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(54) **BIOMARKERS AND METHODS FOR PREDICTING PRETERM BIRTH**

BIOMARKER UND VERFAHREN ZUR VORHERSAGE EINER FRÜHGEBURT

BIOMARQUEURS ET PROCÉDÉS DE PRÉDICTION D'UNE NAISSANCE PRÉMATURÉE

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Description

[0001] The invention relates generally to the field of personalized medicine and, more specifically to compositions and methods for determining the probability for preterm birth in a pregnant female.

BACKGROUND

[0002] According to the World Heath Organization, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation) every year. In almost all countries with reliable data, preterm birth rates are increasing. *See,* World Health Organization; March of Dimes; The Partnership for Maternal, Newborn & Child Health; Save the Children, Born too soon: the global action report on preterm birth, ISBN 9789241503433(2012). An estimated 1 million babies die annually from preterm birth complications. Globally, preterm birth is the leading cause of newborn deaths (babies in the first four weeks of life) and the second leading cause of death after pneumonia in children under five years. Many survivors face a lifetime of disability, including learning disabilities and visual and hearing problems.

[0003] Across 184 countries with reliable data, the rate of preterm birth ranges from 5% to 18% of babies born. Blencowe et al., "National, regional and worldwide estimates of preterm birth." The Lancet, 9;379(9832):2162-72 (2012). While over 60% of preterm births occur in Africa and south Asia, preterm birth is nevertheless a global problem. Countries with the highest numbers include Brazil, India, Nigeria and the United States of America. Of the 11 countries with preterm birth rates over 15%, all but two are in sub-Saharan Africa. In the poorest countries, on average, 12% of babies are born too soon compared with 9% in higher-income countries. Within countries, poorer families are at higher risk. More than three-quarters of premature babies can be saved with feasible, cost-effective care, for example, antenatal steroid injections given to pregnant women at risk of preterm labour to strengthen the babies' lungs.

[0004] Infants born preterm are at greater risk than infants born at term for mortality and a variety of health and developmental problems. Complications include acute respiratory, gastrointestinal, immunologic, central nervous system, hearing, and vision problems, as well as longer-term motor, cognitive, visual, hearing, behavioral, social-emotional, health, and growth problems. The birth of a preterm infant can also bring considerable emotional and economic costs to families and have implications for public-sector services, such as health insurance, educational, and other social support systems. The greatest risk of mortality and morbidity is for those infants born at the earliest gestational ages. However, those infants born nearer to term represent the greatest number of infants born preterm and also experience more complications than infants born at term.

[0005] To prevent preterm birth in women who are less than 24 weeks pregnant with an ultrasound showing cervical opening, a surgical procedure known as cervical cerclage can be employed in which the cervix is stitched closed with strong sutures. For women less than 34 weeks pregnant and in active preterm labor, hospitalization may be necessary as well as the administration of medications to temporarily halt preterm labor an/or promote the fetal lung development. If a pregnant women is determined to be at risk for preterm birth, health care providers can implement various clinical strategies that may include preventive medications, for example, hydroxyprogesterone caproate (Makena) injections and/or vaginal progesterone gel, cervical pessaries, restrictions on sexual activity and/or other physical activities, and alterations of treatments for chronic conditions, such as diabetes and high blood pressure, that increase the risk of preterm labor.

[0006] There is a great need to identify and provide women at risk for preterm birth with proper antenatal care. Women identified as high-risk can be scheduled for more intensive antenatal surveillance and prophylactic interventions. Current strategies for risk assessment are based on the obstetric and medical history and clinical examination, but these strategies are only able to identify a small percentage of women who are at risk for preterm delivery. Reliable early identification of risk for preterm birth would enable planning appropriate monitoring and clinical management to prevent preterm delivery. Such monitoring and management might include: more frequent prenatal care visits, serial cervical length measurements, enhanced education regarding signs and symptoms of early preterm labor, lifestyle interventions for modifiable risk behaviors, cervical pessaries and progesterone treatment. Finally, reliable antenatal identification of risk for preterm birth also is crucial to cost-effective allocation of monitoring resources.

[0007] The present invention addresses this need by providing compositions and methods for determining whether a pregnant woman is at risk for preterm birth. Related advantages are provided as well.

SUMMARY

[0008] In a first aspect, the invention provides an isolated biomarker consisting of the sequence IALGGLLFPASNLR.

[0009] In a second aspect, the invention provides a method of determining probability for preterm birth or term birth in a pregnant female, the method comprising: detecting a measurable feature of each of one or more biomarkers in a biological sample obtained from said pregnant female, and analyzing said measurable feature to determine the probability for preterm birth or term birth in said pregnant female, wherein the one or more biomarkers comprise a biomarker consisting of the sequence IALGGLLFPASNLR; wherein said measurable feature is defined as the presence, absence, or concentration of a biomarker, or a fragment thereof; an altered structure, such as the presence or amount of a post-translational modification; or the presence of an altered conformation in comparison to the conformation of the biomarker in normal control subjects; and wherein the fragment comprises at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 consecutive amino acid residues.

[0010] In a third aspect, the invention provides a method of predicting gestational age at birth (GAB) or time to birth in a pregnant female, the method comprising: detecting a measurable feature of each of one or more biomarkers in a biological sample obtained from said pregnant female, and analyzing said measurable feature to predict GAB or time to birth in said pregnant female, wherein the one or more biomarkers comprise a biomarker consisting of the sequence IALGGLLFPASNLR; wherein said measurable feature is defined as the presence, absence, or concentration of a biomarker, or a fragment thereof; an altered structure, such as the presence or amount of a post-translational modification; or the presence of an altered conformation in comparison to the conformation of the biomarker in normal control subjects; and wherein the fragment comprises at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 consecutive amino acid residues.

[0011] In one embodiment, the method according to the second aspect further comprises:

(a) quantifying an amount of the one or more biomarkers; (b) multiplying said amount by a predetermined coefficient, (c) determining the probability for preterm birth in the pregnant female comprising adding said individual products to obtain a total risk score that corresponds to said probability. In another embodiment, said analyzing of said measurable feature initially comprises prediction of gestational age at birth (GAB) prior to said determining the probability for preterm birth; optionally wherein said prediction of the GAB is used to determine the probability for preterm birth.

[0012] In one embodiment, the method according to the third aspect further comprises:

(a) quantifying an amount of the one or more biomarkers; (b) multiplying and/or thresholding said amount by a predetermined coefficient; (c) determining the predicted GAB in the pregnant female, the determination comprising adding said individual products to obtain a total risk score that corresponds to said predicted GAB; and optionally (d) subtracting the estimated GA at time biological sample was obtained from the predicted GAB to predict time to birth in said pregnant female.

[0013] In one embodiment the methods further comprise calculating the probability for preterm birth or term birth, or GAB or time to birth in said pregnant female based on quantifying an amount of each of the one or more biomarkers. In another embodiment, said analyzing comprises a use of a predictive model; and, optionally, comparing the measurable feature with a reference feature. In another embodiment, said analyzing comprises using one or more of: a linear discriminant analysis model, a support vector machine classification algorithm, a recursive feature elimination model, a prediction analysis of microarray model, a logistic regression model, a multiple regression model, a survival model, a CART algorithm, a flex tree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, a machine learning algorithm, a penalized regression method, and a combination thereof.

[0014] In one embodiment, the biological sample is selected from the group consisting of whole blood, plasma, and serum.

[0015] In one embodiment, said quantifying comprises mass spectrometry (MS) or liquid chromatography-mass spectrometry (LC-MS). In another embodiment, said MS comprises multiple reaction monitoring (MRM) or selected reaction monitoring (SRM); optionally wherein said MRM (or SRM) comprises scheduled MRM (SRM). In another embodiment, said quantifying comprises an assay that utilizes a capture agent. In another embodiment, said capture agent is selected from the group consisting of an antibody, antibody fragment, nucleic acid-based protein binding reagent, small molecule or variant thereof. In another embodiment, said assay is selected from the group consisting of enzyme immunoassay (EIA), enzyme-linked immunosorbent assay (ELISA), and radioimmunoassay (RIA). In another embodiment, said quantifying further comprises mass spectrometry (MS) or co-immunoprecitipation-mass spectrometry (co-IP MS).

[0016] In a further embodiment, the methods comprise detecting one or more risk indicia; optionally wherein the one or more risk indicia are selected from the group consisting of age, prior pregnancy, history of previous low birth weight or preterm delivery, multiple 2nd trimester spontaneous abortion, prior first trimester induced abortion, familial and intergenerational factors, history of infertility, nulliparity, placental abnormalities, cervical and uterine anomalies, gestational bleeding, intrauterine growth restriction, in utero diethylstilbestrol exposure, multiple gestations, infant sex, short stature, low prepregnancy weight/low body mass index, diabetes, hypertension, hypothyroidism, asthma, education level, tobacco use, and urogenital infections.

[0017] The present invention provides biomarkers and methods for predicting the probability of preterm birth in a pregnant female.

[0018] Disclosed herein is a panel of isolated biomarkers comprising N of the biomarkers listed in Tables 1 through 63. In some instances, N is a number selected from the group consisting of 2 to 24. In additional instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. In additional instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR

[0019] In further instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0020] Disclosed herein is a panel of isolated biomarkers comprising N of the biomarkers listed in Tables 1 through 63. In some instances, N is a number selected from the group consisting of 2 to 24. In additional instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0021] Disclosed herein is a biomarker panel comprising at least two of the isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0022] Disclosed herein is a biomarker panel comprising at least two of the isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0023] Disclosed herein is a biomarker panel comprising lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), complement component C8 gamma chain (C8G or CO8G), complement component 1, q subcomponent, B chain (C1QB), fibrinogen beta chain (FIBB or FIB), C-reactive protein (CRP), inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), chorionic somatomammotropin hormone (CSH), and angiotensinogen (ANG or ANGT).

[0024] Disclosed herein is a biomarker panel comprising Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0025] Disclosed herein is a biomarker panel comprising at least two of the isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 51 and the biomarkers set forth in Table 53.

[0026] In some embodiments, the method of determining probability for preterm birth in a pregnant female further comprises detecting a measurable feature of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63 in a biological sample obtained from the pregnant female, and analyzing the measurable feature to determine the probability for preterm birth in the pregnant female. In some embodiments, the invention provides a method of predicting GAB, the method encompassing detecting a measurable feature of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63 in a biological sample obtained from a pregnant female, and analyzing said measurable feature to predict GAB.

