.3245	24%
15356	Metabolite - 3886	35	0.2185	0.2008	26%
15359	Metabolite - 3887	35	0.9902	0.443	0%
15365	sn-Glycerol-3-phosphate	50	0.6605	0.3573	14%
15374	Metabolite - 3893	35	0.4206	0.2789	18%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
15382	Metabolite - 3898	35	0.1721	0.1874	19%
15410	Metabolite - 3908	35	0.0752	0.1546	65%
15411	Metabolite - 3909	35	0.4575	0.2863	−35%
15418	Metabolite - 3911	35	0.2886	0.2274	16%
15496	agmatine	35	0.5278	0.308	25%
15500	carnitine	35	0.3618	0.2584	−24%
15529	Metabolite - 3951	35	0.0523	0.1546	34%
15532	Metabolite - 3952	35	0.5521	0.319	25%
15535	Metabolite - 3955	35	0.0719	0.1546	72%
15541	Metabolite - 3957	35	0.8591	0.4091	3%
15599	Metabolite - 3963	35	0.4048	0.2752	114%
15610	Metabolite - 3970	35	0.0812	0.1546	45%
15620	Metabolite - 3973	35	0.1635	0.1865	179%
15626	Metabolite - 3977	35	0.8247	0.3993	7%
15636	Metabolite - 3981	35	0.6037	0.3354	25%
15641	Metabolite - 3986	35	0.9057	0.4171	2%
15650	1-methyladenosine	35	0.0502	0.1546	51%
15667	2-isopropylmalic acid	50	0.5859	0.3294	−27%
15676	3-methyl-2-oxovaleric acid	35	0.8809	0.4132	5%
15677	3-methyl-L-histidine	35	0.3622	0.2584	16%
15679	xanthurenic acid	50	0.2292	0.2026	43%
15681	4-Guanidinobutanoic acid	35	0.1143	0.1698	38%
15704	heptanedioic acid	35	0.0573	0.1546	38%
15716	L-beta-imidazolelactic acid	50	0.2314	0.2026	55%
15730	suberic acid	35	0.9187	0.421	−3%
15737	hydroxyacetic acid	50	0.2051	0.1961	26%
15743	N-N-dimethylarginine	35	0.1269	0.1705	30%
15753	hippuric acid	35	0.2825	0.2245	26%
15778	benzoic acid	35	0.8138	0.3991	6%
15804	maltose	50	0.8907	0.4163	−6%
15835	L-xylose	50	0.3032	0.233	61%
15948	S-adenosyl-l-homocysteine	35	0.3769	0.2666	24%
15964	D-arabitol	50	0.0555	0.1546	53%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.6621	0.3573	6%
16016	Metabolite - 3994	35	0.1773	0.1876	44%
16034	Metabolite - 4002	50	0.0999	0.1641	53%
16071	Metabolite - 4020	50	0.0376	0.1546	55%
16082	Metabolite - 4027	50	0.1234	0.1705	39%
16107	lysine	50	0.2204	0.2015	72%
16175	Metabolite - 4092	35	0.8448	0.4038	6%
16197	Metabolite - 4112	35	0.1002	0.1641	50%
16217	Metabolite - 4116	35	0.6325	0.3485	22%
16230	Isobar-29-includes-R—S-hydroorotic acid-5-6-dihydroorotic acid	35	0.0858	0.1546	404%
16232	Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.502	0.3001	−19%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.4534	0.2856	49%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.0455	0.1546	103%
16243	L-kynurenine	35	0.2729	0.2215	316%
16276	Isobar-38-includes-N-acetyl-L-methionine-5-hydroxy-1H-indole-3-acetic acid	35	0.8281	0.3999	−4%

TABLE 10-continued

Urine Metabolite Biomarkers to distinguish Non-cancer from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in PCA
16278	Isobar-35-includes-D-arabinose-5-phosphate-D-ribulose-5-phosphate-alpha-D-ribose-5-phosphate	35	0.585	0.3294	16%
16290	Metabolite - 4133	50	0.5451	0.3159	26%
16337	Metabolite - 4167	35	0.6297	0.3485	11%
16338	Metabolite - 4168	35	0.2445	0.2093	239%
16457	Metabolite - 4233	35	0.0367	0.1546	160%
16462	Metabolite - 4234	35	0.3867	0.2688	105%
16496	Metabolite - 4251	50	0.0612	0.1546	68%
16506	Metabolite - 4271	50	0.2168	0.2008	42%
16816	Metabolite - 4494	50	0.3938	0.2707	−8%
16818	Metabolite - 4495	50	0.2517	0.2126	28%
16819	Metabolite - 4496	50	0.1967	0.195	17%
16821	Metabolite - 4498	50	0.1936	0.195	37%
16822	Metabolite - 4499	50	0.0625	0.1546	57%
16823	Metabolite - 4500	50	0.2443	0.2093	159%
16824	iminodiacetic acid	50	0.5004	0.3001	23%
16827	Metabolite - 4502	50	0.0748	0.1546	5%
16829	Metabolite - 4503	50	0.0266	0.1546	60%
16831	Metabolite - 4504	50	0.012	0.1546	56%
16834	Metabolite - 4505	50	0.1015	0.1641	93%
16837	Metabolite - 4507	50	0.4492	0.2848	27%
16848	Metabolite - 4511	50	0.1687	0.1865	62%
16851	Metabolite - 4512	50	0.7087	0.3708	20%
16859	Metabolite - 4516	50	0.1197	0.1705	111%
16860	Metabolite - 4517	50	0.8131	0.3991	7%
16861	Metabolite - 4518	50	0.5277	0.308	47%
16862	Metabolite - 4519	50	0.0624	0.1546	120%
16863	Metabolite - 4520	50	0.4865	0.2937	−24%
16864	Metabolite - 4521	50	0.5658	0.3229	−21%
16865	Metabolite - 4522	50	0.0149	0.1546	54%
16866	Metabolite - 4523	50	0.0831	0.1546	43%
16867	Metabolite - 4524	50	0.9395	0.4275	−3%
16952	Metabolite - 4593	50	0.0167	0.1546	56%
16959	Metabolite - 4595	50	0.1416	0.1744	30%
17028	Metabolite - 4611	50	0.1674	0.1865	35%
17050	Metabolite - 4618	50	0.1343	0.1744	47%
17064	Metabolite - 4624	50	0.1424	0.1744	29%
17072	Metabolite - 4628	50	0.1106	0.1698	133%
17074	Metabolite - 4629	50	0.1355	0.1744	44%
17080	Metabolite - 4632	50	0.2873	0.2274	75%
17083	Metabolite - 4634	50	0.2324	0.2026	39%
17084	Metabolite - 4635	50	0.1653	0.1865	120%
17085	Metabolite - 4636	50	0.0414	0.1546	77%
17086	Metabolite - 4637	50	0.1528	0.1833	114%
17087	Metabolite - 4638	50	0.1281	0.1705	97%
17088	Metabolite - 4639	50	0.0915	0.1595	109%