[0027] In some embodiments, a measurable feature comprises fragments or derivatives of each of the N biomarkers selected from the biomarkers listed in Tables 1 through 63. In some embodiments of the disclosed methods detecting a measurable feature comprises quantifying an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, combinations or portions and/or derivatives thereof in a biological sample obtained from the pregnant female. In additional embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female further encompass detecting a measurable feature for one or more risk indicia associated with preterm birth.

[0028] In some embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of N biomarkers, wherein N is selected from the group consisting of 2 to 24. In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR. In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0029] In other embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0030] In other embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0031] In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), complement component C8 gamma chain (C8G or CO8G), complement component 1, q subcomponent, B chain (C1QB), fibrinogen beta chain (FIBB or FIB), C-reactive protein (CRP), inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), chorionic somatomammotropin hormone (CSH), and angiotensinogen (ANG or ANGT).

[0032] In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 51 and the biomarkers set forth in Table 53.

[0033] In some embodiments of the methods of determining probability for preterm birth in a pregnant female, the probability for preterm birth in the pregnant female is calculated based on the quantified amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63. In some embodiments, the disclosed methods for determining the probability of preterm birth encompass detecting and/or quantifying one or more biomarkers using mass sprectrometry, a capture agent or a combination thereof.

[0034] In some embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass an initial step of providing a biomarker panel comprising N of the biomarkers listed in Tables 1 through 63, including the biomarker of the invention. In some instances, the disclosed methods of determining probability for preterm birth in a pregnant female encompass an initial step of providing a biological sample from the pregnant female.

[0035] In some embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass communicating the probability to a health care provider. In additional embodiments, the communication informs a subsequent treatment decision for the pregnant female. In further embodiments, the treatment decision of one or more selected from the group of consisting of more frequent prenatal care visits, serial cervical length measurements, enhanced education regarding signs and symptoms of early preterm labor, lifestyle interventions for modifiable risk behaviors and progesterone treatment.

[0036] In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass analyzing the measurable feature of one or more isolated biomarkers using a predictive model. In some embodiments of the disclosed methods, a measurable feature of one or more isolated biomarkers is compared with a reference feature.

[0037] In additional embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass using one or more analyses selected from a linear discriminant analysis model, a support vector machine classification algorithm, a recursive feature elimination model, a prediction analysis of microarray model, a logistic regression model, a CART algorithm, a flex tree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, a machine learning algorithm, a penalized regression method, and a combination thereof. In one embodiment, the disclosed methods of determining probability for preterm birth in a pregnant female encompass logistic regression.

[0038] In some embodiments, the invention provides a method of determining probability for preterm birth in a pregnant female, the method encompassing quantifying in a biological sample obtained from the pregnant female an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63; multiplying the amount by a predetermined coefficient, and determining the probability for preterm birth in the pregnant female comprising adding the individual products to obtain a total risk score that corresponds to the probability

[0039] In additional embodiments, the invention provides a method of prediciting GAB, the method comprising: (a) quantifying in a biological sample obtained from said pregnant female an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention; (b) multiplying or thresholding said amount by a predetermined coefficient, (c) determining the predicted GAB birth in said pregnant female comprising adding said individual products to obtain a total risk score that corresponds to said predicted GAB.

[0040] In further embodiments, the invention provides a method of prediciting time to birth in a pregnant female, the method comprising: (a) obtaining a biological sample from said pregnant female; (b) quantifying an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention in said biological sample; (c) multiplying or thresholding said amount by a predetermined coefficient, (d) determining predicted GAB in said pregnant female comprising adding said individual products to obtain a total risk score that corresponds to said predicted GAB; and (e) substracting the estimated gestational age (GA) at time biological sample was obtained from the predicted GAB to predict time to birth in said pregnant female.

[0041] Other features and advantages of the invention will be apparent from the detailed description, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0042]

Figure 1. Scatterplot of actual gestational age at birth versus predicted gestational age from random forest regression model.

Figure 2. Distribution of predicted gestational age from random forest regression model versus actual gestational age at birth (GAB), where actual GAB is given in categories of (i) less than 37 weeks, (ii) 37 to 39 weeks, and (iii) 40 weeks or greater (peaks left to right, respectively).

DETAILED DESCRIPTION

[0043] The present disclosure is based, in part, on the discovery that certain proteins and peptides in biological samples obtained from a pregnant female are differentially expressed in pregnant females that have an increased risk of preterm birth relative to controls. The present disclosure is further based, in part, on the unexpected discovery that panels combining one or more of these proteins and peptides can be utilized in methods of determining the probability for preterm birth in a pregnant female with high sensitivity and specificity. These proteins and peptides disclosed herein serve as biomarkers for classifying test samples, predicting probability of preterm birth, predicting probability of term birth, predicting gestational age at birth (GAB), predicting time to birth and/or monitoring of progress of preventative therapy in a pregnant female, either individually or in a panel of biomarkers.

[0044] The disclosure provides biomarker panels, methods and kits for determining the probability for preterm birth in a pregnant female. One major advantage of the present disclosure is that risk of developing preterm birth can be assessed early during pregnancy so that appropriate monitoring and clinical management to prevent preterm delivery can be initiated in a timely fashion. The present invention is of particular benefit to females lacking any risk factors for preterm birth and who would not otherwise be identified and treated.

[0045] By way of example, the present disclosure includes methods for generating a result useful in determining probability for preterm birth in a pregnant female by obtaining a dataset associated with a sample, where the dataset at least includes quantitative data about biomarkers and panels of biomarkers that have been identified as predictive of preterm birth, and inputting the dataset into an analytic process that uses the dataset to generate a result useful in determining probability for preterm birth in a pregnant female. As described further below, this quantitative data can include amino acids, peptides, polypeptides, proteins, nucleotides, nucleic acids, nucleosides, sugars, fatty acids, steroids, metabolites, carbohydrates, lipids, hormones, antibodies, regions of interest that serve as surrogates for biological macromolecules and combinations thereof.

[0046] In addition to the specific biomarkers identified in this disclosure, for example, by accession number in a public database, sequence, or reference, the invention also contemplates use of biomarker variants that are at least 90% or at least 95% or at least 97% identical to the exemplified sequences and that are now known or later discovered and that have utility for the methods of the invention. These variants may represent polymorphisms, splice variants, mutations, and the like. In this regard, the instant specification discloses multiple art-known proteins in the context of the invention and provides exemplary accession numbers associated with one or more public databases as well as exemplary references to published journal articles relating to these art-known proteins. However, those skilled in the art appreciate that additional accession numbers and journal articles can easily be identified that can provide additional characteristics of the disclosed biomarkers and that the exemplified references are in no way limiting with regard to the disclosed biomarkers. As described herein, various techniques and reagents find use in the methods of the present invention. Suitable samples in the context of the present invention include, for example, blood, plasma, serum, amniotic fluid, vaginal secretions, saliva, and urine. In some embodiments, the biological sample is selected from the group consisting of whole blood, plasma, and serum. In a particular embodiment, the biological sample is serum. As described herein, biomarkers can be detected through a variety of assays and techniques known in the art. As further described herein, such assays include, without limitation, mass spectrometry (MS)-based assays, antibody-based assays as well as assays that combine aspects of the two.

[0047] Protein biomarkers associated with the probability for preterm birth in a pregnant female include, but are not limited to, one or more of the isolated biomarkers listed in Tables 1 through 63. In addition to the specific biomarkers, the disclosure further includes biomarker variants that are about 90%, about 95%, or about 97% identical to the exemplified sequences. Variants, as used herein, include polymorphisms, splice variants, mutations, and the like.

[0048] Additional markers can be selected from one or more risk indicia, including but not limited to, maternal characteristics, medical history, past pregnancy history, and obstetrical history. Such additional markers can include, for example, previous low birth weight or preterm delivery, multiple 2nd trimester spontaneous abortions, prior first trimester induced abortion, familial and intergenerational factors, history of infertility, nulliparity, placental abnormalities, cervical and uterine anomalies, short cervical length measurements, gestational bleeding, intrauterine growth restriction, in utero diethylstilbestrol exposure, multiple gestations, infant sex, short stature, low prepregnancy weight, low or high body mass index, diabetes, hypertension, urogenital infections (i.e. urinary tract infection), asthma, anxiety and depression, asthma, hypertension, hypothyroidism. Demographic risk indicia for preterm birth can include, for example, maternal age, race/ethnicity, single marital status, low socioeconomic status, maternal age, employment-related physical activity, occupational exposures and environment exposures and stress. Further risk indicia can include, inadequate prenatal care, cigarette smoking, use of marijuana and other illicit drugs, cocaine use, alcohol consumption, caffeine intake, maternal weight gain, dietary intake, sexual activity during late pregnancy and leisure-time physical activities. (Preterm Birth: Causes, Consequences, and Prevention, Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes; Behrman RE, Butler AS, editors. Washington (DC): National Academies Press (US); 2007). Additional risk indicia useful for as markers can be identified using learning algorithms known in the art, such as linear discriminant analysis, support vector machine classification, recursive feature elimination, prediction analysis of microarray, logistic regression, CART, FlexTree, LART, random forest, MART, and/or survival analysis regression, which are known to those of skill in the art and are further described herein.

[0049] Disclosed herein are panels of isolated biomarkers comprising N of the biomarkers selected from the group listed in Tables 1 through 63. In the disclosed panels of biomarkers N can be a number selected from the group consisting of 2 to 24. In the disclosed methods, the number of biomarkers that are detected and whose levels are determined, can be 1, or more than 1, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 12, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more. In certain instances the number of biomarkers that are detected, and whose levels are determined, can be 1, or more than 1, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, or more. The methods of this disclosure are useful for determining the probability for preterm birth in a pregnant female.

[0050] While certain of the biomarkers listed in Tables 1 through 63 are useful alone for determining the probability for preterm birth in a pregnant female, methods are also described herein for the grouping of multiple subsets of the biomarkers that are each useful as a panel of three or more biomarkers. In some instances the invention provides panels comprising N biomarkers, wherein N is at least three biomarkers. In other instances N is selected to be any number from 3-23 biomarkers.

[0051] In yet other instances N is selected to be any number from 2-5, 2-10, 2-15, 2-20, or 2-23. In other instances N is selected to be any number from 3-5, 3-10, 3-15, 3-20, or 3-23. In other instances N is selected to be any number from 4-5, 4-10, 4-15, 4-20, or 4-23. In other instances N is selected to be any number from 5-10, 5-15, 5-20, or 5-23. In other instances N is selected to be any number from 6-10, 6-15, 6-20, or 6-23. In other instances N is selected to be any number from 7-10, 7-15, 7-20, or 7-23. In other instances N is selected to be any number from 8-10, 8-15, 8-20, or 8-23. In other instances N is selected to be any number from 9-10, 9-15, 9-20, or 9-23. In other instances N is selected to be any number from 10-15, 10-20, or 10-23. It will be appreciated that N can be selected to encompass similar, but higher order, ranges.

[0052] In certain instances the panel of isolated biomarkers comprises one or more, two or more, three or more, four or more, or five isolated biomarkers comprising an amino acid sequence selected from AFTECCVVASQLR, ELLESYIDGR, ITLPDFTGDLR, TDAPDLPEENQAR and SFRPFVPR. In some instances the panel of isolated biomarkers comprises one or more, two or more, three or more, four or more, or five isolated biomarkers comprising an amino acid sequence selected from FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR.

[0053] In some instances, the panel of isolated biomarkers comprises one or more, two or more, or three of the isolated biomarkers consisting of an amino acid sequence selected from AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. In some instances the panel of isolated biomarkers comprises one or more, two or more, or three of the isolated biomarkers consisting of an amino acid sequence selected from FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR.

[0054] In some instances, the panel of isolated biomarkers comprises one or more, two or more, or three of the isolated biomarkers consisting of an amino acid sequence selected from the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0055] In some instances, the panel of isolated biomarkers comprises one or more peptides comprising a fragment from lipopolysaccharide-binding protein (LBP), Schumann et al., Science 249 (4975), 1429-1431 (1990) (UniProtKB/Swiss-Prot: P18428.3); prothrombin (THRB), Walz et al., Proc. Natl. Acad. Sci. U.S.A. 74 (5), 1969-1972(1977) (NCBI Reference Sequence: NP_000497.1); complement component C5 (C5 or CO5) Haviland, J. Immunol. 146 (1), 362-368 (1991) (GenBank: AAA51925.1); plasminogen (PLMN) Petersen et al., J. Biol. Chem. 265 (11), 6104-6111(1990) (NCBI Reference Sequences: NP_000292.1 NP_001161810.1); and complement component C8 gamma chain (C8G or CO8G), Haefliger et al., Mol. Immunol. 28 (1-2), 123-131 (1991) (NCBI Reference Sequence: NP_000597.2).

[0056] In some instances, the panel of isolated biomarkers comprises one or more peptides comprising a fragment from cell adhesion molecule with homology to complement component 1, q subcomponent, B chain (C1QB), Reid, Biochem. J. 179 (2), 367-371 (1979) (NCBI Reference Sequence: NP_000482.3); fibrinogen beta chain (FIBB or FIB); Watt et al., Biochemistry 18 (1), 68-76 (1979) (NCBI Reference Sequences: NP_001171670.1 and NP_005132.2); C-reactive protein (CRP), Oliveira et al., J. Biol. Chem. 254 (2), 489-502 (1979) (NCBI Reference Sequence: NP_000558.2); inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4) Kim et al., Mol. Biosyst. 7 (5), 1430-1440 (2011) (NCBI Reference Sequences: NP_001159921.1 and NP_002209.2); chorionic somatomammotropin hormone (CSH) Selby et al., J. Biol. Chem. 259 (21), 13131-13138 (1984) (NCBI Reference Sequence: NP_001308.1); and angiotensinogen (ANG or ANGT) Underwood et al., Metabolism 60(8):1150-7 (2011) (NCBI Reference Sequence: NP_000020.1).

[0057] In additional instances, the invention provides a panel of isolated biomarkers comprising N of the biomarkers listed in Tables 1 through 63. In some instances, N is a number selected from the group consisting of 2 to 24. In additional instances the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. In additional instances the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, ITLPDFTGDLR, TDAPDLPEENQAR and SFRPFVPR. In additional instances the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR.

[0058] In additional instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0059] In further instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G). In another instance the invention provides a biomarker panel comprising at least three isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0060] In further instances, the biomarker panel comprises at least two of the isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0061] In some instances, the biomarker panel comprises lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), complement component C8 gamma chain (C8G or CO8G), complement component 1, q subcomponent, B chain (C1QB), fibrinogen beta chain (FIBB or FIB), C-reactive protein (CRP), inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), chorionic somatomammotropin hormone (CSH), and angiotensinogen (ANG or ANGT). In some instances the biomarker panel comprises Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0062] In another instance, the biomarker panel comprises at least two isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), complement component C8 gamma chain (C8G or CO8G), complement component 1, q subcomponent, B chain (C1QB), fibrinogen beta chain (FIBB or FIB), C-reactive protein (CRP), inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), chorionic somatomammotropin hormone (CSH), and angiotensinogen (ANG or ANGT) and the biomarkers set forth in Tables 51 and 53.

[0063] In another instance, the biomarker panel comprises at least two isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0064] It must be noted that, as used in this specification and the appended claims, the singular forms "a", "an" and "the" include plural referents unless the content clearly dictates otherwise. Thus, for example, reference to "a biomarker" includes a mixture of two or more biomarkers, and the like.

[0065] The term "about," particularly in reference to a given quantity, is meant to encompass deviations of plus or minus five percent.

[0066] As used in this application, including the appended claims, the singular forms "a," "an," and "the" include plural references, unless the content clearly dictates otherwise, and are used interchangeably with "at least one" and "one or more."

[0067] As used herein, the terms "comprises," "comprising," "includes," "including," "contains," "containing," and any variations thereof, are intended to cover a non-exclusive inclusion, such that a process, method, product-by-process, or composition of matter that comprises, includes, or contains an element or list of elements does not include only those elements but can include other elements not expressly listed or inherent to such process, method, product-by-process, or composition of matter.

[0068] As used herein, the term "panel" refers to a composition, such as an array or a collection, comprising one or more biomarkers. The term can also refer to a profile or index of expression patterns of one or more biomarkers described herein. The number of biomarkers useful for a biomarker panel is based on the sensitivity and specificity value for the particular combination of biomarker values.

[0069] As used herein, and unless otherwise specified, the terms "isolated" and "purified" generally describes a composition of matter that has been removed from its native environment (e.g., the natural environment if it is naturally occurring), and thus is altered by the hand of man from its natural state. An isolated protein or nucleic acid is distinct from the way it exists in nature.

[0070] The term "biomarker" refers to a biological molecule, or a fragment of a biological molecule, the change and/or the detection of which can be correlated with a particular physical condition or state. The terms "marker" and "biomarker" are used interchangeably throughout the disclosure. For example, the biomarkers of the present invention are correlated with an increased likelihood of preterm birth. Such biomarkers include, but are not limited to, biological molecules comprising nucleotides, nucleic acids, nucleosides, amino acids, sugars, fatty acids, steroids, metabolites, peptides, polypeptides, proteins, carbohydrates, lipids, hormones, antibodies, regions of interest that serve as surrogates for biological macromolecules and combinations thereof (*e.g.*, glycoproteins, ribonucleoproteins, lipoproteins). The term also encompasses portions or fragments of a biological molecule, for example, peptide fragment of a protein or polypeptide that comprises at least 5 consecutive amino acid residues, at least 6 consecutive amino acid residues, at least 7 consecutive amino acid residues, at least 8 consecutive amino acid residues, at least 9 consecutive amino acid residues, at least 10 consecutive amino acid residues, at least 11 consecutive amino acid residues, at least 12 consecutive amino acid residues, at least 13 consecutive amino acid residues, at least 14 consecutive amino acid residues, at least 15 consecutive amino acid residues, at least 5 consecutive amino acid residues, at least 16 consecutive amino acid residues, at least 17consecutive amino acid residues, at least 18 consecutive amino acid residues, at least 19 consecutive amino acid residues, at least 20 consecutive amino acid residues, at least 21 consecutive amino acid residues, at least 22 consecutive amino acid residues, at least 23 consecutive amino acid residues, at least 24 consecutive amino acid residues, at least 25 consecutive amino acid residues,or more consecutive amino acid residues.

[0071] The invention also provides a method of determining probability for preterm birth in a pregnant female, the method comprising detecting a measurable feature of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention, in a biological sample obtained from the pregnant female, and analyzing the measurable feature to determine the probability for preterm birth in the pregnant female. As disclosed herein, a measurable feature comprises fragments or derivatives of each of said N biomarkers selected from the biomarkers listed in Tables 1 through 63. In some embodiments of the disclosed methods detecting a measurable feature comprises quantifying an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention, combinations or portions and/or derivatives thereof in a biological sample obtained from said pregnant female.

[0072] The invention further provides a method of predicting GAB, the method encompassing detecting a measurable feature of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention, in a biological sample obtained from a pregnant female, and analyzing the measurable feature to predict GAB.

[0073] The invention also provides a method of prediciting GAB, the method comprising: (a) quantifying in a biological sample obtained from the pregnant female an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention; (b) multiplying or thresholding the amount by a predetermined coefficient, (c) determining the predicted GAB birth in the pregnant female comprising adding the individual products to obtain a total risk score that corresponds to the predicted GAB.

[0074] The invention further provides a method of prediciting time to birth in a pregnant female, the method comprising: (a) obtaining a biological sample from the pregnant female; (b) quantifying an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention, in the biological sample; (c) multiplying or thresholding the amount by a predetermined coefficient, (d) determining predicted GAB in the pregnant female comprising adding the individual products to obtain a total risk score that corresponds to the predicted GAB; and (e) substracting the estimated gestational age (GA) at time biological sample was obtained from the predicted GAB to predict time to birth in said pregnant female. For methods directed to prediciting time to birth, it is understood that "birth" means birth following spontaneous onset of labor, with or without rupture of membranes.

[0075] Although described and exemplified with reference to methods of determining probability for preterm birth in a pregnant female, the present disclosure is similarly applicable to the methods of predicting GAB, the methods for predicting term birth, methods for determining the probability of term birth in a pregnant female as well methods of prediciting time to birth in a pregnant female. It will be apparent to one skilled in the art that each of the aforementioned methods has specific and substantial utilities and benefits with regard maternal-fetal health considerations.

[0076] In some embodiments, the method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of N biomarkers, wherein N is selected from the group consisting of 2 to 24. In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. In further embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGNLIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALD-LSLK, WWGGQPLWITATK, and LSETNR.

[0077] In additional embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 50 and the biomarkers set forth in Table 52.