TABLE 11

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
53	glutamine	50	0.3616	0.4198	32%
54	tryptophan	35	0.0325	0.3021	47%
57	glutamic acid	50	0.3185	0.411	21%
59	histidine	50	0.2782	0.3951	37%
60	leucine	50	0.1497	0.3451	46%
64	phenylalanine	35	0.0392	0.3021	42%
418	guanine	50	0.0948	0.3377	54%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
512	asparagine	50	0.1243	0.3401	60%
513	creatinine	35	0.0268	0.3021	34%
521	homogentisate	50	0.1224	0.3401	67%
527	lactate	50	0.9146	0.6009	−2%
528	alpha-keto-glutarate	35	0.5059	0.468	−17%
531	3-hydroxy-3-methylglutarate	50	0.3917	0.4342	24%
541	4-hydroxyphenylacetate	50	0.8452	0.5813	6%
542	3-hydroxybutanoic acid	50	0.2058	0.3499	−59%
554	adenine	50	0.2549	0.3783	25%
555	adenosine	35	0.0081	0.3021	81%
563	alpha-L-sorbopyranose	50	0.1978	0.3499	94%
569	caffeine	35	0.029	0.3021	−53%
575	arabinose	50	0.0415	0.3021	72%
577	fructose	50	0.8863	0.591	7%
581	glucose	50	0.061	0.3283	52%
587	gluconic acid	50	0.1217	0.3401	64%
594	niacinamide	35	0.5535	0.4815	−9%
597	phosphoenolpyruvate	35	0.3699	0.4225	50%
605	uracil	50	0.1162	0.3401	35%
607	urocanic acid	35	0.7279	0.5417	11%
608	vitamin-B6	35	0.7072	0.5385	−15%
1101	3-methoxy-4-hydroxyphenylacetate	50	0.0137	0.3021	55%
1107	allantoin	50	0.0607	0.3283	73%
1125	isoleucine	50	0.1449	0.3451	32%
1126	alanine	50	0.2233	0.3499	35%
1284	threonine	50	0.094	0.3377	38%
1299	tyrosine	50	0.0817	0.3308	39%
1302	methionine	35	0.0101	0.3021	54%
1303	malic acid	35	0.627	0.5038	11%
1366	trans-4-hydroxyproline	50	0.7014	0.5382	9%
1413	3-hydroxyphenylacetate	35	0.5846	0.4923	17%
1417	kynurenic acid	50	0.1657	0.3499	68%
1418	5-6-Dihydrothymine	35	0.075	0.3283	46%
1419	5-s-methyl-5-thioadenosine	35	0.3383	0.411	17%
1431	(p-Hydroxyphenyl)lactic acid	50	0.4665	0.4614	42%
1432	alphahydroxybenzeneacetic acid	35	0.7224	0.5417	6%
1437	succinate	50	0.6047	0.497	13%
1444	DL-pipecolic acid	35	0.749	0.5497	18%
1480	guanidineacetic acid	35	0.0242	0.3021	99%
1493	ornithine	50	0.9781	0.6148	−1%
1494	5-oxoproline	50	0.3008	0.4095	24%
1498	N-6-trimethyl-l-lysine	35	0.1516	0.3464	37%
1505	orotic acid	50	0.2192	0.3499	38%
1508	pantothenic acid	35	0.3229	0.411	57%
1519	sucrose	50	0.9951	0.6181	0%
1557	3-methylglutaric acid	35	0.5659	0.4828	−11%
1558	4-acetamidobutyric acid	35	0.026	0.3021	60%
1559	5-6-dihydrouracil	50	0.1436	0.3451	26%
1560	L-methyldopa	35	0.597	0.497	14%
1564	citric acid	50	0.1013	0.3377	44%
1566	3-amino-isobutyrate	50	0.6838	0.5331	16%
1567	4-hydroxy-3-methoxymandelate	50	0.0688	0.3283	53%
1568	4-hydroxymandelate	50	0.2224	0.3499	45%
1569	DL-beta-hydroxyphenylethylamine	35	0.4431	0.4524	17%
1574	histamine	35	0.0188	0.3021	61%
1580	noradrenaline	50	0.2067	0.3499	50%
1585	N-acetyl-L-alanine	35	0.5273	0.4762	14%
1587	N-acetyl-L-leucine	35	0.1465	0.3451	41%
1591	N-acetyl-L-valine	35	0.2387	0.3625	50%
1592	N-acetylneuraminic acid	50	0.0338	0.3021	48%
1598	N-tigloylglycine	35	0.1685	0.3499	29%
1604	uric acid	35	0.3873	0.4336	5%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
1640	ascorbic acid	50	0.6695	0.5267	54%
1648	serine	50	0.0526	0.3216	45%
1649	valine	50	0.1421	0.3451	26%
1708	7-8-dihydrofolic acid	35	0.1975	0.3499	23%
1778	gamma-glu-cys	35	0.4675	0.4614	47%
1827	riboflavine	35	0.2142	0.3499	183%
1860	3-nitro-L-tyrosine	35	0.974	0.6137	−1%
1868	cysteine	50	0.6881	0.534	23%
1898	proline	50	0.2767	0.395	46%
1899	quinolinic acid	50	0.1071	0.3377	40%
2078	pyrophosphate	50	0.3706	0.4225	44%
2092	catechol	35	0.018	0.3021	145%
2132	citrulline	50	0.0991	0.3377	35%
2183	thymidine	35	0.8751	0.5877	3%
2245	Metabolite - 294	35	0.3345	0.411	43%
2342	serotonin	35	0.0762	0.3283	34%
2734	gamma-L-glutamyl-L-tyrosine	35	0.0437	0.3021	66%
2829	N-formyl-L-methionine	35	0.4526	0.4591	23%
2831	adenosine-3-5-cyclic-monophosphate	35	0.008	0.3021	43%
3127	hypoxanthine	35	0.2239	0.3499	51%
3138	pyridoxamine-phosphate	35	0.8095	0.5733	5%
3147	xanthine	35	0.207	0.3499	60%
3155	3-ureidopropionic acid	35	0.1334	0.3451	67%
4966	xylitol	50	0.2152	0.3499	−31%
5493	Metabolite - 1059	35	0.8769	0.5877	−3%
5495	Metabolite - 1060	35	0.8529	0.5835	−2%
5514	Metabolite - 1081	35	0.026	0.3021	11%
5538	Metabolite - 1101	35	0.471	0.4614	59%
5664	Metabolite - 1101	35	0.6342	0.505	−15%
5687	Metabolite - 1110	35	0.306	0.411	23%
5697	acetylcarnitine-	35	0.8627	0.5857	−6%
5702	Metabolite - 1114	35	0.2517	0.3783	65%
5711	2-hydroxybutyric acid	35	0.7942	0.5658	−5%
5719	Metabolite - 1122	35	0.4991	0.4678	12%
5727	Metabolite - 1126	35	0.9422	0.6067	−2%
5797	Metabolite - 1186	35	0.2577	0.3783	30%
6137	Metabolite - 1212	35	0.1231	0.3401	36%
6147	Metabolite - 1216	35	0.5353	0.4784	−9%
6238	normetanephrine	50	0.2336	0.3587	17%
6253	Metabolite - 1283	35	0.4722	0.4614	35%
6278	Metabolite - 1289	35	0.4075	0.4428	13%
6329	urea	50	0.2047	0.3499	24%
6362	Metabolite - 1323-possible-p-cresol-sulfate	35	0.1689	0.3499	56%
6398	Metabolite - 1335	35	0.4993	0.4678	12%
6405	Metabolite - 1338	35	0.4624	0.4614	−16%
6413	Metabolite - 1342-possible-phenylacetylglutamine-or-formyl-N-acetyl-5-methoxykynurenamine	35	0.1592	0.3499	28%
6421	Metabolite - 1345	35	0.2195	0.3499	71%
6437	Metabolite - 1349-possible-N-acetyl-8-O-methyl-Neuraminic acid	35	0.1055	0.3377	40%
6443	Metabolite - 1351	35	0.9453	0.6072	2%
6477	Metabolite - 1364	35	0.3548	0.419	−65%
6486	Metabolite - 1368	35	0.4304	0.4492	45%
6493	salicyluric acid	35	0.462	0.4614	−65%
6528	Metabolite - 1383-possible-salicyluric-glucuronide	35	0.4273	0.4492	−49%
6760	Metabolite - 1455	35	0.0092	0.3021	58%
6764	Metabolite - 1459	35	0.7767	0.5619	13%
6777	Metabolite - 1463	35	0.5723	0.485	−31%
6787	Metabolite - 1465	35	0.2726	0.3914	20%
6847	Metabolite - 1496	35	0.7359	0.5447	15%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
6852	Metabolite - 1498	35	0.4113	0.4428	49%
6987	Metabolite - 1573	35	0.2236	0.3499	16%
7132	Metabolite - 1667	35	0.3277	0.411	−73%
7175	Metabolite - 1655	35	0.1087	0.3377	77%
7177	Metabolite - 1656	35	0.5561	0.4815	23%
7272	Metabolite - 1679	35	0.1129	0.3377	42%
7286	Metabolite - 1682	35	0.8923	0.5935	4%
7359	n-acetyl-L-aspartic acid	35	0.0709	0.3283	67%
7639	oxalic acid	35	0.1367	0.3451	25%
7650	Metabolite - 1834	35	0.4803	0.464	−21%
7660	Metabolite - 1839	35	0.9276	0.6009	−3%
7672	Metabolite - 1843	35	0.1049	0.3377	30%
7933	Metabolite - 1911	35	0.2835	0.4005	42%
8176	Metabolite - 1974	35	0.1493	0.3451	43%
8196	Metabolite - 1979-Cl-adduct-of-isobar-19	35	0.7488	0.5497	−10%
8210	Metabolite - 1981	35	0.9643	0.6134	1%
8336	Metabolite - 2005	35	0.6224	0.5032	−11%
8644	Metabolite - 2051	35	0.5497	0.4815	8%
8677	Metabolite - 2056	35	0.1235	0.3401	24%
9007	Metabolite - 2108	35	0.6911	0.534	17%
9038	Metabolite - 2118	35	0.2102	0.3499	29%
9113	Metabolite - 2133	35	0.2101	0.3499	32%
9165	Metabolite - 2150	35	0.3592	0.4194	29%
9333	Metabolite - 2174	35	0.514	0.4716	15%
9334	Metabolite - 2175	35	0.3253	0.411	73%
9458	Metabolite - 2181	35	0.0095	0.3021	56%
10058	Metabolite - 2242	35	0.3061	0.411	−91%
10087	Metabolite - 2249	35	0.2194	0.3499	79%
10122	Metabolite - 2254	35	0.9247	0.6009	−2%
10136	Metabolite - 2034	35	0.3572	0.419	42%
10156	Metabolite - 2259	35	0.331	0.411	85%
10240	4-acetominophen-sulfate	35	0.6091	0.497	15%
10245	Metabolite - 2269-	35	0.715	0.5393	5%
10247	Metabolite - 2270	35	0.135	0.3451	−49%
10252	Metabolite - 2271	35	0.2042	0.3499	38%
10286	Metabolite - 2272	35	0.1989	0.3499	80%
10309	Metabolite - 2277	35	0.0163	0.3021	59%
10347	Metabolite - 2285	35	0.1474	0.3451	44%
10407	Metabolite - 2059	35	0.3262	0.411	22%
10424	Metabolite - 2292	35	0.0485	0.3188	−36%
10433	Metabolite - 2293-possible-O-desmethylvenlafaxine-glucuronide	35	0.3264	0.411	−91%
10490	Metabolite - 2319	35	0.6803	0.5319	8%
10526	Metabolite - 2323	35	0.8122	0.5733	7%
10544	Metabolite - 2329	35	0.5016	0.4678	11%
10555	Metabolite - 2348	35	0.3735	0.4225	−36%
10570	Metabolite - 2366	35	0.5627	0.4824	13%
10629	Metabolite - 2386	35	0.2987	0.4088	19%
10644	Metabolite - 2387	35	0.374	0.4225	39%
10667	Metabolite - 2389	35	0.207	0.3499	−22%
10672	Metabolite - 2390	35	0.0744	0.3283	69%
10737	Isobar-1-includes-mannose-fructose-glucose-galactose-alpha-L-sorbopyranose-Inositol-D-allose-D--altrose-D-psicone	35	0.9075	0.6009	−4%
10741	Isobar-2-includes-2-aminoisobutyric acid-3-amino-isobutyrate-2-amino-butyrate-4-aminobutanoic acid-dimethylglycine-choline-	35	0.7125	0.5393	−9%
10743	Isobar-4-includes-Gluconic acid-DL-arabinose-D-ribose-L-	35	0.0298	0.3021	48%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
	xylose-DL-lyxose-D-xylulose				
10746	Isobar-6-includes-valine-betaine	35	0.5275	0.4762	14%
10785	Metabolite - 2506	35	0.886	0.591	3%
10825	Metabolite - 2546	35	0.3726	0.4225	15%
10872	Metabolite - 2550	35	0.1131	0.3377	100%
10906	Metabolite - 2557-possible-Pantoprazole-metabolite	35	0.7733	0.5619	−8%
11053	Metabolite - 2567	35	0.0376	0.3021	42%
11085	Metabolite - 2588	35	0.3891	0.4336	64%
11110	Metabolite - 2591	35	0.0842	0.3353	−35%
11173	Metabolite - 2607	35	0.7772	0.5619	12%
11219	Metabolite - 2686	35	0.818	0.5733	5%
11264	Metabolite - 2698	35	0.2618	0.38	−43%
11271	Metabolite - 2700	35	0.4829	0.4648	29%
11292	Metabolite - 2703	35	0.0818	0.3308	25%
11299	Metabolite - 2706	35	0.4803	0.464	21%
11390	Metabolite - 2726	35	0.1731	0.3499	31%
11411	Metabolite - 2746	35	0.6339	0.505	−9%
11438	phosphate	50	0.2251	0.3499	27%
11484	Metabolite - 2752	35	0.077	0.3283	35%
11661	Metabolite - 2781	35	0.0671	0.3283	30%
11777	glycine	50	0.0787	0.3283	44%
11808	Metabolite - 2807	35	0.9564	0.6099	2%
11851	Metabolite - 2811	35	0.497	0.4678	28%
12025	cis-aconitic acid	50	0.8152	0.5733	12%
12055	galactose	50	0.9486	0.6079	3%
12102	o-phosphoethanolamine	50	0.4724	0.4614	25%
12104	Metabolite - 2852	35	0.2242	0.3499	199%
12109	Metabolite - 2853	35	0.6302	0.5048	14%
12129	beta-hydroxyisovaleric acid	50	0.0907	0.3377	43%
12300	Metabolite - 2868	35	0.3468	0.4142	109%
12358	(1'R,1'S)_biopterin	35	0.8705	0.5877	3%
12426	Metabolite - 2416	35	0.329	0.411	44%
12463	Metabolite - 2893-possible-demethylated-Rosiglitazone	35	0.8121	0.5733	7%
12474	Metabolite - 2897	35	0.5015	0.4678	16%
12593	Metabolite - 2973	50	0.8428	0.5812	3%
12641	meso-erythritol	50	0.2553	0.3783	30%
12644	Metabolite - 3016	50	0.7026	0.5382	5%
12648	Metabolite - 3020	50	0.0318	0.3021	62%
12666	Metabolite - 3033	50	0.0908	0.3377	47%
12711	Metabolite - 3053	35	0.8572	0.5835	−8%
12720	Metabolite - 3056	35	0.1203	0.3401	30%
12765	inositol	50	0.986	0.6153	−1%
12770	Metabolite - 3090	50	0.0682	0.3283	25%
12771	Metabolite - 3091	50	0.1481	0.3451	83%
12795	Metabolite - 3113	50	0.9736	0.6137	−1%
12856	Metabolite - 3123	35	0.7353	0.5447	−8%
12902	Metabolite - 3127	35	0.5559	0.4815	14%
12904	Metabolite - 2457	35	0.7826	0.5634	10%
12924	Metabolite - 3131	35	0.3436	0.4141	31%
12938	Metabolite - 2459	35	0.662	0.5223	11%
13018	Metabolite - 3138	35	0.6504	0.5163	12%
13136	Metabolite - 3163-possible-methylcytidine-benserazide-Pyr-Gln-OH-or-glycerophosphocholine-	35	0.3216	0.411	17%
13153	Metabolite - 3169	35	0.264	0.3811	132%
13179	Metabolite - 3176	35	0.4698	0.4614	30%
13214	Metabolite - 3183-possible-gamma-L-glutamyl-L-phenylalanine	35	0.1413	0.3451	45%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
13217	Metabolite - 3184	35	0.1112	0.3377	37%
13249	Metabolite - 3215	35	0.0274	0.3021	40%
13251	Metabolite - 3216	35	0.0408	0.3021	17%
13265	Metabolite - 3221	35	0.2155	0.3499	34%
13297	Metabolite - 3231	35	0.7164	0.5393	6%
13318	DL-indole-3-lactic acid	35	0.7541	0.5513	12%
13356	Metabolite - 3246-possible-Ala-GLy-glycyl-sarcosine-or-ureido-butyric acid	35	0.0524	0.3216	76%
13459	Metabolite - 3305	35	0.1936	0.3499	47%
13484	Metabolite - 3309	35	0.491	0.4678	13%
13493	Metabolite - 3311-	35	0.1657	0.3499	−40%
13505	Metabolite - 3313	35	0.6134	0.4974	17%
13534	Metabolite - 3320-possible-pimpinellin-or-tetrahydroxybenzophenone	35	0.559	0.4815	34%
13545	Metabolite - 3322	35	0.0622	0.3283	90%
13589	Metabolite - 3327	35	0.2577	0.3783	37%
13594	Metabolite - 3329	35	0.0616	0.3283	149%
13704	Metabolite - 3355	35	0.6078	0.497	11%
13744	Metabolite - 3364	35	0.2939	0.4065	−19%
13775	Metabolite - 3370	35	0.1617	0.3499	35%
13791	Metabolite - 3373	35	0.3232	0.411	1137%
13803	Metabolite - 3377	35	0.4791	0.464	37%
13817	Metabolite - 3380	35	0.094	0.3377	53%
13820	beta-nicotinamide-mononucleotide	35	0.0454	0.3059	45%
13847	Metabolite - 3387	35	0.3384	0.411	23%
13904	Metabolite - 3402	35	0.3627	0.4198	−38%
13968	Metabolite - 3409	35	0.9107	0.6009	4%
14036	Metabolite - 3427	35	0.1123	0.3377	58%
14066	Metabolite - 3433	35	0.4093	0.4428	12%
14084	Metabolite - 3436	35	0.8736	0.5877	2%
14115	Metabolite - 3440	35	0.8294	0.575	−5%
14125	Metabolite - 3443	35	0.0154	0.3021	−54%
14170	Metabolite - 3457	35	0.6072	0.497	−11%
14220	Metabolite - 3470	35	0.0626	0.3283	84%
14249	Metabolite - 3476	35	0.7481	0.5497	−9%
14368	Metabolite - 3489	35	0.1826	0.3499	−28%
14406	Metabolite - 3493	35	0.4363	0.4492	17%
14453	Metabolite - 3507	35	0.8289	0.575	−5%
14471	Metabolite - 3516	35	0.3193	0.411	−21%
14506	Metabolite - 3543	35	0.3275	0.411	111%
14539	Metabolite - 3564	35	0.2138	0.3499	107%
14595	Metabolite - 3576	35	0.1745	0.3499	63%
14640	Metabolite - 3604	35	0.9887	0.6156	0%
14641	Metabolite - 3605	35	0.5637	0.4824	24%
14731	Metabolite - 3659	35	0.5691	0.4839	14%
14732	Metabolite - 3660	35	0.627	0.5038	25%
14733	Metabolite - 3661	35	0.4336	0.4492	28%
14759	Metabolite - 3667	35	0.828	0.575	4%
14762	Metabolite - 3668	35	0.7262	0.5417	−6%
14766	Metabolite - 3670	35	0.8506	0.5835	−4%
14769	Metabolite - 3691	35	0.0162	0.3021	135%
14808	Metabolite - 3701	35	0.1711	0.3499	61%
14835	Metabolite - 3706	35	0.353	0.419	19%
14840	Metabolite - 3708	35	0.202	0.3499	184%
14907	Metabolite - 3734	35	0.1065	0.3377	49%
14983	Metabolite - 3754	35	0.9841	0.6153	−1%
14984	Metabolite - 3755	35	0.3568	0.419	−60%
15017	Metabolite - 3761	35	0.3351	0.411	15%
15057	Metabolite - 3771	35	0.7946	0.5658	−9%
15064	Metabolite - 3773	35	0.4963	0.4678	17%
15096	N-acetyl-D-glucosamine	50	0.0305	0.3021	81%
15121	Metabolite - 3786	35	0.9216	0.6009	−3%
15124	porphobilinogen	35	0.3291	0.411	22%
15125	(2-Aminoethyl)phosphonate	35	0.0419	0.3021	25%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
15128	DL-homocysteine	35	0.4331	0.4492	20%
15129	D-alanyl-D-alanine	35	0.2018	0.3499	27%
15130	diaminopimelic acid	35	0.0787	0.3283	49%
15131	dethiobiotin	35	0.4377	0.4492	74%
15187	Metabolite - 3800	35	0.1005	0.3377	82%
15197	Metabolite - 3802	35	0.3395	0.411	40%
15201	Metabolite - 3803	35	0.1397	0.3451	45%
15202	Metabolite - 3804	35	0.0505	0.3216	62%
15203	Metabolite - 3805	35	0.1828	0.3499	32%
15207	Metabolite - 3806	35	0.1977	0.3499	95%
15211	Metabolite - 3807	35	0.0352	0.3021	30%
15220	Metabolite - 3813	35	0.3153	0.411	26%
15228	Metabolite - 3817	35	0.0645	0.3283	62%
15240	Metabolite - 3824	35	0.837	0.5787	8%
15249	Metabolite - 3828	35	0.176	0.3499	43%
15251	Metabolite - 3830	35	0.5535	0.4815	20%
15253	Metabolite - 3832-possible-phenol-sulfate	35	0.9729	0.6137	1%
15258	Metabolite - 3834-Peptide	35	0.5236	0.476	27%
15275	Metabolite - 3840	35	0.5876	0.4932	12%
15276	Metabolite - 3841	35	0.7884	0.5652	−12%
15278	Metabolite - 3843	35	0.1684	0.3499	48%
15284	Metabolite - 3847	35	0.9363	0.6044	2%
15294	Metabolite - 3855	35	0.9278	0.6009	−2%
15312	Metabolite - 3873	35	0.1113	0.3377	41%
15315	Metabolite - 3876	35	0.6801	0.5319	−17%
15324	Metabolite - 3878	35	0.9543	0.6099	−1%
15326	Metabolite - 3879	35	0.5214	0.4756	40%
15328	azelaic acid	35	0.5573	0.4815	27%
15335	mannitol	50	0.7785	0.5619	10%
15336	tartaric acid	35	0.1794	0.3499	69%
15356	Metabolite - 3886	35	0.3988	0.4403	17%
15359	Metabolite - 3887	35	0.8182	0.5733	6%
15365	sn-Glycerol-3-phosphate	50	0.5348	0.4784	23%
15374	Metabolite - 3893	35	0.4706	0.4614	15%
15382	Metabolite - 3898	35	0.287	0.4018	14%
15410	Metabolite - 3908	35	0.1311	0.3451	50%
15411	Metabolite - 3909	35	0.559	0.4815	−17%
15418	Metabolite - 3911	35	0.6533	0.517	7%
15496	agmatine	35	0.8254	0.575	−7%
15500	carnitine	35	0.191	0.3499	−31%
15529	Metabolite - 3951	35	0.0572	0.3283	34%
15532	Metabolite - 3952	35	0.3275	0.411	49%
15535	Metabolite - 3955	35	0.0891	0.3377	71%
15541	Metabolite - 3957	35	0.7242	0.5417	5%
15599	Metabolite - 3963	35	0.5152	0.4716	72%
15610	Metabolite - 3970	35	0.3254	0.411	24%
15620	Metabolite - 3973	35	0.2969	0.4084	94%
15626	Metabolite - 3977	35	0.2082	0.3499	65%
15636	Metabolite - 3981	35	0.3746	0.4225	49%
15641	Metabolite - 3986	35	0.6892	0.534	9%
15650	1-methyladenosine	35	0.0431	0.3021	54%
15667	2-isopropylmalic acid	50	0.9286	0.6009	−3%
15676	3-methyl-2-oxovaleric acid	35	0.7554	0.5513	−9%
15677	3-methyl-L-histidine	35	0.0247	0.3021	50%
15679	xanthurenic acid	50	0.428	0.4492	25%
15681	4-Guanidinobutanoic acid	35	0.1785	0.3499	33%
15704	heptanedioic acid	35	0.0437	0.3021	42%
15716	L-beta-imidazolelactic acid	50	0.4297	0.4492	31%
15730	suberic acid	35	0.5965	0.497	13%
15737	hydroxyacetic acid	50	0.1005	0.3377	38%
15743	N—N-dimethylarginine	35	0.1977	0.3499	25%
15753	hippuric acid	35	0.6063	0.497	11%
15778	benzoic acid	35	0.2541	0.3783	−35%
15804	maltose	50	0.4101	0.4428	−43%
15835	L-xylose	50	0.4221	0.4492	47%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
15948	S-adenosyl-l-homocysteine	35	0.1118	0.3377	40%
15964	D-arabitol	50	0.0578	0.3283	52%
16002	Metabolite - 3992-possible-Cl-adduct-of-Formate-dimer	35	0.5021	0.4678	−9%
16016	Metabolite - 3994	35	0.0348	0.3021	90%
16034	Metabolite - 4002	50	0.5041	0.468	17%
16071	Metabolite - 4020	50	0.0755	0.3283	44%
16082	Metabolite - 4027	50	0.1596	0.3499	33%
16107	lysine	50	0.6063	0.497	−30%
16175	Metabolite - 4092	35	0.4353	0.4492	22%
16197	Metabolite - 4112	35	0.122	0.3401	43%
16217	Metabolite - 4116	35	0.5789	0.4891	30%
16230	Isobar-29-includes-R—S-hydroorotic acid-5-6-dihydroorotic acid	35	0.2117	0.3499	135%
16232	Isobar-17-includes-arginine-N-alpha-acetyl-ornithine	35	0.4014	0.4413	−23%
16233	Isobar-13-includes-5-keto-D-gluconic acid-2-keto-L-gulonic acid-D-glucuronic acid-D-galacturonic acid	35	0.3895	0.4336	63%
16235	Isobar-19-includes-D-saccharic acid-1-5-anhydro-D-glucitol-2-deoxy-D-galactose-2-deoxy-D-glucose-L-fucose-L-rhamnose	35	0.5538	0.4815	22%
16243	L-kynurenine	35	0.2602	0.3798	353%
16276	Isobar-38-includes-N-acetyl-L-methionine-5-hydroxy-1H-indole-3-acetic acid	35	0.3469	0.4142	−19%
16278	Isobar-35-includes-D-arabinose-5-phosphate-D-ribulose-5-phosphate-alpha-D-ribose-5-phosphate	35	0.874	0.5877	−3%
16290	Metabolite - 4133	50	0.8566	0.5835	−7%
16337	Metabolite - 4167	35	0.9854	0.6153	−1%
16338	Metabolite - 4168	35	0.2875	0.4018	183%
16457	Metabolite - 4233	35	0.0702	0.3283	115%
16462	Metabolite - 4234	35	0.7005	0.5382	30%
16496	Metabolite - 4251	50	0.0239	0.3021	99%
16506	Metabolite - 4271	50	0.7894	0.5652	9%
16816	Metabolite - 4494	50	0.4086	0.4428	−7%
16818	Metabolite - 4495	50	0.7053	0.5385	8%
16819	Metabolite - 4496	50	0.4299	0.4492	10%
16821	Metabolite - 4498	50	0.9186	0.6009	3%
16822	Metabolite - 4499	50	0.132	0.3451	42%
16823	Metabolite - 4500	50	0.5079	0.4682	59%
16824	iminodiacetic acid	50	0.1695	0.3499	60%
16827	Metabolite - 4502	50	0.0356	0.3021	6%
16829	Metabolite - 4503	50	0.1744	0.3499	30%
16831	Metabolite - 4504	50	0.0255	0.3021	47%
16834	Metabolite - 4505	50	0.1844	0.3499	68%
16837	Metabolite - 4507	50	0.9737	0.6137	1%
16848	Metabolite - 4511	50	0.5473	0.4815	22%
16851	Metabolite - 4512	50	0.5346	0.4784	−25%
16859	Metabolite - 4516	50	0.1479	0.3451	95%
16860	Metabolite - 4517	50	0.9134	0.6009	−3%
16861	Metabolite - 4518	50	0.5481	0.4815	45%
16862	Metabolite - 4519	50	0.0417	0.3021	147%
16863	Metabolite - 4520	50	0.49	0.4678	−23%
16864	Metabolite - 4521	50	0.5999	0.497	−17%
16865	Metabolite - 4522	50	0.0317	0.3021	45%
16866	Metabolite - 4523	50	0.1397	0.3451	35%