[0078] In additional embodiments, the method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0079] In additional embodiments, the method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0080] In further embodiments, the disclosed method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), complement component C8 gamma chain (C8G or CO8G), complement component 1, q subcomponent, B chain (C1QB), fibrinogen beta chain (FIBB or FIB), C-reactive protein (CRP), inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), chorionic somatomammotropin hormone (CSH), and angiotensinogen (ANG or ANGT).

[0081] In further embodiments, the disclosed method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0082] In further embodiments, the disclosed method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0083] In further embodiments, the disclosed method of determining probability for preterm birth in a pregnant female and related methods disclosed herein further comprise detecting a measurable feature of each of at least two isolated biomarkers selected from the group consisting of the biomarkers set forth in Table 51 and the biomarkers set forth in Table 53.

[0084] As provided by the invention, the methods of determining probability for preterm birth in a pregnant female further encompass detecting a measurable feature for one or more risk indicia associated with preterm birth. In additional embodiments the risk indicia are selected form the group consisting of previous low birth weight or preterm delivery, multiple 2nd trimester spontaneous abortions, prior first trimester induced abortion, familial and intergenerational factors, history of infertility, nulliparity, placental abnormalities, cervical and uterine anomalies, gestational bleeding, intrauterine growth restriction, in utero diethylstilbestrol exposure, multiple gestations, infant sex, short stature, low prepregnancy weight, low or high body mass index, diabetes, hypertension, and urogenital infections.

[0085] A "measurable feature" is any property, characteristic or aspect that can be determined and correlated with the probability for preterm birth in a subject. The term further encompasses any property, characteristic or aspect that can be determined and correlated in connection with a prediction of GAB, a prediction of term birth, or a prediction of time to birth in a pregnant female. For a biomarker, such a measurable feature can include, for example, the presence, absence, or concentration of the biomarker, or a fragment thereof, in the biological sample, an altered structure, such as, for example, the presence or amount of a post-translational modification, such as oxidation at one or more positions on the amino acid sequence of the biomarker or, for example, the presence of an altered conformation in comparison to the conformation of the biomarker in normal control subjects, and/or the presence, amount, or altered structure of the biomarker as a part of a profile of more than one biomarker. In addition to biomarkers, measurable features can further include risk indicia including, for example, maternal characteristics, age, race, ethnicity, medical history, past pregnancy history, obstetrical history. For a risk indicium, a measurable feature can include, for example, previous low birth weight or preterm delivery, multiple 2nd trimester spontaneous abortions, prior first trimester induced abortion, familial and intergenerational factors, history of infertility, nulliparity, placental abnormalities, cervical and uterine anomalies, short cervical length meansurements, gestational bleeding, intrauterine growth restriction, in utero diethylstilbestrol exposure, multiple gestations, infant sex, short stature, low prepregnancy weight/low body mass index, diabetes, hypertension, urogenital infections, hypothyroidism,asthma, low educational attainment, cigarette smoking, drug use and alcohol consumption.

[0086] In some embodiments of the disclosed methods of determining probability for preterm birth in a pregnant female, the probability for preterm birth in the pregnant female is calculated based on the quantified amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention. In some embodiments, the disclosed methods for determining the probability of preterm birth encompass detecting and/or quantifying one or more biomarkers using mass sprectrometry, a capture agent or a combination thereof.

[0087] In some embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass an initial step of providing a biomarker panel comprising N of the biomarkers listed in Tables 1 through 63, including the biomarker of the invention. In some instances, the disclosed methods of determining probability for preterm birth in a pregnant female encompass an initial step of providing a biological sample from the pregnant female.

[0088] In some embodiments, the disclosed methods of determining probability for preterm birth in a pregnant female encompass communicating the probability to a health care provider. The disclosed of predicting GAB, the methods for predicting term birth, methods for determining the probability of term birth in a pregnant female as well methods of prediciting time to birth in a pregnant female similarly encompass communicating the probability to a health care provider. As stated above, although described and exemplified with reference to determining probability for preterm birth in a pregnant female, all embodiments described throughout this disclosure are similarly applicable to the methods of predicting GAB, the methods for predicting term birth, methods for determining the probability of term birth in a pregnant female as well methods of prediciting time to birth in a pregnant female. Specifically, he biomarkers and panels recited throughout this application with express reference to methods for preterm birth can also be used in methods for predicting GAB, the methods for predicting term birth, methods for determining the probability of term birth in a pregnant female as well methods of prediciting time to birth in a pregnant female. It will be apparent to one skilled in the art that each of the aforementioned methods have specific and substantial utilities and benefits with regard maternal-fetal health considerations.

[0089] In additional embodiments, the communication informs a subsequent treatment decision for the pregnant female. In some embodiments, the method of determining probability for preterm birth in a pregnant female encompasses the additional feature of expressing the probability as a risk score.

[0090] As used herein, the term "risk score" refers to a score that can be assigned based on comparing the amount of one or more biomarkers in a biological sample obtained from a pregnant female to a standard or reference score that represents an average amount of the one or more biomarkers calculated from biological samples obtained from a random pool of pregnant females. Because the level of a biomarker may not be static throughout pregnancy, a standard or reference score has to have been obtained for the gestational time point that corresponds to that of the pregnant female at the time the sample was taken. The standard or reference score can be predetermined and built into a predictor model such that the comparison is indirect rather than actually performed every time the probability is determined for a subject. A risk score can be a standard (*e.g.*, a number) or a threshold (*e.g.,* a line on a graph). The value of the risk score correlates to the deviation, upwards or downwards, from the average amount of the one or more biomarkers calculated from biological samples obtained from a random pool of pregnant females. In certain embodiments, if a risk score is greater than a standard or reference risk score, the pregnant female can have an increased likelihood of preterm birth. In some embodiments, the magnitude of a pregnant female's risk score, or the amount by which it exceeds a reference risk score, can be indicative of or correlated to that pregnant female's level of risk.

[0091] In the context of the present invention, the term "biological sample," encompasses any sample that is taken from pregnant female and contains one or more of the biomarkers listed in Tables 1 through 63 and includes the biomarker of the invention. Suitable samples in the context of the present invention include, for example, blood, plasma, serum, amniotic fluid, vaginal secretions, saliva, and urine. In some embodiments, the biological sample is selected from the group consisting of whole blood, plasma, and serum. In a particular embodiment, the biological sample is serum. As will be appreciated by those skilled in the art, a biological sample can include any fraction or component of blood, without limitation, T cells, monocytes, neutrophils, erythrocytes, platelets and microvesicles such as exosomes and exosome-like vesicles. In a particular embodiment, the biological sample is serum.

[0092] Preterm birth refers to delivery or birth at a gestational age less than 37 completed weeks. Other commonly used subcategories of preterm birth have been established and delineate moderately preterm (birth at 33 to 36 weeks of gestation), very preterm (birth at <33 weeks of gestation), and extremely preterm (birth at ≤28 weeks of gestation). With regard to the methods disclosed herein, those skilled in the art understand that the cut-offs that delineate preterm birth and term birth as well as the cut-offs that delineate subcategories of preterm birth can be adjusted in practicing the methods disclosed herein, for example, to maximize a particular health benefit. It is further understood that such adjustments are well within the skill set of individuals considered skilled in the art and encompassed within the scope of the inventions disclosed herein. Gestational age is a proxy for the extent of fetal development and the fetus's readiness for birth. Gestational age has typically been defined as the length of time from the date of the last normal menses to the date of birth. However, obstetric measures and ultrasound estimates also can aid in estimating gestational age. Preterm births have generally been classified into two separate subgroups. One, spontaneous preterm births are those occurring subsequent to spontaneous onset of preterm labor or preterm premature rupture of membranes regardless of subsequent labor augmentation or cesarean delivery. Two, indicated preterm births are those occurring following induction or cesarean section for one or more conditions that the woman's caregiver determines to threaten the health or life of the mother and/or fetus. In some cases the methods of the invention are directed to determining the probability for spontaneous preterm birth. In additional cases the methods of the invention are directed to predicting gestational birth.

[0093] As used herein, the term "estimated gestational age" or "estimated GA" refers to the GA determined based on the date of the last normal menses and additional obstetric measures, ultrasound estimates or other clinical parameters including, without limitation, those described in the preceding paragraph. In contrast the term "predicted gestational age at birth" or "predicted GAB" refers to the GAB determined based on the methods of the invention as dislosed herein. As used herein, "term birth" refers to birth at a gestational age equal or more than 37 completed weeks.

[0094] In some embodiments, the pregnant female is between 17 and 28 weeks of gestation at the time the biological sample is collected. In other embodiments, the pregnant female is between 16 and 29 weeks, between 17 and 28 weeks, between 18 and 27 weeks, between 19 and 26 weeks, between 20 and 25 weeks, between 21 and 24 weeks, or between 22 and 23 weeks of gestation at the time the biological sample is collected. In further embodiments, the the pregnant female is between about 17 and 22 weeks, between about 16 and 22 weeks between about 22 and 25 weeks, between about 13 and 25 weeks, between about 26 and 28, or between about 26 and 29 weeks of gestation at the time the biological sample is collected. Accordingly, the gestational age of a pregnant female at the time the biological sample is collected can be 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 weeks.

[0095] In some embodiments of the claimed methods the measurable feature comprises fragments or derivatives of each of the N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention. In additional embodiments of the claimed methods, detecting a measurable feature comprises quantifying an amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention, combinations or portions and/or derivatives thereof in a biological sample obtained from said pregnant female.

[0096] The term "amount" or "level" as used herein refers to a quantity of a biomarker that is detectable or measurable in a biological sample and/or control. The quantity of a biomarker can be, for example, a quantity of polypeptide, the quantity of nucleic acid, or the quantity of a fragment or surrogate. The term can alternatively include combinations thereof. The term "amount" or "level" of a biomarker is a measurable feature of that biomarker.