TABLE 11-continued

Urine Metabolite Biomarkers to distinguish Lower Grade PCA from Higher Grade PCA.

COMP_ID	COMPOUND	LIB_ID	p-value	q-value	% Change in Higher PCA
16867	Metabolite - 4524	50	0.4657	0.4614	41%
16952	Metabolite - 4593	50	0.1068	0.3377	32%
16959	Metabolite - 4595	50	0.206	0.3499	26%
17028	Metabolite - 4611	50	0.191	0.3499	30%
17050	Metabolite - 4618	50	0.7146	0.5393	−14%
17064	Metabolite - 4624	50	0.4442	0.4524	15%
17072	Metabolite - 4628	50	0.6112	0.4971	29%
17074	Metabolite - 4629	50	0.2339	0.3587	32%
17080	Metabolite - 4632	50	0.3386	0.411	64%
17083	Metabolite - 4634	50	0.2892	0.402	32%
17084	Metabolite - 4635	50	0.9283	0.6009	−6%
17085	Metabolite - 4636	50	0.1467	0.3451	50%
17086	Metabolite - 4637	50	0.1763	0.3499	99%
17087	Metabolite - 4638	50	0.4336	0.4492	37%
17088	Metabolite - 4639	50	0.2348	0.3587	58%

Example 5

Random Forest Analysis for the Classification of Tissue Samples

[0136] The data obtained in Example 1 concerning the tissue samples was used to create a random forest model. Random Forest Analysis was carried out on the data obtained from tissue samples in Example 1 to classify them as Normal (N), Localized (i.e. lower grade) cancer tumor (T) or Metastatic tumor (M). The first analysis resulted in 90.5% correct classification of the three tissue types. The metastatic tumors were correctly classified 100% of the time while the normal tissue and the localized prostate cancer tumors were correctly classified 87% and 83%, respectively (Table 12).

TABLE 12

Confusion matrix for metastatic (M), normal prostate (N) and localized prostate cancer tumor (T) tissue types.

		Predicted Tissue Type			
		Metastatic Tumor	Normal Tissue	Localized Tumor	error
Actual Tissue Type	Metastatic Tumor (M)	14	0	0	0.00
	Normal Tissue (N)	0	14	2	0.13
	Localized Tumor (T)	0	2	10	0.17

OOB Error = 9.5%

[0137] Based on the OOB Error rate of 9.5%, the Random Forest model that was created could be used to predict whether a subject has a metastatic tumor (M), a localized tumor (T), or normal tissue (N) with about 90.5% accuracy from analysis of the levels of the biomarkers in samples from the subject.

[0138] The importance plot is shown in FIG. **1**. The important metabolites for this classification are listed in Table 13.

TABLE 13

Most important biomarker metabolites to distinguish N, T, M tissue types.

Metabolite	Library
n-hexadecanoic acid (palmitate)	50
tetradecanoic acid (myristate)	50
inosine	61
octadecanoic acid (stearate(	50
3-amino-isobutyrate	50
n-dodecanoate (laurate)	50
(2-aminoethyl)phosphonate	61
Metabolite - 3778	61
glycerol	50
(p-hydroxyphenyl)lactic acid	50
palmitoleic acid	50
N-acetyl-D-galactosamine	50
Metabolite - 3102	50
meso-erythritol	50
Metabolite - 1597	61
uracil	50
uridine	61
Metabolite - 4075	50
Isobar - 24 includes L-arabitol & adonitol	61
Metabolite - 2867	61
Metabolite - 4620	61
sn-glycerol-3-phosphate	50
Metabolite - 4117 (possible-propranolol or 2-heptyl-3-hydroxy-quinolone	61
Metabolite - 1114	61
DL-homocysteine	61
leucine	50
xanthine	61
Metabolite - 1576	61
Metabolite - 2973	50
Metabolite - 3810	61

[0139] Based on this analysis one sample appeared to be an outlier. Sample T3, which was reported as localized prostate tumor tissue, appears to be an outlier. From the random forest comparing all three tissue types, 80% of the trees in the random forest classified T3 as an "N" or normal while only

17% correctly classed it as "T" and only 3% classified it as "M" or metastatic. This result indicates that the sample may be a mixture of normal and cancerous tissue or that the sample is at an early stage of cancer.

[0140] Random Forest Analysis was also carried out on the tissue samples from the prostate to classify them as Normal prostate (N) or Localized prostate cancer tumor (T). This analysis resulted in 86% correct classification of the two tissue types. The normal tissue and the localized prostate cancer tumors were correctly classified 87% and 83% respectively (Table 14).

TABLE 14

Confusion matrix comparing Normal prostate tissue (N) with Localized prostate tumor tissue (T).

		Predicted Tissue Type		
		Normal Tissue	Localized Tumor	error
Actual Tissue Type	Normal Tissue (N)	14	2	0.13
	Localized Tumor (T)	2	10	0.17

OOB Error = 14%

[0141] Based on the OOB Error rate of 14%, the Random Forest model that was created could be used to predict whether a subject has normal tissue (N), or localized tumor (T) tissue with about 86% accuracy from analysis of the levels of biomarkers in samples from the subject.

[0142] The important metabolites for this classification are listed in Table 15 and shown in the importance plot in FIG. **2**.

TABLE 15

Most important biomarker metabolites to distinguish Normal prostate tissue (N) and Cancerous prostate tumor tissue (T).

Metabolite	Library
N-acetyl-D-galactosamine	50
Metabolite - 3778	61
uridine	61
Metabolite - 4117 possible propanolol or 2-heptyl-3-hydroxy-quinolone	61
Metabolite - 1114	61
Metabolite - 3810	61
DL-homocysteine	61
Metabolite - 3094	50
Metabolite - 4616	61
Metabolite - 1576	61
Metabolite - 3139	61
sn-glycerol-3-phospate	50
Metabolite - 2973	50
carnitine	61
Metabolite - 2041	61
Isobar 3 includes inositol-1-phosphate, mannose-6-phospate, glucose-6-phosphate, D-mannose-1-phoaphate, alpha-D-glucose-1-phosphate	61
kynurenic acid	61
n-hexadecanoic acid (palmitate)	50
cysteine	50
Metabolite - 4027	50
Metabolite - 3027	50
glutamic acid	50
Metabolite - 2688	61
Metabolite - 1111 possible methylnitronitrosoguanidine or ethyl-thiocarbamoylacetate	61

TABLE 15-continued

Most important biomarker metabolites to distinguish Normal prostate tissue (N) and Cancerous prostate tumor tissue (T).

Metabolite	Library
Metabolite - 2055	61
Metabolite - 3176 possible creatine	61
uracil	50
glycine	50
Metabolite - 3165	61
Metabolite - 1595 possible glutathione-metabolite	61

[0143] Since the metastatic tumors were obtained from sites distal to the prostate, we determined if these tissues were distinguished from the normal and cancerous prostate tissue due to the metastasis or due to the location of the tumor. To test this, the metastatic tumor tissue samples from liver were compared with the non-liver metastatic tumor tissues using Random Forest. The confusion matrix resulting from this analysis is provided in Table 16 and the results are essentially random chance; the liver and non-liver origins of the tumors appear to be indistinguishable. Thus, the classification of the metastatic tumor tissue is based on the metabolite biomarkers for metastasis and not on the source tissue of the metastatic tumor.

TABLE 16

Confusion matrix comparing metastatic tumors from liver tissue with metastatic tumors from non-liver tissue.

		Predicted Tissue Source		
		Liver	Non-liver	error
Actual Tissue Source	Liver	5	3	0.38
	Non-liver	5	5	0.50

OOB Error = 43%

[0144] Based on the OOB Error rate of 43%, the Random Forest model that was created could be used to predict whether a subject has a metastatic tumor from liver tissue, compared to non-liver tissue, with about 57% accuracy from analysis of the levels of biomarkers in liver tissue samples from the subject, but the Error Rate may essentially be random chance and may indicate that the source (i.e. liver or non-liver) of the tumor tissue is not predicted by these biomarkers.

Example 6

Random Forest Analysis for the Classification of Urine Samples from Control Subjects, Subjects with Low Grade PCA and Subjects with High Grade PCA

[0145] Random Forest Analysis was carried out on the data obtained from urine samples in Example 4 to classify them as Non-cancer (Control) or Prostate cancer. The control samples were urine obtained from subjects with a Gleason score (major) of 0 or from prostate cancer (PCA) subjects with a Gleason score (major) >=4. The analysis resulted in 63% correct classification of the urine sample types. The control subjects

were correctly classified 62% of the time while the subjects with prostate cancer (PCA) were correctly classified 64% of the time (Table 17).

TABLE 17

Confusion matrix for control vs PCA in Urine.

		Predicted		
		Control	PCA	error
Actual	Control	33	20	0.38
	PCA	5	9	0.36

OOB Error = 37%

[0146] Based on the OOB Error rate of 37%, the Random Forest model that was created could be used to predict whether a subject has prostate cancer (PCA), compared to being cancer-free, with about 63% accuracy from analysis of the levels of biomarkers in urine from the subject.

[0147] The importance plot is shown in FIG. **3**. The important metabolites for this classification are listed in Table 18.

TABLE 18

Most important urine biomarker metabolites to distinguish Control from PCA.

Metabolite	Library
(2-aminoethyl)phosphonate	35
Metabolite - 2051	35
Metabolite - 3805	35
Guanidineacetic acid	35
catechol	35
N-acetyl-L-valine	35
DL-beta-hydroxyphenylethylamine	35
N-acetyl-D-glucosamine	50
Metabolite - 1974	35
Metabolite - 4636	50
Metabolite - 2811	35
Metabolite - 3176	35
Metabolite - 1979	35
histamine	35
alpha-L-sorbopyranose	50
xylitol	50
Metabolite - 4504	50
Metabolite - 2285	35
3-methoxy-4-hydroxyphenylacetate	50
Metabolite - 2181	35
Metabolite - 1455	35
adenosine	35
Isobar 6: includes valine & betaine	35
Metabolite - 3169	35
Metabolite - 3470	35
Metabolite - 4502	50
Metabolite - 2746	35
Metabolite - 4503	50
Metabolite - 3476	35
Metabolite - 3443	35

[0148] Random Forest Analysis was also carried out on the biomarkers identified in Example 4 from urine samples to classify them as lower grade prostate cancer (Gleason score major 3) or higher grade prostate cancer (Gleason score major >=4). In this analysis resulted in 61% correct classification of the two cancer grades. The lower grade and the higher grade prostate cancers were correctly classified 58% and 71% respectively (Table 19).

TABLE 19

Confusion matrix comparing urine from subjects with lower grade prostate cancer and higher grade prostate cancer.

		Predicted Grade		
		Low	High	error
Actual Grade	Low	25	18	0.42
	High	4	10	0.29

OOB Error = 39%

[0149] Based on the OOB Error rate of 39%, the Random Forest model that was created could be used to predict whether a subject has a lower grade prostate cancer or a higher grade prostate cancer with about 61% accuracy from analysis of the levels of biomarkers in urine from the subject.

[0150] The importance plot is shown in FIG. **4**. The important metabolites for this classification are listed in Table 20.

TABLE 20

Most important urine biomarker metabolites to distinguish subjects with lower grade prostate cancer and higher grade prostate cancer.

Metabolite	Library
Metabolite - 3805	35
Histamine	35
Metabolite - 1455	35
Catechol	35
xylitol	50
Metabolite - 4636	50
Metabolite - 3691	35
Adenosine	35
Glycine	50
Metabolite - 3661	35
Metabolite - 3955	35
Methionine	35
Isobar 6 includes valine, betaine	35
guanidineacetic acid	35
Metabolite - 3817	35
N-acetyl-D-glucosamine	50
Metabolite - 3806	35
Metabolite - 2277	35
3-methoxy-4-hydroxyphenylacetate	50
Metabolite - 4502	50
Metabolite - 4519	50
Guanine	50
Metabolite - 2181	35
Alpha-L-sorbopyranose	50
Metabolite - 2270	35
Metabolite - 1498	35
Metabolite - 3443	35
tryptophan	35
Metabolite - 2051	35
gamma-L-glutamy-L-tyrosine	35

Example 7

Random Forest Analysis for the Classification of Plasma Samples from Control Subjects, Subjects with Lower Grade PCA and Subjects with Higher Grade PCA

[0151] Random Forest Analysis was carried out on data obtained in Example 3 from plasma samples to classify them as Non-cancer (Control) or Prostate cancer. The control samples were plasma obtained from subjects with a Gleason score (major) of 0 or from prostate cancer (PCA) subjects

with a Gleason score (major) 3. The analysis resulted in 65% correct classification of the plasma sample types. The control subjects were correctly classified 68% of the time while the subjects with prostate cancer (PCA) were correctly classified 60% of the time (Table 21).

TABLE 21

Confusion matrix for Control vs Lower Grade PCA in Plasma.

		Predicted		
		Control	PCA	error
Actual	Control	36	17	0.32
	PCA	17	26	0.40

OOB Error = 35%

[0152] Based on the OOB Error rate of 35%, the Random Forest model that was created could be used to predict whether a subject has a lower grade prostate cancer or does not have prostate cancer with about 65% accuracy from analysis of the levels of biomarkers in plasma from the subject.

[0153] The importance plot is shown in FIG. **5**. The important metabolites for this classification are listed in Table 22.

TABLE 22

Most important plasma biomarker metabolites to distinguish Control from Lower Grade PCA.

Metabolite	Library
Metabolite - 1185	35
5-oxoproline	50
IHWESASLLR	35
Metabolite - 3765	35
Metabolite - 2753	35
Hydroxyproline form of bradykinin	35
D-alany-D-alanine	35
Metabolite - 5437	50
Metabolite - 2256	35
Metabolite - 5366	50
Metabolite - 4611	50
Alpha keto glutarate	35
Metabolite - 3167	35
Alpha-tocopherol	50
Metabolite - 3377	35
Metabolite - 1127	35
Iminodiacetic acid	50
Trans-4-hydroxyproline	50
Metabolite - 2111	35
Metabolite - 2853	35
Metabolite - 2185	35
Metabolite - 3030	50
Metabolite - 3017	50
Metabolite - 1083	35
N-acetyl-L-valine	35
Metabolite - 1597	35
Creatinine	35
Isobar 36 includes D-sorbitol-6-phosphate, mannitol-1-phosphate	35
Metabolite - 2914	50
Pyridoxal-phosphate	35

[0154] Random Forest Analysis was also carried out on the biomarkers from plasma samples in Example 3 to classify them as control (Gleason score major 0) or higher grade prostate cancer (Gleason score major >=4, PCA). In this analysis resulted in 73% correct classification of the plasma sample types. The control and the higher grade prostate cancers were correctly classified 58% and 71% respectively (Table 23).

TABLE 23

Confusion matrix comparing plasma from subjects without prostate cancer (Control) and with higher grade prostate cancer (High PCA).

		Predicted		
		Control	High PCA	error
Actual	Control	36	17	0.32
	High PCA	2	13	0.07

OOB Error = 27%

[0155] Based on the OOB Error rate of 27%, the Random Forest model that was created could be used to predict whether a subject has a higher grade prostate cancer or does not have prostate cancer with about 63% accuracy from analysis of the levels of biomarkers in plasma from the subject.

[0156] The importance plot is shown in FIG. **6**. The important biomarker metabolites for this classification are listed in Table 24.

TABLE 24

Most important plasma biomarker metabolites to distinguish subjects without prostate cancer from those with higher grade prostate cancer.

Metabolite	Library
Metabolite - 1185	35
Metabolite - 3377	35
Metabolite - 2329	35
Metabolite - 3603	35
Metabolite - 1127	35
Metabolite - 3305	35
Metabolite - 2389	35
Metabolite - 3088	50
Trans-4-hydroxyproline	50
Metabolite - 1104	35
Isobar 17 includes arginine, N-alpha-acetyl-ornithine	35
Metabolite - 4769	50
Metabolite - 2141	35
Metabolite - 3030	50
Metabolite - 2867	35
Metabolite - 3707	35
Metabolite - 3098	50
Palmitoleic acid	50
Metabolite - 2711	35
Tetradecanoic acid	50
Metabolite - 2287	35
Metabolite - 2407	35
DL-indole-3-lactic acid	50
Metabolite - 1286	35
Heptadecanoic acid	50
Metabolite - 3033	50
5-oxoproline	50
Metabolite - 3576	35
Tartaric acid	35
Metabolite - 1831 possible Cl adduct of citrulline	35

[0157] Random Forest Analysis was also carried out on the biomarkers from plasma samples to classify them as lower grade prostate cancer (Gleason score major 3) or higher grade prostate cancer (Gleason score major >=4). This analysis resulted in 67% correct classification of the two cancer grades. The lower grade and the higher grade prostate cancers were correctly classified 65% and 71% respectively (Table 25).

TABLE 25

Confusion matrix classifying plasma from subjects with lower grade prostate cancer and higher grade prostate cancer.

		Predicted Grade		
		Low	High	error
Actual Grade	Low	28	15	0.35
	High	4	10	0.29

OOB Error = 33%

[0158] Based on the OOB Error rate of 33%, the Random Forest model that was created could be used to predict whether a subject has a lower grade prostate cancer or a higher grade prostate cancer with about 67% accuracy from analysis of the levels of biomarkers in plasma from the subject.

[0159] The importance plot is shown in FIG. **7**. The important metabolites for this classification are listed in Table 26.

TABLE 26

Most important plasma biomarker metabolites to distinguish subjects with lower grade prostate cancer and higher grade prostate cancer.

Metabolite	Library
Metabolite - 2329	35
Heptadecanoic acid	50
Metabolite - 3088	50
Metabolite - 3322	35
Palmitoleic acid	50
Isobar 6 includes valine and betaine	35
Tetradecanoic acid	50
Pyridoxal-phosphate	35
4-methyl-2-oxopentanoate	50
Metabolite - 3534	35
Metabolite - 2711	35
Isobar 17 includes arginine, N-alpha-acetyl-ornithine.	35

TABLE 26-continued

Most important plasma biomarker metabolites to distinguish subjects with lower grade prostate cancer and higher grade prostate cancer.

Metabolite	Library
Octadecanoic acid	50
Caffeine	35
Metabolite - 2389	35
Metabolite - 3377	35
Metabolite - 3305	35
Leucine	50
Metabolite - 2407	35
Metabolite - 3900	35
Metabolite - 3992 possible Cl adduct of formate dimmer	35
Metabolite - 3089	50
Trans-4-hydroxypyruvate	50
Metabolite - 5437	50
N-hexadecanoic acid	50
Paraxanthine	35
Metabolite - 3603	35
M2130	35
Oleic acid	50
Metabolite - 1286	35

Example 8

Analytical Characterization of Unnamed Biomarkers Compounds

[0160] Table 27 below includes analytical characteristics of each of the isobars and the unnamed metabolites listed in Tables 1-26 above. The table includes, for each listed Isobar and Metabolite, the retention time (RT), retention index (RI), mass, quant mass, and polarity obtained using the analytical methods described above. "Mass" refers to the mass of the C12 isotope of the parent ion used in quantification of the compound. The values for "Quant Mass" give an indication of the analytical method used for quantification: "Y" indicates GC-MS and "1" indicates LC-MS. "Polarity" indicates the polarity of the quantitative ion as being either positive (+) or negative (−).