[0097] In some embodiments, calculating the probability for preterm birth in a pregnant female is based on the quantified amount of each of N biomarkers selected from the biomarkers listed in Tables 1 through 63, including the biomarker of the invention. Any existing, available or conventional separation, detection and quantification methods can be used herein to measure the presence or absence (*e.g.,* readout being present vs. absent; or detectable amount vs. undetectable amount) and/or quantity (*e.g.,* readout being an absolute or relative quantity, such as, for example, absolute or relative concentration) of biomarkers, peptides, polypeptides, proteins and/or fragments thereof and optionally of the one or more other biomarkers or fragments thereof in samples. In some embodiments, detection and/or quantification of one or more biomarkers comprises an assay that utilizes a capture agent. In further embodiments, the capture agent is an antibody, antibody fragment, nucleic acid-based protein binding reagent, small molecule or variant thereof. In additional embodiments, the assay is an enzyme immunoassay (EIA), enzyme-linked immunosorbent assay (ELISA), and radioimmunoassay (RIA). In some embodiments, detection and/or quantification of one or more biomarkers further comprises mass spectrometry (MS). In yet further embodiments, the mass spectrometry is co-immunoprecitipation-mass spectrometry (co-IP MS), where coimmunoprecipitation, a technique suitable for the isolation of whole protein complexes is followed by mass spectrometric analysis.

[0098] As used herein, the term "mass spectrometer" refers to a device able to volatilize/ionize analytes to form gas-phase ions and determine their absolute or relative molecular masses. Suitable methods of volatilization/ionization are matrix-assisted laser desorption ionization (MALDI), electrospray, laser/light, thermal, electrical, atomized/sprayed and the like, or combinations thereof. Suitable forms of mass spectrometry include, but are not limited to, ion trap instruments, quadrupole instruments, electrostatic and magnetic sector instruments, time of flight instruments, time of flight tandem mass spectrometer (TOF MS/MS), Fourier-transform mass spectrometers, Orbitraps and hybrid instruments composed of various combinations of these types of mass analyzers. These instruments can, in turn, be interfaced with a variety of other instruments that fractionate the samples (for example, liquid chromatography or solid-phase adsorption techniques based on chemical, or biological properties) and that ionize the samples for introduction into the mass spectrometer, including matrix-assisted laser desorption (MALDI), electrospray, or nanospray ionization (ESI) or combinations thereof.

[0099] Generally, any mass spectrometric (MS) technique that can provide precise information on the mass of peptides, and preferably also on fragmentation and/or (partial) amino acid sequence of selected peptides (*e.g.,* in tandem mass spectrometry, MS/MS; or in post source decay, TOF MS), can be used in the methods disclosed herein. Suitable peptide MS and MS/MS techniques and systems are well-known *per se* (see, e.g., Methods in Molecular Biology, vol. 146: "Mass Spectrometry of Proteins and Peptides", by Chapman, ed., Humana Press 2000; Biemann 1990. Methods Enzymol 193: 455-79; or Methods in Enzymology, vol. 402: "Biological Mass Spectrometry", by Burlingame, ed., Academic Press 2005) and can be used in practicing the methods disclosed herein. Accordingly, in some embodiments, the disclosed methods comprise performing quantitative MS to measure one or more biomarkers. Such quantitiative methods can be performed in an automated (Villanueva, et al., Nature Protocols (2006) 1(2):880-891) or semi-automated format. In particular embodiments, MS can be operably linked to a liquid chromatography device (LC-MS/MS or LC-MS) or gas chromatography device (GC-MS or GC-MS/MS). Other methods useful in this context include isotope-coded affinity tag (ICAT), tandem mass tags (TMT), or stable isotope labeling by amino acids in cell culture (SILAC), followed by chromatography and MS/MS.

[0100] As used herein, the terms "multiple reaction monitoring (MRM)" or "selected reaction monitoring (SRM)" refer to an MS-based quantification method that is particularly useful for quantifying analytes that are in low abundance. In an SRM experiment, a predefined precursor ion and one or more of its fragments are selected by the two mass filters of a triple quadrupole instrument and monitored over time for precise quantification. Multiple SRM precursor and fragment ion pairs can be measured within the same experiment on the chromatographic time scale by rapidly toggling between the different precursor/fragment pairs to perform an MRM experiment. A series of transitions (precursor/fragment ion pairs) in combination with the retention time of the targeted analyte (*e.g.,* peptide or small molecule such as chemical entity, steroid, hormone) can constitute a definitive assay. A large number of analytes can be quantified during a single LC-MS experiment. The term "scheduled," or "dynamic" in reference to MRM or SRM, refers to a variation of the assay wherein the transitions for a particular analyte are only acquired in a time window around the expected retention time, significantly increasing the number of analytes that can be detected and quantified in a single LC-MS experiment and contributing to the selectivity of the test, as retention time is a property dependent on the physical nature of the analyte. A single analyte can also be monitored with more than one transition. Finally, included in the assay can be standards that correspond to the analytes of interest (*e.g.,* same amino acid sequence), but differ by the inclusion of stable isotopes. Stable isotopic standards (SIS) can be incorporated into the assay at precise levels and used to quantify the corresponding unknown analyte. An additional level of specificity is contributed by the co-elution of the unknown analyte and its corresponding SIS and properties of their transitions (*e.g.,* the similarity in the ratio of the level of two transitions of the unknown and the ratio of the two transitions of its corresponding SIS).

[0101] Mass spectrometry assays, instruments and systems suitable for biomarker peptide analysis can include, without limitation, matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) MS; MALDI-TOF post-source-decay (PSD); MALDI-TOF/TOF; surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF) MS; electrospray ionization mass spectrometry (ESI-MS); ESI-MS/MS; ESI-MS/$(MS)_n$ (n is an integer greater than zero); ESI 3D or linear (2D) ion trap MS; ESI triple quadrupole MS; ESI quadrupole orthogonal TOF (Q-TOF); ESI Fourier transform MS systems; desorption/ionization on silicon (DIOS); secondary ion mass spectrometry (SIMS); atmospheric pressure chemical ionization mass spectrometry (APCI-MS); APCI-MS/MS; APCI- $(MS)_n$; ion mobility spectrometry (IMS); inductively coupled plasma mass spectrometry (ICP-MS)atmospheric pressure photoionization mass spectrometry (APPI-MS); APPI-MS/MS; and APPI- $(MS)_n$. Peptide ion fragmentation in tandem MS (MS/MS) arrangements can be achieved using manners established in the art, such as, e.g., collision induced dissociation (CID). As described herein, detection and quantification of biomarkers by mass spectrometry can involve multiple reaction monitoring (MRM), such as described among others by Kuhn et al. Proteomics 4: 1175-86 (2004). Scheduled multiple-reaction-monitoring (Scheduled MRM) mode acquisition during LC-MS/MS analysis enhances the sensitivity and accuracy of peptide quantitation. Anderson and Hunter, Molecular and Cellular Proteomics 5(4):573 (2006). As described herein, mass spectrometry-based assays can be advantageously combined with upstream peptide or protein separation or fractionation methods, such as for example with the chromatographic and other methods described herein below. As further described herein, shotgun quantitative proteomics can be combined with SRM/MRM-based assays for high-throughput identification and verification of prognostic biomarkers of preterm birth.

[0102] A person skilled in the art will appreciate that a number of methods can be used to determine the amount of a biomarker, including mass spectrometry approaches, such as MS/MS, LC-MS/MS, multiple reaction monitoring (MRM) or SRM and production monitoring (PIM) and also including antibody based methods such as immunoassays such as Western blots, enzyme-linked immunosorbant assay (ELISA), immunoprecipitation, immunohistochemistry, immunofluorescence, radioimmunoassay, dot blotting, and FACS. Accordingly, in some embodiments, determining the level of the at least one biomarker comprises using an immunoassay and/or mass spectrometric methods. In additional embodiments, the mass spectrometric methods are selected from MS, MS/MS, LC-MS/MS, SRM, PIM, and other such methods that are known in the art. In other embodiments, LC-MS/MS further comprises ID LC-MS/MS, 2D LC-MS/MS or 3D LC-MS/MS. Immunoassay techniques and protocols are generally known to those skilled in the art (Price and Newman, Principles and Practice of Immunoassay, 2nd Edition, Grove's Dictionaries, 1997; and Gosling, Immunoassays: A Practical Approach, Oxford University Press, 2000.) A variety of immunoassay techniques, including competitive and non-competitive immunoassays, can be used (Self et al., Curr. Opin. Biotechnol., 7:60-65 (1996).

[0103] In further embodiments, the immunoassay is selected from Western blot, ELISA, immunoprecipitation, immunohistochemistry, immunofluorescence, radioimmunoassay (RIA), dot blotting, and FACS. In certain embodiments, the immunoassay is an ELISA. In yet a further embodiment, the ELISA is direct ELISA (enzyme-linked immunosorbent assay), indirect ELISA, sandwich ELISA, competitive ELISA, multiplex ELISA, ELISPOT technologies, and other similar techniques known in the art. Principles of these immunoassay methods are known in the art, for example John R. Crowther, The ELISA Guidebook, 1st ed., Humana Press 2000, ISBN 0896037282. Typically ELISAs are performed with antibodies but they can be performed with any capture agents that bind specifically to one or more biomarkers of the invention and that can be detected. Multiplex ELISA allows simultaneous detection of two or more analytes within a single compartment (e.g., microplate well) usually at a plurality of array addresses (Nielsen and Geierstanger 2004. J Immunol Methods 290: 107-20 (2004) and Ling et al. 2007. Expert Rev Mol Diagn 7: 87-98 (2007)).

[0104] In some embodiments, Radioimmunoassay (RIA) can be used to detect one or more biomarkers in the methods of the invention. RIA is a competition-based assay that is well known in the art and involves mixing known quantities of radioactavely-labelled (e.g.,^{125}I or ^{131}I-labelled) target analyte with antibody specific for the analyte, then adding non-labelled analyte from a sample and measuring the amount of labelled analyte that is displaced (see, e.g., An Introduction to Radioimmunoassay and Related Techniques, by Chard T, ed., Elsevier Science 1995, ISBN 0444821198 for guidance).

[0105] A detectable label can be used in the assays described herein for direct or indirect detection of the biomarkers in the methods of the invention. A wide variety of detectable labels can be used, with the choice of label depending on the sensitivity required, ease of conjugation with the antibody, stability requirements, and available instrumentation and disposal provisions. Those skilled in the art are familiar with selection of a suitable detectable label based on the assay detection of the biomarkers in the methods of the invention. Suitable detectable labels include, but are not limited to, fluorescent dyes (*e.g.,* fluorescein, fluorescein isothiocyanate (FITC), Oregon Green™, rhodamine, Texas red, tetrarhodimine isothiocynate (TRITC), Cy3, Cy5, etc.), fluorescent markers (*e.g.,* green fluorescent protein (GFP), phycoerythrin, etc.), enzymes (*e.g.,* luciferase, horseradish peroxidase, alkaline phosphatase, etc.), nanoparticles, biotin, digoxigenin, metals, and the like.