TABLE 27

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Isobar 1 includes mannose, fructose, glucose, galactose, alpha-L-sorbopyranose, Inositol, D-allose	1.45	1481.0	215	1	−
Isobar 13 includes 5-keto-D-gluconic acid, 2-keto-L-gulonic acid, D-glucuronic acid	1.40	1530.0	193.1	1	−
Isobar 17 includes arginine, N-alpha-acetyl-ornithine	1.49	1620.0	175.2	1	+
Isobar 18 includes D-fructose 1-phosphate, beta-D-fructose 6-phosphate	1.33	1475.0	259.1	1	−
Isobar 19 includes D-saccharic acid, 2-deoxy-D-galactose, 2-deoxy-D-glucose, L-fucose, L-rhamnose	1.55	1700.0	209	1	−
Isobar 2 includes 3-amino-isobutyrate, 2-amino-butyrate, 4-aminobutanoic acid, dimethylglycine, choline	1.60	1671.0	104.1	1	+
Isobar 20 includes fumaric acid, 3-methyl-2-oxobutanoate	4.45	4800.0	160.9	1	−

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Isobar 21 includes gamma-aminobutyryl-L-histidine, L-anserine	1.59	1620.0	263.1	1	+
Isobar 22 includes glutamic acid, O-acetyl-L-serine	1.55	1635.0	148	1	+
Isobar 24 includes L-arabitol, adonitol	1.43	1545.0	153.1	1	+
Isobar 25 includes L-gulono-1,4-lactone, glucono-gamma-lactone	1.67	1615.0	222.9	1	–
Isobar 27 includes L-kynurenine, alpha-2-diamino-gamma-oxobenzenebutanoic acid	8.23	8470.0	209.1	1	+
Isobar 29 includes R,S-hydroorotic acid, 5,6-dihydroorotic acid	2.17	2095.0	157.1	1	–
Isobar 3 includes inositol 1-phosphate, mannose 6-phosphate, glucose 6-phosphate, D-mannose 1-phosphate, alpha-D-glucose 1-phosphate, alpha-D-galactose 1 phosphate	1.45	1467.0	304.7	1	–
Isobar 30 includes maltotetraose, stachyose	1.67	1770.0	710.8	1	–
Isobar 31 includes maltotriose, melezitose	1.64	1752.0	548.8	1	–
Isobar 32 includes N-acetyl-D-glucosamine, N-acetyl-D-mannosamine	1.57	1685.0	222	1	+
Isobar 36 includes D-sorbitol 6-phosphate, mannitol-1-phosphate	1.37	1470.0	261.1	1	–
Isobar 38 includes N-acetyl-L-methionine, 5-hydroxy-1H-indole-3-acetic acid	9.12	9220.0	192	1	+
Isobar 4 includes Gluconic acid, DL-arabinose, D-ribose, L-xylose, DL-lyxose, D-xylulose	1.52	1587.0	195	1	–
Isobar 40 includes Maltotetraose, stachyose	1.67	2282.0	710.8	1	–
Isobar 5 includes asparagine, ornithine	1.50	1395.0	133.1	1	+
Isobar 6 includes valine, betaine	2.13	2160.0	118.1	1	+
Isobar 9 includes sucrose, beta-D-lactose, D-trehalose, D-cellobiose, D-Maltose, palatinose, melibiose, alpha-D-lactose	1.60	1605.0	386.9	1	–
Metabolite - 1069 - possible dehydroepiandrosterone sulfate	12.55	14450.0	367.2	1	–
Metabolite - 1070	9.00	9169.0	378.3	1	+
Metabolite - 1085 - possible isolobinine or 4-aminoestra-1,3,5(10)-triene-3,17beta-diol	15.82	15964.0	288.1	1	+
Metabolite - 1086	4.56	4811.0	294.1	1	+
Metabolite - 1088	13.12	14225.0	369.1	1	–
Metabolite - 1104	2.43	2410.0	201	1	–
Metabolite - 1110	11.66	11841.0	269.1	1	–
Metabolite - 1111 - possible methylnitronitrosoguanidine or ethyl thiocarbamoylacetate	2.69	2700.0	148.1	1	+
Metabolite - 1113 - possible acetylcarnitine	4.91	5290.0	204.2	1	+
Metabolite - 1114	2.19	2198.0	104.1	1	+
Metabolite - 1116	4.20	4780.0	103.4	1	–
Metabolite - 1121	16.29	16429.0	303.3	1	+
Metabolite - 1122	4.45	4701.0	233.1	1	+
Metabolite - 1126	3.04	3188.0	175.1	1	+
Metabolite - 1127	12.18	12369.0	363.1	1	+
Metabolite - 1129	5.16	5419.0	260.1	1	+
Metabolite - 1133-retired Na adduct of EDTA	1.63	1636.0	315	1	+
Metabolite - 1142-possible 5-hydroxypentanoate or beta-hydroxyisovaleric acid	8.54	8739.0	163	1	–

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 1183	8.56	8765.0	365.8	1	+
Metabolite - 1185	8.70	9150.0	506.8	1	+
Metabolite - 1186	8.83	9000.0	529.6	1	+
Metabolite - 1187	8.80	9017.0	559.9	1	+
Metabolite - 1188	8.83	9017.0	619.9	1	+
Metabolite - 1203 - possible HXGXA	9.11	9288.0	510.2	1	+
Metabolite - 1208	15.33	15494.0	319.4	1	–
Metabolite - 1211 - possible IHWESASLLR	9.90	9800.0	606.5	1	+
Metabolite - 1215	8.96	9390.0	550.1	1	+
Metabolite - 1216	1.60	1631.4	343.9	1	–
Metabolite - 1220	15.24	15402.5	319.2	1	+
Metabolite - 1244	15.28	15436.8	343.4	1	–
Metabolite - 1248 - possible avermectin aglycone	8.06	8275.4	302.3	1	+
Metabolite - 1283	9.04	9244.5	434.8	1	+
Metabolite - 1286	14.41	14579.8	229	1	+
Metabolite - 1288	2.11	2120.5	302	1	–
Metabolite - 1289	8.96	9139.7	338.4	1	+
Metabolite - 1303	9.01	9178.0	527.8	1	+
Metabolite - 1323-possible p-cresol sulfate	9.31	10000.0	187	1	–
Metabolite - 1327 - possible bilirubin	13.22	13300.0	585.4	1	+
Metabolite - 1329	2.69	2791.0	210.1	1	+
Metabolite - 1330	10.67	11097.7	436.3	1	+
Metabolite - 1333	3.05	3794.0	321.9	1	+
Metabolite - 1335	8.74	9162.2	367.2	1	+
Metabolite - 1338	10.76	11193.0	241.1	1	–
Metabolite - 1342 - possible phenylacetylglutamine or formyl-N-acetyl-5-methoxykynurenamine	9.04	9459.4	265.2	1	+
Metabolite - 1349	3.50	3876.0	323.9	1	+
Metabolite - 1351	1.77	1936.5	177.9	1	+
Metabolite - 1364	10.35	10765.1	397.2	1	+
Metabolite - 1368	8.18	8607.4	184.1	1	+
Metabolite - 1383 - possible salicyluric glucuronide	8.66	9077.9	370.1	1	–
Metabolite - 1389 - possible glucuronide form of X-1359	13.62	14111.3	425.3	1	–
Metabolite - 1392	10.90	11350.3	415.2	1	+
Metabolite - 1394 - possible Losartan	12.28	12752.0	423.2	1	+
Metabolite - 1455	2.38	2350.0	131.1	1	+
Metabolite - 1457	1.59	1675.0	188.2	1	+
Metabolite - 1465	3.45	3600.0	162.1	1	+
Metabolite - 1496	1.53	1562.0	133	1	–
Metabolite - 1497	13.87	14031.5	332.2	1	+
Metabolite - 1498	1.56	1650.0	143.1	1	–
Metabolite - 1573	1.63	1669.0	170.9	1	–
Metabolite - 1575	2.25	2243.5	219.1	1	+
Metabolite - 1576	2.51	2530.0	247.1	1	+
Metabolite - 1593	2.67	2690.0	395.9	1	–
Metabolite - 1594	3.15	3325.0	263.1	1	+
Metabolite - 1595 - possible glutathione metabolite	3.14	3400.0	290.1	1	+
Metabolite - 1596	3.66	3902.0	185	1	–
Metabolite - 1597	3.66	4100.0	265.9	1	+
Metabolite - 1608	8.08	8253.0	348.1	1	–
Metabolite - 1609	8.31	8529.0	378	1	+
Metabolite - 1616	12.73	12910.3	331.2	1	+
Metabolite - 1653	16.84	16977.0	454.3	1	+
Metabolite - 1655	1.31	1374.0	107	1	+
Metabolite - 1656	1.46	1509.0	154.9	1	–
Metabolite - 1679	8.52	8705.8	283.1	1	–
Metabolite - 1680	8.50	8681.0	851.1	1	+
Metabolite - 1682	8.78	8961.0	339.1	1	–
Metabolite - 1713	2.73	3050.0	174	1	–
Metabolite - 1718	8.43	8390.0	457.9	1	+
Metabolite - 1817	1.37	1552.3	252	1	+
Metabolite - 1819	1.36	1539.6	244.8	1	–

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 1829	1.43	1600.0	135	1	–
Metabolite - 1831 - possible Cl adduct of citrulline	1.46	1638.7	209.9	1	–
Metabolite - 1834	1.64	1960.0	104	1	–
Metabolite - 1835	1.86	1999.3	152.1	1	–
Metabolite - 1836	2.10	2215.5	205.9	1	–
Metabolite - 1911	11.42	11799.6	464.1	1	+
Metabolite - 1914	10.35	10719.8	239.1	1	+
Metabolite - 1915	14.37	14798.6	507.2	1	–
Metabolite - 1963	13.15	13550.8	464.1	1	+
Metabolite - 1970	12.88	13271.2	852.9	1	+
Metabolite - 1974	5.93	6300.0	160.2	1	+
Metabolite - 1975	5.95	6093.0	344	1	+
Metabolite - 1977	3.56	4060.0	260.9	1	+
Metabolite - 1979 - Cl adduct of isobar 19	1.52	1690.3	199	1	–
Metabolite - 1980	13.20	13250.0	391.1	1	+
Metabolite - 1981	7.94	8150.0	158.1	1	+
Metabolite - 1988	11.14	11515.0	190.1	1	+
Metabolite - 2005	8.62	9048.0	232.1	1	+
Metabolite - 2027	1.56	1729.3	184.1	1	+
Metabolite - 2036	14.30	14300.0	616.3	1	+
Metabolite - 2041	13.84	14198.1	246.3	1	+
Metabolite - 2051	1.45	1634.0	309	1	+
Metabolite - 2053	1.35	1482.3	324.9	1	–
Metabolite - 2055	1.37	1502.0	269.9	1	+
Metabolite - 2056	1.37	1499.0	165.1	1	–
Metabolite - 2064	8.00	8312.0	193.2	1	+
Metabolite - 2072	1.57	1736.1	273.7	1	–
Metabolite - 2074	2.24	2380.9	280.1	1	+
Metabolite - 2075	2.71	2728.0	134.1	1	+
Metabolite - 2099	7.82	8135.9	469.2	1	+
Metabolite - 2100	1.33	1532.9	499	1	+
Metabolite - 2105	8.15	8442.0	433.6	1	+
Metabolite - 2108	8.76	8800.0	277.1	1	+
Metabolite - 2109	8.99	9266.0	321.1	1	+
Metabolite - 2111	9.19	9442.3	365.1	1	+
Metabolite - 2118	13.10	13367.8	547.1	1	+
Metabolite - 2121	14.18	14467.4	561.2	1	+
Metabolite - 2129	15.83	16363.2	526.3	1	+
Metabolite - 2130	16.28	16625.5	792.4	1	+
Metabolite - 2139	8.09	8500.0	218.1	1	+
Metabolite - 2141	9.39	9605.0	409.1	1	+
Metabolite - 2143	10.11	10327.0	585.1	1	+
Metabolite - 2150	13.27	13616.5	466.1	1	+
Metabolite - 2174	2.50	2569.0	250.1	1	+
Metabolite - 2175	3.84	4148.4	144	1	+
Metabolite - 2180	8.32	8663.0	490	1	+
Metabolite - 2181	8.37	8715.5	298	1	+
Metabolite - 2185	9.22	9499.4	246.2	1	+
Metabolite - 2194	13.65	13961.3	544.2	1	+
Metabolite - 2198	13.97	14284.8	530.1	1	+
Metabolite - 2212	15.96	16271.0	478.2	1	+
Metabolite - 2232	2.26	2318.0	754.8	1	–
Metabolite - 2237	10.14	10039.0	453.1	1	+
Metabolite - 2242	11.61	11926.0	254.3	1	+
Metabolite - 2249	14.21	14570.9	267.2	1	–
Metabolite - 2250	14.26	14668.4	286.3	1	+
Metabolite - 2254	1.53	1687.6	217.2	1	+
Metabolite - 2255 - hydroxyproline form of bradykinin	9.08	9394.0	539.1	1	+
Metabolite - 2256	9.93	9867.0	460.8	1	+
Metabolite - 2259	11.25	11586.0	383.2	1	–
Metabolite - 2269	10.36	10727.0	255.1	1	–
Metabolite - 2271	12.95	13348.8	413.2	1	–
Metabolite - 2272	7.96	8377.0	189.1	1	–
Metabolite - 2277	10.07	10457.0	201.1	1	–
Metabolite - 2279	12.38	12781.0	490.1	1	+
Metabolite - 2281	13.93	14325.1	505.2	1	–
Metabolite - 2285	2.00	2146.0	699.6	1	–
Metabolite - 2287	12.95	13335.6	502.8	1	+
Metabolite - 2292	2.40	2900.0	343.9	1	–