[0106] For mass-sectrometry based analysis, differential tagging with isotopic reagents, *e.g.,* isotope-coded affinity tags (ICAT) or the more recent variation that uses isobaric tagging reagents, iTRAQ (Applied Biosystems, Foster City, Calif.), or tandem mass tags, TMT, (Thermo Scientific, Rockford, IL), followed by multidimensional liquid chromatography (LC) and tandem mass spectrometry (MS/MS) analysis can provide a further methodology in practicing the methods of the inventon.

[0107] A chemiluminescence assay using a chemiluminescent antibody can be used for sensitive, non-radioactive detection of protein levels. An antibody labeled with fluorochrome also can be suitable. Examples of fluorochromes include, without limitation, DAPI, fluorescein, Hoechst 33258, R-phycocyanin, B-phycoerythrin, R-phycoerythrin, rhodamine, Texas red, and lissamine. Indirect labels include various enzymes well known in the art, such as horseradish peroxidase (HRP), alkaline phosphatase (AP), beta-galactosidase, urease, and the like. Detection systems using suitable substrates for horseradish-peroxidase, alkaline phosphatase, beta-galactosidase are well known in the art.

[0108] A signal from the direct or indirect label can be analyzed, for example, using a spectrophotometer to detect color from a chromogenic substrate; a radiation counter to detect radiation such as a gamma counter for detection of ^{125}I; or a fluorometer to detect fluorescence in the presence of light of a certain wavelength. For detection of enzyme-linked antibodies, a quantitative analysis can be made using a spectrophotometer such as an EMAX Microplate Reader (Molecular Devices; Menlo Park, Calif.) in accordance with the manufacturer's instructions. If desired, assays used to practice the invention can be automated or performed robotically, and the signal from multiple samples can be detected simultaneously.

[0109] In some embodiments, the methods described herein encompass quantification of the biomarkers using mass spectrometry (MS). In further embodiments, the mass spectrometry can be liquid chromatography-mass spectrometry (LC-MS), multiple reaction monitoring (MRM) or selected reaction monitoring (SRM). In additional embodiments, the MRM or SRM can further encompass scheduled MRM or scheduled SRM.

[0110] As described above, chromatography can also be used in practicing the methods of the invention. Chromatography encompasses methods for separating chemical substances and generally involves a process in which a mixture of analytes is carried by a moving stream of liquid or gas ("mobile phase") and separated into components as a result of differential distribution of the analytes as they flow around or over a stationary liquid or solid phase ("stationary phase"), between the mobile phase and said stationary phase. The stationary phase can be usually a finely divided solid, a sheet of filter material, or a thin film of a liquid on the surface of a solid, or the like. Chromatography is well understood by those skilled in the art as a technique applicable for the separation of chemical compounds of biological origin, such as, *e.g.,* amino acids, proteins, fragments of proteins or peptides, *etc.*

[0111] Chromatography can be columnar (*i.e.,* wherein the stationary phase is deposited or packed in a column), preferably liquid chromatography, and yet more preferably high-performance liquid chromatography (HPLC), or ultra high performance/pressure liquid chromatography (UHPLC). Particulars of chromatography are well known in the art (Bidlingmeyer, Practical HPLC Methodology and Applications, John Wiley & Sons Inc., 1993). Exemplary types of chromatography include, without limitation, high-performance liquid chromatography (HPLC), UHPLC, normal phase HPLC (NP-HPLC), reversed phase HPLC (RP-HPLC), ion exchange chromatography (IEC), such as cation or anion exchange chromatography, hydrophilic interaction chromatography (HILIC), hydrophobic interaction chromatography (HIC), size exclusion chromatography (SEC) including gel filtration chromatography or gel permeation chromatography, chromatofocusing, affinity chromatography such as immuno-affinity, immobilised metal affinity chromatography, and the like. Chromatography, including single-, two- or more-dimensional chromatography, can be used as a peptide fractionation method in conjunction with a further peptide analysis method, such as for example, with a downstream mass spectrometry analysis as described elsewhere in this specification.

[0112] Further peptide or polypeptide separation, identification or quantification methods can be used, optionally in conjunction with any of the above described analysis methods, for measuring biomarkers in the present disclosure. Such methods include, without limitation, chemical extraction partitioning, isoelectric focusing (IEF) including capillary isoelectric focusing (CIEF), capillary isotachophoresis (CITP), capillary electrochromatography (CEC), and the like, one-dimensional polyacrylamide gel electrophoresis (PAGE), two-dimensional polyacrylamide gel electrophoresis (2D-PAGE), capillary gel electrophoresis (CGE), capillary zone electrophoresis (CZE), micellar electrokinetic chromatography (MEKC), free flow electrophoresis (FFE), etc.

[0113] In the context of the invention, the term "capture agent" refers to a compound that can specifically bind to a target, in particular a biomarker. The term includes antibodies, antibody fragments, nucleic acid-based protein binding reagents (*e.g.* aptamers, Slow Off-rate Modified Aptamers (SOMAmer™)), protein-capture agents, natural ligands (*i.e.* a hormone for its receptor or vice versa), small molecules or variants thereof.

[0114] Capture agents can be configured to specifically bind to a target, in particular a biomarker. Capture agents can include but are not limited to organic molecules, such as polypeptides, polynucleotides and other non polymeric molecules that are identifiable to a skilled person. In the embodiments disclosed herein, capture agents include any agent that can be used to detect, purify, isolate, or enrich a target, in particular a biomarker. Any art-known affinity capture technologies can be used to selectively isolate and enrich/concentrate biomarkers that are components of complex mixtures of biological media for use in the disclosed methods.

[0115] Antibody capture agents that specifically bind to a biomarker can be prepared using any suitable methods known in the art. *See, e.g.,* Coligan, Current Protocols in Immunology (1991); Harlow & Lane, Antibodies: A Laboratory Manual (1988); Goding, Monoclonal Antibodies: Principles and Practice (2d ed. 1986). Antibody capture agents can be any immunoglobulin or derivative therof, whether natural or wholly or partially synthetically produced. All derivatives thereof which maintain specific binding ability are also included in the term. Antibody capture agents have a binding domain that is homologous or largely homologous to an immunoglobulin binding domain and can be derived from natural sources, or partly or wholly synthetically produced. Antibody capture agents can be monoclonal or polyclonal antibodies. In some embodiments, an antibody is a single chain antibody. Those of ordinary skill in the art will appreciate that antibodies can be provided in any of a variety of forms including, for example, humanized, partially humanized, chimeric, chimeric humanized, *etc.* Antibody capture agents can be antibody fragments including, but not limited to, Fab, Fab', F(ab')2, scFv, Fv, dsFv diabody, and Fd fragments. An antibody capture agent can be produced by any means. For example, an antibody capture agent can be enzymatically or chemically produced by fragmentation of an intact antibody and/or it can be recombinantly produced from a gene encoding the partial antibody sequence. An antibody capture agent can comprise a single chain antibody fragment. Alternatively or additionally, antibody capture agent can comprise multiple chains which are linked together, for example, by disulfide linkages.; and, any functional fragments obtained from such molecules, wherein such fragments retain specific-binding properties of the parent antibody molecule. Because of their smaller size as functional components of the whole molecule, antibody fragments can offer advantages over intact antibodies for use in certain immunochemical techniques and experimental applications.

[0116] Suitable capture agents useful for practicing the invention also include aptamers. Aptamers are oligonucleotide sequences that can bind to their targets specifically via unique three dimensional (3-D) structures. An aptamer can include any suitable number of nucleotides and different aptamers can have either the same or different numbers of nucleotides. Aptamers can be DNA or RNA or chemically modified nucleic acids and can be single stranded, double stranded, or contain double stranded regions, and can include higher ordered structures. An aptamer can also be a photoaptamer, where a photoreactive or chemically reactive functional group is included in the aptamer to allow it to be covalently linked to its corresponding target. Use of an aptamer capture agent can include the use of two or more aptamers that specifically bind the same biomarker. An aptamer can include a tag. An aptamer can be identified using any known method, including the SELEX (systematic evolution of ligands by exponential enrichment), process. Once identified, an aptamer can be prepared or synthesized in accordance with any known method, including chemical synthetic methods and enzymatic synthetic methods and used in a variety of applications for biomarker detection. Liu et al., Curr Med Chem. 18(27):4117-25 (2011). Capture agents useful in practicing the methods of the invention also include SO-MAmers (Slow Off-Rate Modified Aptamers) known in the art to have improved off-rate characteristics. Brody et al., J Mol Biol. 422(5):595-606 (2012). SOMAmers can be generated using using any known method, including the SELEX method.

[0117] It is understood by those skilled in the art that biomarkers can be modified prior to analysis to improve their resolution or to determine their identity. For example, the biomarkers can be subject to proteolytic digestion before analysis. Any protease can be used. Proteases, such as trypsin, that are likely to cleave the biomarkers into a discrete number of fragments are particularly useful. The fragments that result from digestion function as a fingerprint for the biomarkers, thereby enabling their detection indirectly. This is particularly useful where there are biomarkers with similar molecular masses that might be confused for the biomarker in question. Also, proteolytic fragmentation is useful for high molecular weight biomarkers because smaller biomarkers are more easily resolved by mass spectrometry. In another example, biomarkers can be modified to improve detection resolution. For instance, neuraminidase can be used to remove terminal sialic acid residues from glycoproteins to improve binding to an anionic adsorbent and to improve detection resolution. In another example, the biomarkers can be modified by the attachment of a tag of particular molecular weight that specifically binds to molecular biomarkers, further distinguishing them. Optionally, after detecting such modified biomarkers, the identity of the biomarkers can be further determined by matching the physical and chemical characteristics of the modified biomarkers in a protein database (*e.g.,* SwissProt).