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 2293 - possible O-desmethylvenlafaxine glucuronide	8.86	9084.0	440.1	1	+
Metabolite - 2313	1.56	1685.6	352.9	1	–
Metabolite - 2316	8.82	9163.6	100.1	1	+
Metabolite - 2319	12.24	12626.0	367.2	1	–
Metabolite - 2323	7.55	7796.0	188.9	1	–
Metabolite - 2329	11.76	12177.6	541.2	1	–
Metabolite - 2347	13.65	14091.0	450.1	1	+
Metabolite - 2348	13.91	14293.5	448.3	1	+
Metabolite - 2366	8.47	8870.2	271	1	+
Metabolite - 2368	9.27	9615.5	573.2	1	–
Metabolite - 2370	16.13	16561.2	476.4	1	–
Metabolite - 2386	11.94	12320.3	539.2	1	–
Metabolite - 2387	8.55	9050.0	182.1	1	–
Metabolite - 2388	16.16	16900.0	259.1	1	–
Metabolite - 2389	1.49	1641.5	314.9	1	–
Metabolite - 2390	6.09	6410.0	517.4	1	+
Metabolite - 2391	10.14	10485.7	159.1	1	+
Metabolite - 2392	13.08	13460.4	379	1	–
Metabolite - 2406	14.69	15063.0	274.4	1	+
Metabolite - 2407	15.72	16127.6	637.3	1	+
Metabolite - 2466	9.19	8760.0	624.8	1	+
Metabolite - 2486	1.52	1667.0	635.7	1	–
Metabolite - 2506	14.05	14437.5	624.4	1	–
Metabolite - 2507	14.44	14843.0	481.4	1	–
Metabolite - 2546	1.63	1747.3	129.1	1	+
Metabolite - 2548 - possible Cl adduct of uric acid	5.97	6430.0	202.9	1	–
Metabolite - 2550 - possible Riluzole glucuronide	11.09	11490.0	411.1	1	+
Metabolite - 2557 - possible Pantoprazole metabolite	11.79	11968.1	354.2	1	+
Metabolite - 2558 - possible N1-methyl-2-pyridone-5-carboxamide and others	8.14	8800.0	153.1	1	+
Metabolite - 2567	7.79	8464.7	247.1	1	+
Metabolite - 2591	9.99	10189.4	279.3	1	+
Metabolite - 2592	10.59	10600.0	697.4	1	–
Metabolite - 2607	10.01	10354.0	578.2	1	+
Metabolite - 2686	1.40	1593.0	219	1	–
Metabolite - 2688	1.42	1614.0	182	1	–
Metabolite - 2690	1.62	1786.2	441.1	1	+
Metabolite - 2691	1.69	1835.8	294.1	1	–
Metabolite - 2698	3.88	4500.0	157	1	+
Metabolite - 2703	8.86	9054.8	384.1	1	+
Metabolite - 2706	10.20	10428.3	247.2	1	+
Metabolite - 2711	2.22	2300.0	123	1	+
Metabolite - 2724	4.12	4499.3	206.1	1	+
Metabolite - 2726	8.30	8854.0	375.2	1	+
Metabolite - 2752	2.92	3200.0	189.1	1	+
Metabolite - 2753	3.38	3750.0	147	1	+
Metabolite - 2766	8.09	8395.0	397	1	+
Metabolite - 2768	9.13	9340.0	322.8	1	–
Metabolite - 2774	3.53	3796.0	230.9	1	+
Metabolite - 2778	7.97	8251.5	376.1	1	+
Metabolite - 2781	10.01	10224.6	202.2	1	–
Metabolite - 2806	1.38	1491.0	185.1	1	+
Metabolite - 2807	8.74	8920.3	380.8	1	+
Metabolite - 2809	8.74	8923.5	699.8	1	+
Metabolite - 2821	6.80	7680.0	119.1	1	+
Metabolite - 2824	12.72	12903.0	773.2	1	+
Metabolite - 2827	8.70	8877.0	419.5	1	+
Metabolite - 2846	9.19	9369.8	596.6	1	+
Metabolite - 2849 - related to citric acid?	3.17	3375.0	482.6	1	–
Metabolite - 2853	8.74	8923.5	578.4	1	+
Metabolite - 2867	9.65	9908.0	235.3	1	+
Metabolite - 2888 - possible sulfated Rosiglitazone	9.87	10153.9	452	1	–
Metabolite - 2893 - possible demethylated Rosiglitazone	9.99	10292.8	344.1	1	+

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 2897	10.96	10100.0	245.2	1	–
Metabolite - 2898	11.17	11463.3	213.1	1	–
Metabolite - 2900	13.35	13544.7	621.8	1	+
Metabolite - 2914	3.75	1096.1	214	Y	+
Metabolite - 2915	3.77	1099.0	174	Y	+
Metabolite - 2924 2-hydroxy butanoic acid	4.38	1170.7	130.9	Y	+
Metabolite - 2973	4.74	1213.4	281	Y	+
Metabolite - 2974	4.76	1215.6	187	Y	+
Metabolite - 2978	5.01	1244.1	261.8	Y	+
Metabolite - 2981	5.21	1265.2	210.9	Y	+
Metabolite - 3002	6.74	1440.8	296.1	Y	+
Metabolite - 3003	6.79	1446.6	218.1	Y	+
Metabolite - 3004	6.81	1449.0	210.9	Y	+
Metabolite - 3012	7.17	1489.8	232	Y	+
Metabolite - 3014 - meso erythritol	7.43	1520.6	217.1	Y	+
Metabolite - 3016	7.58	1537.5	186	Y	+
Metabolite - 3017	7.61	1541.4	246.1	Y	+
Metabolite - 3019	7.74	1556.4	260.1	Y	+
Metabolite - 3020	7.81	1564.1	292	Y	+
Metabolite - 3022	7.98	1584.9	142	Y	+
Metabolite - 3023	8.04	1590.9	274.1	Y	+
Metabolite - 3025	8.11	1600.3	274.1	Y	+
Metabolite - 3027	8.21	1610.6	142	Y	+
Metabolite - 3030	8.62	1659.7	320	Y	+
Metabolite - 3033	8.88	1689.4	116.9	Y	+
Metabolite - 3034	8.92	1694.9	299	Y	+
Metabolite - 3040	9.27	1735.7	274.1	Y	+
Metabolite - 3044	1.52	1615.3	150.1	1	+
Metabolite - 3051	8.69	8878.6	835.8	1	+
Metabolite - 3053	8.83	9042.0	170.2	1	+
Metabolite - 3055 - possible NH3 adduct of hippuric acid	9.20	9443.0	196.8	1	+
Metabolite - 3056	9.19	9432.0	185.2	1	+
Metabolite - 3058	9.70	1786.9	335.1	Y	+
Metabolite - 3064	13.80	13968.2	516.1	1	+
Metabolite - 3067	10.02	1824.2	132	Y	+
Metabolite - 3073	10.17	1838.8	362.1	Y	+
Metabolite - 3074	10.22	1844.5	204.1	Y	+
Metabolite - 3075	10.36	1857.9	204	Y	+
Metabolite - 3077	10.44	1866.2	308.1	Y	+
Metabolite - 3078	10.65	1887.0	203.1	Y	+
Metabolite - 3081	10.89	1911.5	204	Y	+
Metabolite - 3085 = Inositol 2	11.04	1926.1	217	Y	+
Metabolite - 3086	11.16	1938.5	221	Y	+
Metabolite - 3088	11.23	1946.1	372.2	Y	+
Metabolite - 3089	11.28	1951.5	116.9	Y	+
Metabolite - 3090	11.31	1955.0	243.1	Y	+
Metabolite - 3091	11.41	1966.2	232.1	Y	+
Metabolite - 3093	11.50	1975.6	204	Y	+
Metabolite - 3094	11.55	1980.6	299	Y	+
Metabolite - 3097	11.64	1990.4	204	Y	+
Metabolite - 3098	11.75	2003.0	308	Y	+
Metabolite - 3099	11.77	2005.2	204	Y	+
Metabolite - 3101	11.93	2022.2	290	Y	+
Metabolite - 3102	11.99	2028.2	217.1	Y	+
Metabolite - 3103	12.09	2039.8	290.1	Y	+
Metabolite - 3108	12.24	2056.5	246	Y	+
Metabolite - 3109	12.56	2092.6	202.1	Y	+
Metabolite - 3113	12.73	2113.5	406.2	Y	+
Metabolite - 3123	8.97	8763.0	334	1	+
Metabolite - 3125	11.88	12095.0	187.1	1	+
Metabolite - 3127	8.61	8812.0	260.1	1	–
Metabolite - 3129	8.80	9012.0	337.1	1	+
Metabolite - 3130	9.09	9328.0	158.2	1	+
Metabolite - 3131	10.49	10770.0	192.9	1	+
Metabolite - 3132	10.14	10177.0	260.2	1	+
Metabolite - 3134	14.33	14487.3	483.1	1	+
Metabolite - 3135	14.96	15107.7	467.2	1	+
Metabolite - 3138	8.63	8749.0	229.2	1	+
Metabolite - 3139	8.82	8934.5	176.1	1	+

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 3143	9.81	10070.0	160.1	1	+
Metabolite - 3146	14.96	15105.0	499.1	1	–
Metabolite - 3160	12.11	12247.3	361	1	+
Metabolite - 3163 - possible methylcytidine, benserazide, Pyr-Gln-OH, or glycerophosphocholine	4.57	4837.5	258	1	+
Metabolite - 3165	8.38	8472.2	265	1	+
Metabolite - 3166	8.69	8850.0	394.2	1	+
Metabolite - 3167	8.86	8929.0	197.1	1	+
Metabolite - 3169	9.27	9384.5	250	1	+
Metabolite - 3176 - possible creatine	1.42	1750.0	132	1	+
Metabolite - 3178 - possible NH3 adduct of isobar 42	3.15	3670.0	210	1	+
Metabolite - 3180	4.14	4500.0	139	1	+
Metabolite - 3181	8.59	8621.4	165.1	1	+
Metabolite - 3183 - possible gamma-L-glutamyl-L-phenylalanine	9.37	9441.0	295.2	1	+
Metabolite - 3184	10.28	10364.4	223	1	+
Metabolite - 3189	12.06	12190.0	391	1	+
Metabolite - 3215	1.67	1733.8	173.8	1	+
Metabolite - 3216	1.68	1743.8	405.7	1	+
Metabolite - 3218	2.20	2257.0	148.1	1	+
Metabolite - 3220	3.73	4044.1	233.1	1	+
Metabolite - 3221	7.97	8050.0	204.1	1	+
Metabolite - 3231	3.08	3287.0	104.1	1	+
Metabolite - 3238	11.77	11827.4	220	1	+
Metabolite - 3243	11.34	11371.0	376.8	1	+
Metabolite - 3245	2.14	2168.3	816.7	1	–
Metabolite - 3246 - possible Ala-GLy, glycyl sarcosine, or ureido-butyric acid	4.73	5260.0	147.1	1	+
Metabolite - 3303	9.51	9799.5	170.1	1	+
Metabolite - 3309	8.37	8686.3	512.9	1	+
Metabolite - 3311	11.27	11597.0	308.2	1	+
Metabolite - 3313	8.10	8529.6	196.9	1	–
Metabolite - 3314	8.92	9143.5	264.8	1	+
Metabolite - 3317	8.42	8702.3	429.6	1	+
Metabolite - 3320 - possible pimpinellin or tetrahydroxybenzophenone	10.74	11300.0	245	1	–
Metabolite - 3322	11.82	12044.0	383.2	1	–
Metabolite - 3327	11.56	11784.0	385.3	1	–
Metabolite - 3364	9.06	9172.1	189	1	–
Metabolite - 3365	1.87	2068.3	115.1	1	+
Metabolite - 3370	8.11	8529.1	226.2	1	+
Metabolite - 3377	8.86	8963.9	270.2	1	+
Metabolite - 3379	1.51	1539.0	414.1	1	+
Metabolite - 3380	8.26	8602.1	164.1	1	+
Metabolite - 3381	2.31	2775.0	335	1	+
Metabolite - 3387	9.21	9377.5	463.1	1	+
Metabolite - 3390	8.14	8800.0	595.9	1	–
Metabolite - 3401	1.73	1863.3	131.1	1	+
Metabolite - 3402	8.90	8900.0	343.2	1	+
Metabolite - 3409	10.35	10636.4	259.1	1	+
Metabolite - 3426	10.71	11051.7	163	1	+
Metabolite - 3430 - possible gly-leu, acetyl-lys, ala-val	2.78	3319.7	189.1	1	+
Metabolite - 3433	8.41	8681.7	327.1	1	–
Metabolite - 3436	8.91	9157.1	157	1	–
Metabolite - 3440	9.99	10317.6	252.8	1	–
Metabolite - 3441	1.51	1565.4	515	1	+
Metabolite - 3443	9.23	9420.6	194.8	1	–
Metabolite - 3457	3.81	4193.3	212.9	1	+
Metabolite - 3474	15.67	16524.3	228.3	1	+
Metabolite - 3475	1.66	1711.9	365.2	1	+
Metabolite - 3476	1.65	1709.7	377	1	–
Metabolite - 3484	13.59	13710.7	983.4	1	+
Metabolite - 3489	3.26	3840.0	226	1	+
Metabolite - 3493	9.57	9912.3	335.9	1	+