[0118] It is further appreciated in the art that biomarkers in a sample can be captured on a substrate for detection. Traditional substrates include antibody-coated 96-well plates or nitrocellulose membranes that are subsequently probed for the presence of the proteins. Alternatively, protein-binding molecules attached to microspheres, microparticles, microbeads, beads, or other particles can be used for capture and detection of biomarkers. The protein-binding molecules can be antibodies, peptides, peptoids, aptamers, small molecule ligands or other protein-binding capture agents attached to the surface of particles. Each protein-binding molecule can include unique detectable label that is coded such that it can be distinguished from other detectable labels attached to other protein-binding molecules to allow detection of biomarkers in multiplex assays. Examples include, but are not limited to, color-coded microspheres with known fluorescent light intensities (see e.g., microspheres with xMAP technology produced by Luminex (Austin, Tex.); microspheres containing quantum dot nanocrystals, for example, having different ratios and combinations of quantum dot colors (e.g., Qdot nanocrystals produced by Life Technologies (Carlsbad, Calif.); glass coated metal nanoparticles (see *e.g.,* SERS nanotags produced by Nanoplex Technologies, Inc. (Mountain View, Calif.); barcode materials (see e.g., sub-micron sized striped metallic rods such as Nanobarcodes produced by Nanoplex Technologies, Inc.), encoded microparticles with colored bar codes (see e.g., CellCard produced by Vitra Bioscience, vitrabio.com), glass microparticles with digital holographic code images (see *e.g.,* CyVera microbeads produced by Illumina (San Diego, Calif.); chemiluminescent dyes, combinations of dye compounds; and beads of detectably different

[0119] Biochips can be used for capture and detection of the biomarkers of the invention. Many protein biochips are known in the art. These include, for example, protein biochips produced by Packard BioScience Company (Meriden Conn.), Zyomyx (Hayward, Calif.) and Phylos (Lexington, Mass.). In general, protein biochips comprise a substrate having a surface. A capture reagent or adsorbent is attached to the surface of the substrate. Frequently, the surface comprises a plurality of addressable locations, each of which location has the capture agent bound there. The capture agent can be a biological molecule, such as a polypeptide or a nucleic acid, which captures other biomarkers in a specific manner. Alternatively, the capture agent can be a chromatographic material, such as an anion exchange material or a hydrophilic material. Examples of protein biochips are well known in the art.

[0120] Measuring mRNA in a biological sample can be used as a surrogate for detection of the level of the corresponding protein biomarker in a biological sample. Thus, any of the biomarkers or biomarker panels described herein can also be detected by detecting the appropriate RNA. Levels of mRNA can measured by reverse transcription quantitative polymerase chain reaction (RT-PCR followed with qPCR). RT-PCR is used to create a cDNA from the mRNA. The cDNA can be used in a qPCR assay to produce fluorescence as the DNA amplification process progresses. By comparison to a standard curve, qPCR can produce an absolute measurement such as number of copies of mRNA per cell. Northern blots, microarrays, Invader assays, and RT-PCR combined with capillary electrophoresis have all been used to measure expression levels of mRNA in a sample. See Gene Expression Profiling: Methods and Protocols, Richard A. Shimkets, editor, Humana Press, 2004.

[0121] Some embodiments disclosed herein relate to diagnostic and prognostic methods of determining the probability for preterm birth in a pregnant female. The detection of the level of expression of one or more biomarkers and/or the determination of a ratio of biomarkers can be used to determine the probability for preterm birth in a pregnant female. Such detection methods can be used, for example, for early diagnosis of the condition, to determine whether a subject is predisposed to preterm birth, to monitor the progress of preterm birth or the progress of treatment protocols, to assess the severity of preterm birth, to forecast the outcome of preterm birth and/or prospects of recovery or birth at full term, or to aid in the determination of a suitable treatment for preterm birth.

[0122] The quantitation of biomarkers in a biological sample can be determined, without limitation, by the methods described above as well as any other method known in the art. The quantitative data thus obtained is then subjected to an analytic classification process. In such a process, the raw data is manipulated according to an algorithm, where the algorithm has been pre-defined by a training set of data, for example as described in the examples provided herein. An algorithm can utilize the training set of data provided herein, or can utilize the guidelines provided herein to generate an algorithm with a different set of data.

[0123] In some embodiments, analyzing a measurable feature to determine the probability for preterm birth in a pregnant female encompasses the use of a predictive model. In further embodiments, analyzing a measurable feature to determine the probability for preterm birth in a pregnant female encompasses comparing said measurable feature with a reference feature. As those skilled in the art can appreciate, such comparison can be a direct comparison to the reference feature or an indirect comparison where the reference feature has been incorporated into the predictive model. In further embodiments, analyzing a measurable feature to determine the probability for preterm birth in a pregnant female encompasses one or more of a linear discriminant analysis model, a support vector machine classification algorithm, a recursive feature elimination model, a prediction analysis of microarray model, a logistic regression model, a CART algorithm, a flex tree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, a machine learning algorithm, a penalized regression method, or a combination thereof. In particular embodiments, the analysis comprises logistic regression.

[0124] An analytic classification process can use any one of a variety of statistical analytic methods to manipulate the quantitative data and provide for classification of the sample. Examples of useful methods include linear discriminant analysis, recursive feature elimination, a prediction analysis of microarray, a logistic regression, a CART algorithm, a FlexTree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, machine learning algorithms; etc.

[0125] For creation of a random forest for prediction of GAB one skilled in the art can consider a set of k subjects (pregnant women) for whom the gestational age at birth (GAB) is known, and for whom N analytes (transitions) have been measured in a blood specimen taken several weeks prior to birth. A regression tree begins with a root node that contains all the subjects. The average GAB for all subjects can be cacluclated in the root node. The variance of the GAB within the root node will be high, because there is a mixture of women with different GAB's. The root node is then divided (partitioned) into two branches, so that each branch contains women with a similar GAB. The average GAB for subjects in each branch is again caluclated. The variance of the GAB within each branch will be lower than in the root node, because the subset of women within each branch has relatively more similar GAB's than those in the root node. The two branches are created by selecting an analyte and a threshold value for the analyte that creates branches with similar GAB. The analyte and threshold value are chosen from among the set of all analytes and threshold values, usually with a random subset of the analytes at each node. The procedure continues recursively producing branches to create leaves (terminal nodes) in which the subjects have very similar GAB's. The predicted GAB in each terminal node is the average GAB for subjects in that terminal node. This procedure creates a single regression tree. A random forest can consist of several hundred or several thousand such trees.

[0126] Classification can be made according to predictive modeling methods that set a threshold for determining the probability that a sample belongs to a given class. The probability preferably is at least 50%, or at least 60%, or at least 70%, or at least 80% or higher. Classifications also can be made by determining whether a comparison between an obtained dataset and a reference dataset yields a statistically significant difference. If so, then the sample from which the dataset was obtained is classified as not belonging to the reference dataset class. Conversely, if such a comparison is not statistically significantly different from the reference dataset, then the sample from which the dataset was obtained is classified as belonging to the reference dataset class.

[0127] The predictive ability of a model can be evaluated according to its ability to provide a quality metric, e.g. AUROC (area under the ROC curve) or accuracy, of a particular value, or range of values. Area under the curve measures are useful for comparing the accuracy of a classifier across the complete data range. Classifiers with a greater AUC have a greater capacity to classify unknowns correctly between two groups of interest. In some embodiments, a desired quality threshold is a predictive model that will classify a sample with an accuracy of at least about 0.5, at least about 0.55, at least about 0.6, at least about 0.7, at least about 0.75, at least about 0.8, at least about 0.85, at least about 0.9, at least about 0.95, or higher. As an alternative measure, a desired quality threshold can refer to a predictive model that will classify a sample with an AUC of at least about 0.7, at least about 0.75, at least about 0.8, at least about 0.85, at least about 0.9, or higher.

[0128] As is known in the art, the relative sensitivity and specificity of a predictive model can be adjusted to favor either the selectivity metric or the sensitivity metric, where the two metrics have an inverse relationship. The limits in a model as described above can be adjusted to provide a selected sensitivity or specificity level, depending on the particular requirements of the test being performed. One or both of sensitivity and specificity can be at least about 0.7, at least about 0.75, at least about 0.8, at least about 0.85, at least about 0.9, or higher.

[0129] The raw data can be initially analyzed by measuring the values for each biomarker, usually in triplicate or in multiple triplicates. The data can be manipulated, for example, raw data can be transformed using standard curves, and the average of triplicate measurements used to calculate the average and standard deviation for each patient. These values can be transformed before being used in the models, *e.g.* log-transformed, Box-Cox transformed (Box and Cox, Royal Stat. Soc., Series B, 26:211-246(1964). The data are then input into a predictive model, which will classify the sample according to the state. The resulting information can be communicated to a patient or health care provider.

[0130] To generate a predictive model for preterm birth, a robust data set, comprising known control samples and samples corresponding to the preterm birth classification of interest is used in a training set. A sample size can be selected using generally accepted criteria. As discussed above, different statistical methods can be used to obtain a highly accurate predictive model. Examples of such analysis are provided in Example 2.

[0131] In one embodiment, hierarchical clustering is performed in the derivation of a predictive model, where the Pearson correlation is employed as the clustering metric. One approach is to consider a preterm birth dataset as a "learning sample" in a problem of "supervised learning." CART is a standard in applications to medicine (Singer, Recursive Partitioning in the Health Sciences, Springer(1999)) and can be modified by transforming any qualitative features to quantitative features; sorting them by attained significance levels, evaluated by sample reuse methods for Hotelling's T^2 statistic; and suitable application of the lasso method. Problems in prediction are turned into problems in regression without losing sight of prediction, indeed by making suitable use of the Gini criterion for classification in evaluating the quality of regressions.

[0132] This approach led to what is termed FlexTree (Huang, Proc. Nat. Acad. Sci. U.S.A 101:10529-10534(2004)). FlexTree performs very well in simulations and when applied to multiple forms of data and is useful for practicing the claimed methods. Software automating FlexTree has been developed. Alternatively, LARTree or LART can be used (Turnbull (2005) Classification Trees with Subset Analysis Selection by the Lasso, Stanford University). The name reflects binary trees, as in CART and FlexTree; the lasso, as has been noted; and the implementation of the lasso through what is termed LARS by Efron et al. (2004) Annals of Statistics 32:407-451 (2004). See, also, Huang et al.., Proc. Natl. Acad. Sci. USA. 101(29):10529-34 (2004). Other methods of analysis that can be used include logic regression. One method of logic regression Ruczinski, Journal of Computational and Graphical Statistics 12:475-512 (2003). Logic regression resembles CART in that its classifier can be displayed as a binary tree. It is different in that each node has Boolean statements about features that are more general than the simple "and" statements produced by CART.

[0133] Another approach is that of nearest shrunken centroids (Tibshirani, Proc. Natl. Acad. Sci. U.S.A 99:6567-72(2002)). The technology is k-means-like, but has the advantage that by shrinking cluster centers, one automatically selects features, as is the case in the lasso, to focus attention on small numbers of those that are informative. The approach is available as PAM software and is widely used. Two further sets of algorithms that can be used are random forests (Breiman, Machine Learning 45:5-32 (2001)) and MART (Hastie, The Elements of Statistical Learning, Springer (2001)). These two methods are known in the art as "committee methods," that involve predictors that "vote" on outcome.