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 3498	7.80	8368.7	279.1	1	+
Metabolite - 3507	10.01	10631.8	396.2	1	+
Metabolite - 3516	10.27	10895.1	411.3	1	+
Metabolite - 3517	10.27	10891.5	382.3	1	+
Metabolite - 3522	10.38	11005.0	362.3	1	+
Metabolite - 3526	10.42	11049.9	404.3	1	+
Metabolite - 3531	10.52	11400.0	384.3	1	+
Metabolite - 3534	10.54	11174.3	426.3	1	+
Metabolite - 3539	10.62	11259.8	435.2	1	+
Metabolite - 3543	10.67	11305.2	406.5	1	+
Metabolite - 3545	10.69	11331.3	448.4	1	+
Metabolite - 3554	10.91	11547.0	521.5	1	+
Metabolite - 3564	11.15	11792.0	471.7	1	+
Metabolite - 3576	1.38	1539.7	108	1	−
Metabolite - 3578	1.36	1525.2	296	1	+
Metabolite - 3603	8.41	8971.0	313.6	1	+
Metabolite - 3604	8.99	9551.9	214.2	1	−
Metabolite - 3605	9.59	10191.4	229.9	1	−
Metabolite - 3615	13.61	14343.6	868	1	+
Metabolite - 3624	10.36	10984.4	205.1	1	+
Metabolite - 3653 - Possible stachydrine	4.05	4700.0	144.1	1	+
Metabolite - 3659	10.28	10447.6	427.2	1	+
Metabolite - 3660	10.32	10622.4	387.1	1	+
Metabolite - 3667	9.17	9120.0	301.1	1	+
Metabolite - 3668	9.63	9536.0	379.1	1	+
Metabolite - 3670	10.23	10459.0	213	1	−
Metabolite - 3694	8.05	8483.7	364.1	1	+
Metabolite - 3698	8.31	8640.2	273.1	1	+
Metabolite - 3701	1.34	1455.6	141.2	1	+
Metabolite - 3706	9.93	9717.0	348	1	+
Metabolite - 3707	13.07	13339.5	241	1	+
Metabolite - 3708	1.66	1625.3	159.9	1	+
Metabolite - 3752	8.61	8750.4	276.1	1	+
Metabolite - 3754	9.02	9152.5	190.2	1	+
Metabolite - 3755	9.81	9800.0	418.2	1	+
Metabolite - 3756	10.02	10319.0	160.9	1	+
Metabolite - 3758	12.44	12714.0	309.1	1	−
Metabolite - 3761	8.34	8750.0	212	1	+
Metabolite - 3765	9.22	9630.0	467.8	1	+
Metabolite - 3771	1.68	1761.0	227	1	−
Metabolite - 3772	2.22	2274.0	109	1	+
Metabolite - 3773	2.26	2275.3	153	1	+
Metabolite - 3778	7.37	7200.0	307.3	1	+
Metabolite - 3783	1.37	1464.0	271.1	1	+
Metabolite - 3786	10.19	9787.3	241.2	1	−
Metabolite - 3800	2.00	2400.0	255	1	−
Metabolite - 3802	2.18	2200.0	137.1	1	+
Metabolite - 3803	2.22	2435.0	198.1	1	+
Metabolite - 3804	2.44	2694.5	259	1	+
Metabolite - 3805	2.49	2600.0	229.1	1	+
Metabolite - 3806	2.80	3155.3	212.1	1	+
Metabolite - 3808	3.28	3719.0	288.8	1	−
Metabolite - 3810	3.74	4500.0	188.1	1	−
Metabolite - 3813	3.81	4312.0	212.1	1	+
Metabolite - 3816	4.16	5310.0	173.1	1	−
Metabolite - 3817	4.73	4701.0	143.1	1	+
Metabolite - 3824	7.88	8197.7	202.1	1	+
Metabolite - 3828	8.20	8495.7	245.2	1	+
Metabolite - 3830	8.42	8725.0	189	1	−
Metabolite - 3832 - possible phenol sulfate	8.73	8995.8	173	1	−
Metabolite - 3833	8.81	9100.0	261.1	1	−
Metabolite - 3834 - Peptide	9.20	9285.0	372	1	+
Metabolite - 3837	9.26	9466.8	212.1	1	−
Metabolite - 3841	9.45	9638.0	245.1	1	−
Metabolite - 3843	9.54	9721.9	263.1	1	+
Metabolite - 3847	9.65	9816.6	206	1	+
Metabolite - 3848	9.73	9924.4	192	1	+
Metabolite - 3855	9.94	10142.0	243	1	−
Metabolite - 3873	9.94	10142.5	219.9	1	+
Metabolite - 3876	9.99	10195.0	273	1	−

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 3877	10.02	10227.0	211	1	–
Metabolite - 3878	10.44	10673.0	245	1	+
Metabolite - 3879	11.07	11336.5	243	1	–
Metabolite - 3886	1.77	1903.3	255	1	–
Metabolite - 3887	2.33	2576.0	224.1	1	–
Metabolite - 3893	3.26	3724.5	409	1	+
Metabolite - 3896	3.38	3868.0	245.2	1	+
Metabolite - 3898	3.57	4100.0	194.9	1	+
Metabolite - 3900	4.53	4871.7	173.1	1	–
Metabolite - 3908	7.98	8301.7	150	1	+
Metabolite - 3909	8.21	8497.8	160.1	1	+
Metabolite - 3911	8.27	8568.2	116.1	1	+
Metabolite - 3951	8.41	8705.4	367.1	1	+
Metabolite - 3952	8.70	9150.0	297.2	1	+
Metabolite - 3955	8.68	8951.7	357.1	1	–
Metabolite - 3957	9.54	9720.8	159.3	1	–
Metabolite - 3960	8.49	8744.1	417.1	1	+
Metabolite - 3963	10.53	10787.0	652.1	1	+
Metabolite - 3966	11.53	11830.0	491.2	1	+
Metabolite - 3968	1.39	1436.0	327.8	1	+
Metabolite - 3970	4.52	4906.0	226	1	+
Metabolite - 3972	6.16	6304.0	432.6	1	–
Metabolite - 3973	9.57	9765.0	296.9	1	+
Metabolite - 3974	10.12	10349.0	604.1	1	+
Metabolite - 3977	11.03	11312.0	187.1	1	–
Metabolite - 3980	8.16	8480.4	353.1	1	+
Metabolite - 3981	10.01	10234.0	431	1	+
Metabolite - 3984	12.76	13134.0	489.1	1	+
Metabolite - 3986	13.12	13514.5	489.1	1	+
Metabolite - 3992 - possible Cl adduct of Formate dimer	1.40	1600.0	129.2	1	–
Metabolite - 3994	1.63	1640.4	427	1	+
Metabolite - 3996	5.06	1236.0	176	Y	+
Metabolite - 3997	2.87	2876.0	564.9	1	–
Metabolite - 3998	5.22	1252.7	171	Y	+
Metabolite - 4002	5.69	1305.2	174	Y	+
Metabolite - 4003	3.94	4397.0	205	1	+
Metabolite - 4010	6.80	1432.8	218.1	Y	+
Metabolite - 4013	8.05	8399.5	547	1	–
Metabolite - 4014	7.17	1474.9	252	Y	+
Metabolite - 4015	7.37	1498.4	160	Y	+
Metabolite - 4017	7.62	1527.3	174	Y	+
Metabolite - 4018	8.35	8589.3	664	1	–
Metabolite - 4019	7.68	1534.5	174	Y	+
Metabolite - 4020	7.91	1561.5	220.1	Y	+
Metabolite - 4027	8.67	1650.2	274.1	Y	+
Metabolite - 4030 - possible glutethimide or securinine	11.88	12214.7	218.1	1	+
Metabolite - 4031 - possible norlevorphenol, isobutylphendienamide, amprolium	14.26	14607.0	244.2	1	+
Metabolite - 4032	8.95	1682.6	156.1	Y	+
Metabolite - 4042	10.23	1831.9	57.9	Y	+
Metabolite - 4043 lysine	10.29	1838.6	317.2	Y	+
Metabolite - 4046	10.80	1890.5	353.1	Y	+
Metabolite - 4051	11.56	1970.2	357.1	Y	+
Metabolite - 4053	11.87	2004.6	217.1	Y	+
Metabolite - 4058	12.46	2070.6	315.1	Y	+
Metabolite - 4075	13.27	2171.5	103	Y	+
Metabolite - 4078	16.49	16789.0	663.4	1	+
Metabolite - 4080	14.02	2270.2	299	Y	+
Metabolite - 4084	14.98	2393.9	441.3	Y	+
Metabolite - 4091 - possible gamma-glutamyl-glutamic acid	2.03	2084.7	277	1	+
Metabolite - 4092	5.23	5668.0	256.1	1	+
Metabolite - 4096 - possible gamma-glu-gly-leu	8.60	8763.6	318.2	1	+
Metabolite - 4112	8.46	8643.5	254.2	1	+
Metabolite - 4116	10.26	10582.0	272.2	1	+

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 4117 - possible propranolol or 2-heptyl-3-hydroxy-quinolone	14.70	15040.2	260.3	1	+
Metabolite - 4133	4.35	1108.9	198	Y	+
Metabolite - 4134	5.51	1239.0	60.9	Y	+
Metabolite - 4147	10.07	1767.1	290.2	Y	+
Metabolite - 4148	10.23	1786.3	249.2	Y	+
Metabolite - 4150	11.34	1910.4	306.3	Y	+
Metabolite - 4163	1.35	1444.1	225.3	1	+
Metabolite - 4167	11.03	10920.4	286.2	1	+
Metabolite - 4168	13.69	13793.3	686.4	1	+
Metabolite - 4196	12.14	2000.4	290.2	Y	+
Metabolite - 4234	10.57	10467.0	564.4	1	+
Metabolite - 4235	10.91	10789.1	652.3	1	+
Metabolite - 4238	9.29	9192.0	828.5	1	+
Metabolite - 4251	4.09	1130.7	217	Y	+
Metabolite - 4271	9.69	1777.4	419.2	Y	+
Metabolite - 4272	10.28	1840.2	669.3	Y	+
Metabolite - 4274	10.37	1857.0	158.1	Y	+
Metabolite - 4275	10.68	1887.0	271.1	Y	+
Metabolite - 4331	13.95	14040.0	679	1	+
Metabolite - 4354	3.90	1074.3	110	Y	+
Metabolite - 4355	6.76	1396.9	102	Y	+
Metabolite - 4360	9.15	1678.2	347.2	Y	+
Metabolite - 4361	9.40	1706.2	232.2	Y	+
Metabolite - 4362	10.02	1779.9	319.2	Y	+
Metabolite - 4365	11.05	1892.9	204	Y	+
Metabolite - 4428	7.92	8236.5	229.2	1	+
Metabolite - 4448	9.54	9831.4	362.3	1	+
Metabolite - 4494	6.45	1363.2	221	Y	+
Metabolite - 4495	6.59	1381.0	117	Y	+
Metabolite - 4496	6.76	1398.2	204	Y	+
Metabolite - 4497	7.05	1431.6	218.1	Y	+
Metabolite - 4498	7.06	1434.9	103	Y	+
Metabolite - 4499	7.22	1453.0	189	Y	+
Metabolite - 4500	7.30	1460.7	172	Y	+
Metabolite - 4501 imino diacetic acid	7.96	1538.4	232.1	Y	+
Metabolite - 4502	8.34	1581.3	273.1	Y	+
Metabolite - 4503	8.39	1589.0	227.2	Y	+
Metabolite - 4504	8.46	1597.1	244.1	Y	+
Metabolite - 4505	8.79	1633.4	285	Y	+
Metabolite - 4507	8.89	1644.9	245	Y	+
Metabolite - 4509	9.52	1720.6	204	Y	+
Metabolite - 4510	9.70	1740.1	254	Y	+
Metabolite - 4511	10.09	1788.4	206	Y	+
Metabolite - 4512	10.14	1790.7	345.1	Y	+
Metabolite - 4514	10.31	1812.3	342.2	Y	+
Metabolite - 4516	11.00	1886.5	217	Y	+
Metabolite - 4517	11.06	1892.7	217	Y	+
Metabolite - 4518	11.15	1902.4	295	Y	+
Metabolite - 4519	11.51	1941.8	193	Y	+
Metabolite - 4520	11.83	1978.1	325.1	Y	+
Metabolite - 4521	11.89	1983.4	383.1	Y	+
Metabolite - 4522	12.26	2025.4	217.1	Y	+
Metabolite - 4523	12.46	2047.0	258.1	Y	+
Metabolite - 4524	12.66	2071.3	210.1	Y	+
Metabolite - 4550	13.25	13286.2	568.2	1	+
Metabolite - 4567	3.50	3910.5	203.2	1	+
Metabolite - 4593	3.37	1011.1	170.9	Y	+
Metabolite - 4595	5.65	1274.4	130	Y	+
Metabolite - 4598	6.69	1392.2	169.9	Y	+
Metabolite - 4611	8.07	1546.6	292.1	Y	+
Metabolite - 4615	7.93	8250.0	222.1	1	+
Metabolite - 4617	8.39	8588.0	241.3	1	+
Metabolite - 4618	8.93	1651.1	349.2	Y	+
Metabolite - 4620	8.82	9001.0	312.1	1	+
Metabolite - 4624	10.01	1779.1	342.2	Y	+
Metabolite - 4628	10.11	1786.4	267.1	Y	+
Metabolite - 4629	10.29	1806.9	274.1	Y	+
Metabolite - 4632	10.59	1840.6	166	Y	+
Metabolite - 4633	10.69	1851.2	129	Y	+

TABLE 27-continued

Analytical Characteristics of Isobars and Unnamed Metabolites.

COMPOUND	RT	RI	MASS	QUANT_MASS	Polarity
Metabolite - 4634	11.00	1884.3	333.1	Y	+
Metabolite - 4635	11.19	1908.7	192.9	Y	+
Metabolite - 4636	11.50	1937.7	483.3	Y	+
Metabolite - 4637	11.95	1988.1	193	Y	+
Metabolite - 4638	12.25	2021.4	203.1	Y	+
Metabolite - 4639	12.87	2092.4	156.1	Y	+
Metabolite - 4649	5.33	5997.0	164.1	1	+
Metabolite - 4667	5.36	5652.8	320.1	1	–
Metabolite - 4706	8.92	9069.8	219	1	–
Metabolite - 4767	8.77	1626.2	116.9	Y	+
Metabolite - 4768	9.04	1661.7	279.1	Y	+
Metabolite - 4769	11.30	1916.4	156	Y	+
Metabolite - 4787	11.13	10895.5	289.4	1	+
Metabolite - 4791	10.29	1796.4	366.4	Y	+
Metabolite - 4795	14.83	2350.3	309	Y	+
Metabolite - 4796	3.53	1043.6	117	Y	+
Metabolite - 4806	4.20	1122.8	104.9	Y	+
Metabolite - 4866	9.18	9069.0	506.7	1	+
Metabolite - 4868 - confirmed Bradykinin	9.44	9356.0	531.2	1	+
Metabolite - 4869	10.25	10112.8	534.5	1	+
Metabolite - 4931	1.50	1659.5	431	1	+
Metabolite - 4986	11.56	1956.4	204.1	Y	+
Metabolite - 5086	9.51	9738.3	388.2	1	+
Metabolite - 5087	9.69	9924.9	432.3	1	+
Metabolite - 5089	9.85	10075.9	476.3	1	+
Metabolite - 5107	11.87	11986.0	516.7	1	+
Metabolite - 5108	12.00	12116.5	538.7	1	+
Metabolite - 5109	12.12	12248.5	560.7	1	+
Metabolite - 5110	12.24	12350.5	582.6	1	+
Metabolite - 5126	9.78	10017.0	358.3	1	+
Metabolite - 5128	3.12	3462.8	558	1	–
Metabolite - 5147	8.21	8508.0	262.2	1	+
Metabolite - 5166	12.90	12999.4	491.5	1	+
Metabolite - 5167	12.97	13070.0	506.2	1	+
Metabolite - 5170	8.93	9156.3	279.1	1	+
Metabolite - 5186	1.55	1709.7	163.9	1	+
Metabolite - 5187	3.53	3985.5	489.1	1	+
Metabolite - 5189	16.33	16650.0	528.2	1	+
Metabolite - 5207	7.41	1493.6	151	Y	+
Metabolite - 5209	8.10	1573.6	218.2	Y	+
Metabolite - 5210	8.47	1616.4	254.1	Y	+
Metabolite - 5211	8.77	1652.1	326.2	Y	+
Metabolite - 5212	8.88	1665.1	306.1	Y	+
Metabolite - 5213	8.97	1675.3	111.1	Y	+
Metabolite - 5214	11.54	1960.0	117	Y	+
Metabolite - 5215	11.98	2008.0	163	Y	+
Metabolite - 5226	3.73	1073.9	102	Y	+
Metabolite - 5227	6.59	1398.6	151	Y	+
Metabolite - 5228	6.97	1442.5	181.1	Y	+
Metabolite - 5229	7.13	1461.6	211.1	Y	+
Metabolite - 5232	12.19	2031.5	134	Y	+
Metabolite - 5346	8.33	1573.0	202	Y	+
Metabolite - 5349	10.10	1782.2	312.1	Y	+
Metabolite - 5366	12.49	2044.7	204	Y	+
Metabolite - 5403	5.92	1300.2	319	Y	+
Metabolite - 5419	9.05	1664.1	349.2	Y	+
Metabolite - 5427	10.67	1853.0	192.9	Y	+
Metabolite - 5437	12.17	2017.4	204	Y	+
Metabolite - 5489	8.10	1550.3	247.1	Y	+
Metabolite - 5847	12.35	2040.0	288.2	Y	+
Metabolite - 5906	7.82	1541.2	313.9	Y	+
Metabolite - 5907	8.69	1643.2	229.1	Y	+

[0161] While the invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one skilled in the art that various changes and modifications can be made without departing from the spirit and scope of the invention.

1. A method of diagnosing whether a subject has prostate cancer, comprising:

analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, wherein the one or more biomarkers are selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24, and

comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to diagnose whether the subject has prostate cancer.

2. The method of claim **1**, wherein the one or more biomarkers are selected from those biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having p values of less than 0.05 and/or those biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having q values of less than 0.10.

3. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of two or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

4. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of three or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

5. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of four or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

6. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of five or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

7. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of ten or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

8. The method of claim **1**, wherein the method comprises analyzing the biological sample to determine the level of fifteen or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24.

9. The method of claim **1**, wherein the biological sample is prostate tissue and the one or more biomarkers are selected from Tables 1 and/or 2.

10. The method of claim **1**, wherein the biological sample is blood plasma and the one or more biomarkers are selected from Tables 4, 6, 7, 22, 24, and/or 26.

11. The method of claim **1**, wherein the biological sample is urine and the one or more biomarkers are selected from Tables 5, 9, 10, and/or 18.

12. The method of claim **1**, wherein the sample is analyzed using one or more techniques selected from the group consisting of gas chromatography, liquid chromatography, mass spectrometry, ELISA, and antibody linkage.

13. A method of determining whether a subject is predisposed to developing prostate cancer, comprising:

analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, wherein the one or more biomarkers are selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24; and

comparing the level(s) of the one or more biomarkers in the sample to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers in order to determine whether the subject is predisposed to developing prostate cancer.

14. A method of monitoring progression/regression of prostate cancer in a subject comprising:

analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer in the sample, wherein the one or more biomarkers are selected from Tables 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 and the first sample is obtained from the subject at a first time point;

analyzing a second biological sample from a subject to determine the level(s) of the one or more biomarkers, wherein the second sample is obtained from the subject at a second time point; and

comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to monitor the progression/regression of prostate cancer in the subject.

15. The method of claim **14**, wherein the method further comprises comparing the level(s) of one or more biomarkers in the first sample, the level(s) of one or more biomarkers in the second sample, and/or the results of the comparison of the level(s) of the one or more biomarkers in the first and second samples to prostate cancer-positive and/or prostate cancer-negative reference levels of the one or more biomarkers.

16. A method of assessing the efficacy of a composition for treating prostate cancer comprising:

analyzing, from a subject having prostate cancer and currently or previously being treated with a composition, a biological sample to determine the level(s) of one or more biomarkers for prostate cancer selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and

comparing the level(s) of the one or more biomarkers in the sample to (a) levels of the one or more biomarkers in a previously-taken biological sample from the subject, wherein the previously-taken biological sample was obtained from the subject before being treated with the composition, (b) prostate cancer-positive reference levels of the one or more biomarkers, and/or (c) prostate cancer-negative reference levels of the one or more biomarkers.

17. A method for assessing the efficacy of a composition in treating prostate cancer, comprising:

analyzing a first biological sample from a subject to determine the level(s) of one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26 the first sample obtained from the subject at a first time point;

administering the composition to the subject;

analyzing a second biological sample from the subject to determine the level(s) of the one or more biomarkers, the second sample obtained from the subject at a second time point after administration of the composition;

comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the efficacy of the composition for treating prostate cancer.

18. A method of assessing the relative efficacy of two or more compositions for treating prostate cancer comprising:

analyzing, from a first subject having prostate cancer and currently or previously being treated with a first composition, a first biological sample to determine the level(s) of one or more biomarkers selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26;

analyzing, from a second subject having prostate cancer and currently or previously being treated with a second composition, a second biological sample to determine the level(s) of the one or more biomarkers; and

comparing the level(s) of one or more biomarkers in the first sample to the level(s) of the one or more biomarkers in the second sample in order to assess the relative efficacy of the first and second compositions for treating prostate cancer.

19. A method for screening a composition for activity in modulating one or more biomarkers of prostate cancer, comprising:

contacting one or more cells with a composition;

analyzing at least a portion of the one or more cells or a biological sample associated with the cells to determine the level(s) of one or more biomarkers of prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and

comparing the level(s) of the one or more biomarkers with predetermined standard levels for the biomarkers to determine whether the composition modulated the level (s) of the one or more biomarkers.

20. The method of claim **19**, wherein the predetermined standard levels for the biomarkers are level(s) of the one or more biomarkers in the one or more cells in the absence of the composition.

21. The method of claim **19**, wherein the predetermined standard levels for the biomarkers are level(s) of the one or more biomarkers in one or more control cells not contacted with the composition.

22. The method of claim **19**, wherein the method is conducted in vivo.

23. The method of claim **19**, wherein the method is conducted in vitro.

24. A method for identifying a potential drug target for prostate cancer comprising:

identifying one or more biochemical pathways associated with one or more biomarkers for prostate cancer selected from Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 18, 20, 22, 24, and/or 26; and

identifying a protein affecting at least one of the one or more identified biochemical pathways, the protein being a potential drug target for prostate cancer.

25. A method for treating a subject having prostate cancer comprising administering to the subject an effective amount of one or more biomarkers selected from Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 that are decreased in prostate cancer.

26. A method of distinguishing low grade prostate cancer from high grade prostate cancer in a subject having prostate cancer, comprising:

analyzing a biological sample from a subject to determine the level(s) of one or more biomarkers for low grade prostate cancer and/or high grade prostate cancer in the sample, wherein the one or more biomarkers are selected from Tables 3, 8, 11, 20, and/or 26 and

comparing the level(s) of the one or more biomarkers in the sample to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or to high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer in order to determine whether the subject has low grade or high grade prostate cancer.

27. The method of claim **26**, wherein the biological sample is prostate tissue and the one or more biomarkers are selected from Table 3.

28. The method of claim **26**, wherein the biological sample is blood plasma and the one or more biomarkers are selected from Table 8 and/or 26.

29. The method of claim **26**, wherein the biological sample is urine and the one or more biomarkers are selected from Table 11 and/or 20.

30. The method of claim **26**, wherein the one or more biomarkers are selected from those biomarkers in Tables 3, 8, 11, 20, and/or 26 having p values of less than 0.05 and/or those biomarkers in Tables 3, 8, 11, 20, and/or 26 having q values of less than 0.10.

31. The method of claim **1**, wherein the one or more biomarkers comprise one or more biomarkers selected from the group consisting of sarcosine, citric acid, spermine, and malic acid.

32. The method of claim **1**, wherein the comparing step comprises comparing a ratio of a level of one or more biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having p values of less than 0.05 and/or those biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having q values of less than 0.10 to prostate cancer-positive and/or prostate cancer-negative reference levels in order to diagnose whether the subject has prostate cancer.

33. The method of claim **32**, wherein the ratio of the level of one or more biomarkers comprises the level of a biomarker selected from the group consisting of sarcosine, spermine, and malic acid.

34. The method of claim **1**, wherein the comparing step comprises comparing a ratio of the levels of one or more biomarkers to prostate cancer-positive and/or prostate cancer-negative reference levels in order to diagnose whether the subject has prostate cancer, wherein the ratio of levels is selected from the group consisting of the ratio of the levels of sarcosine and citric acid, sarcosine and spermine, and citric acid and malic acid.

35. The method of claim **26**, wherein the one or more biomarkers comprise one or more biomarkers selected from the group consisting of sarcosine, citric acid, spermine, and malic acid.

36. The method of claim **26**, wherein the comparing step comprises comparing a ratio of the levels of one or more biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having p values of less than 0.05 and/or those biomarkers in Tables 1, 2, 4, 5, 6, 7, 9, 10, 13, 15, 18, 22, and/or 24 having q values of less than 0.10 to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer in order to determine whether the subject has low grade or high grade prostate cancer.

37. The method of claim **36**, wherein the ratio of the levels of one or more biomarkers comprises the level of a biomarker selected from the group consisting of sarcosine, spermine, and malic acid.

38. The method of claim **26**, wherein the comparing step comprises comparing a ratio of the levels of one or more biomarkers to low grade prostate cancer-positive reference levels that distinguish over high grade prostate cancer and/or high grade prostate cancer-positive reference levels that distinguish over low grade prostate cancer in order to determine whether the subject has low grade or high grade prostate cancer, wherein the ratio is selected from the group consisting of the ratio of levels of sarcosine and citric acid, sarcosine and spermine, and citric acid and malic acid.

* * * * *

专利名称(译)	前列腺癌的生物标志物及其使用方法		
公开(公告)号	US20100292331A1	公开(公告)日	2010-11-18
申请号	US12/441945	申请日	2007-09-18
[标]申请(专利权)人(译)	METABALON		
申请(专利权)人(译)	METABALON INC.		
当前申请(专利权)人(译)	METABOLON INC.		
[标]发明人	MITCHELL MATTHEW W BERGER ALVIN LAWTON KAY A		
发明人	MITCHELL, MATTHEW W. BERGER, ALVIN LAWTON, KAY A.		
IPC分类号	A61K31/195 C12Q1/02 G01N33/00 G01N33/53 A61K31/194 A61K31/132 A61P35/04		
CPC分类号	G01N33/57434 G01N33/6812 Y10T436/201666 Y10T436/173845 G01N33/68		
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其他公开文献	US8518650		
外部链接	Espacenet USPTO		

摘要(译)

提供了用于鉴定和评估生物化学和/或基因实体的套件的方法，所述生物化学和/或基因实体可用作用于早期预测前列腺癌，疾病分级，靶标识别/验证和药物功效监测的生物标记物。还提供了作为前列腺癌生物标志物的小分子实体套件。