[0134] To provide significance ordering, the false discovery rate (FDR) can be determined. First, a set of null distributions of dissimilarity values is generated. In one embodiment, the values of observed profiles are permuted to create a sequence of distributions of correlation coefficients obtained out of chance, thereby creating an appropriate set of null distributions of correlation coefficients (Tusher et al., Proc. Natl. Acad. Sci. U.S.A 98, 5116-21 (2001)). The set of null distribution is obtained by: permuting the values of each profile for all available profiles; calculating the pair-wise correlation coefficients for all profile; calculating the probability density function of the correlation coefficients for this permutation; and repeating the procedure for N times, where N is a large number, usually 300. Using the N distributions, one calculates an appropriate measure (mean, median, *etc*.) of the count of correlation coefficient values that their values exceed the value (of similarity) that is obtained from the distribution of experimentally observed similarity values at given significance level.

[0135] The FDR is the ratio of the number of the expected falsely significant correlations (estimated from the correlations greater than this selected Pearson correlation in the set of randomized data) to the number of correlations greater than this selected Pearson correlation in the empirical data (significant correlations). This cut-off correlation value can be applied to the correlations between experimental profiles. Using the aforementioned distribution, a level of confidence is chosen for significance. This is used to determine the lowest value of the correlation coefficient that exceeds the result that would have obtained by chance. Using this method, one obtains thresholds for positive correlation, negative correlation or both. Using this threshold(s), the user can filter the observed values of the pair wise correlation coefficients and eliminate those that do not exceed the threshold(s). Furthermore, an estimate of the false positive rate can be obtained for a given threshold. For each of the individual "random correlation" distributions, one can find how many observations fall outside the threshold range. This procedure provides a sequence of counts. The mean and the standard deviation of the sequence provide the average number of potential false positives and its standard deviation.

[0136] In an alternative analytical approach, variables chosen in the cross-sectional analysis are separately employed as predictors in a time-to-event analysis (survival analysis), where the event is the occurrence of preterm birth, and subjects with no event are considered censored at the time of giving birth. Given the specific pregnancy outcome (preterm birth event or no event), the random lengths of time each patient will be observed, and selection of proteomic and other features, a parametric approach to analyzing survival can be better than the widely applied semi-parametric Cox model. A Weibull parametric fit of survival permits the hazard rate to be monotonically increasing, decreasing, or constant, and also has a proportional hazards representation (as does the Cox model) and an accelerated failure-time representation. All the standard tools available in obtaining approximate maximum likelihood estimators of regression coefficients and corresponding functions are available with this model.

[0137] In addition the Cox models can be used, especially since reductions of numbers of covariates to manageable size with the lasso will significantly simplify the analysis, allowing the possibility of a nonparametric or semi-parametric approach to prediction of time to preterm birth. These statistical tools are known in the art and applicable to all manner of proteomic data. A set of biomarker, clinical and genetic data that can be easily determined, and that is highly informative regarding the probability for preterm birth and predicted time to a preterm birth event in said pregnant female is provided. Also, algorithms provide information regarding the probability for preterm birth in the pregnant female.

[0138] Accordingly, one skilled in the art understands that the probability for preterm birth according to the invention can be determined using either a quantitative or a categorical variable. For example, in practicing the methods of the invention the measurable feature of each of N biomarkers can be subjected to categorical data analysis to determine the probability for preterm birth as a binary categorical outcome. Alternatively, the methods of the invention may analyze the measurable feature of each of N biomarkers by initially calculating quantitative variables, in particular, predicted gestational age at birth. The predicted gestational age at birth can subsequently be used as a basis to predict risk of preterm birth. By initially using a quantitative variable and subsequently converting the quantitative variable into a categorical variable the methods of the invention take into account the continuum of measurements detected for the measurable features. For example, by predicting the gestational age at birth rather than making a binary prediction of preterm birth versus term birth, it is possible to tailor the treatment for the pregnant female. For example, an earlier predicted gestational age at birth will result in more intensive prenatal intervention, *i.e.* monitoring and treatment, than a predicted gestational age that approaches full term.

[0139] Among women with a predicted GAB of j days plus or minus k days, p(PTB) can estimated as the proportion of women in the PAPR clinical trial (*see* Example 1) with a predicted GAB of j days plus or minus k days who actually deliver before 37 weeks gestational age. More generally, for women with a predicted GAB of j days plus or minus k days, the probability that the actual gestational age at birth will be less than a specified gestational age, p(actual GAB < specified GAB), was estimated as the proportion of women in the PAPR clinical trial with a predicted GAB of j days plus or minus k days who actually deliver before the specified gestational age.

[0140] In the development of a predictive model, it can be desirable to select a subset of markers, i.e. at least 3, at least 4, at least 5, at least 6, up to the complete set of markers. Usually a subset of markers will be chosen that provides for the needs of the quantitative sample analysis, e.g. availability of reagents, convenience of quantitation, etc., while maintaining a highly accurate predictive model. The selection of a number of informative markers for building classification models requires the definition of a performance metric and a user-defined threshold for producing a model with useful predictive ability based on this metric. For example, the performance metric can be the AUC, the sensitivity and/or specificity of the prediction as well as the overall accuracy of the prediction model.

[0141] As will be understood by those skilled in the art, an analytic classification process can use any one of a variety of statistical analytic methods to manipulate the quantitative data and provide for classification of the sample. Examples of useful methods include, without limitation, linear discriminant analysis, recursive feature elimination, a prediction analysis of microarray, a logistic regression, a CART algorithm, a FlexTree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, and machine learning algorithms.

[0142] As described in Example 2, various methods are used in a training model. The selection of a subset of markers can be for a forward selection or a backward selection of a marker subset. The number of markers can be selected that will optimize the performance of a model without the use of all the markers. One way to define the optimum number of terms is to choose the number of terms that produce a model with desired predictive ability (*e.g.* an AUC>0.75, or equivalent measures of sensitivity/specificity) that lies no more than one standard error from the maximum value obtained for this metric using any combination and number of terms used for the given algorithm.

Table 1. Transitions with p-values less than 0.05 in univariate Cox Proportional Hazards analyses to predict Gestational Age at Birth

Transition	Protein	p-value Cox univariate
ITLPDFTGDLR_624.34_920.4	LBP_HUMAN	0.006
ELLESYIDGR_597.8_710.3	THRB_HUMAN	0.006
TDAPDLPEENQAR_728.34_613.3	CO5_HUMAN	0.007
AFTECCVVASQLR_770.87_574.3	CO5_HUMAN	0.009
SFRPFVPR_335.86_272.2	LBP_HUMAN	0.011
ITLPDFTGDLR_624.34_288.2	LBP_HUMAN	0.012
SFRPFVPR_335.86_635.3	LBP_HUMAN	0.015
ELLESYIDGR_597.8_839.4	THRB_HUMAN	0.018
LEQGENVFLQATDK_796.4_822.4	C1QB_HUMAN	0.019
ETAASLLQAGYK_626.33_679.4	THRB_HUMAN	0.021
VTGWGNLK_437.74_617.3	THRB_HUMAN	0.021
EAQLPVIENK_570.82_699.4	PLMN_HUMAN	0.023
EAQLPVIENK_570.82_329.1	PLMN_HUMAN	0.023
FLQEQGHR_338.84_497.3	CO8G_HUMAN	0.025
IRPFFPQQ_516.79_661.4	FIBB_HUMAN	0.028
ETAASLLQAGYK_626.33_879.5	THRB_HUMAN	0.029
AFTECCVVASQLR_770.87_673.4	CO5_HUMAN	0.030
TLLPVSKPEIR_418.26_288.2	CO5_HUMAN	0.030
LSSPAVITDK_515.79_743.4	PLMN_HUMAN	0.033
YEVQGEVFTKPQLWP_910.96_392.2	CRP_HUMAN	0.036
LQGTLPVEAR_542.31_571.3	CO5_HUMAN	0.036
VRPQQLVK_484.31_609.3	ITIH4_HUMAN	0.036
IEEIAAK_387.22_531.3	CO5_HUMAN	0.041
TLLPVSKPEIR_418.26_514.3	CO5_HUMAN	0.042
VQEAHLTEDQIFYFPK_655.66_701.4	CO8G_HUMAN	0.047
ISLLLIESWLEPVR_834.49_371.2	CSH_HUMAN	0.048
ALQDQLVLVAAK_634.88_289.2	ANGT_HUMAN	0.048
YEFLNGR_449.72_293.1	PLMN_HUMAN	0.049

Table 2. Transitions selected by the Cox stepwise AIC analysis

Transition	**coef**	**exp(coef)**	**se(coef)**	**z**	**Pr(>|z|)**
Collection.Window.GA.in.Days	1.28E-01	1.14E+00	2.44E-02	5.26	1.40E-07
ITLPDFTGDLR_624.34_920.4	2.02E+00	7.52E+00	1.14E+00	1.77	0.07667
TPSAAYLWVGTGASEAEK_919.45_849.4	2.85E+01	2.44E+12	3.06E+00	9.31	<2e-16
TATSEYQTFFNPR_781.37_386.2	5.14E+00	1.70E+02	6.26E-01	8.21	2.20E-16
TASDFITK_441.73_781.4	-1.25E+00	2.86E-01	1.58E+00	-0.79	0.42856
IITGLLEFEVYLEYLQNR_738.4_530.3	1.30E+01	4.49E+05	1.45E+00	9	<2e-16
IIGGSDADIK_494.77_762.4	-6.43E+01	1.16E-28	6.64E+00	-9.68	<2e-16
YTTEIIK_434.25_603.4	6.96E+01	1.75E+30	7.06E+00	9.86	<2e-16
EDTPNSVWEPAK_686.82_315.2	7.91E+00	2.73E+03	2.66E+00	2.98	0.00293
LYYGDDEK_501.72_726.3	8.74E+00	6.23E+03	1.57E+00	5.57	2.50E-08
VRPQQLVK_484.31_609.3	4.64E+01	1.36E+20	3.97E+00	11.66	< 2e-16
GGEIEGFR_432.71_379.2	-3.33E+00	3.57E-02	2.19E+00	-1.52	0.12792
DGSPDVTTADIGANTPDATK_973.45_844.4	-1.52E+01	2.51E-07	1.41E+00	-10.8	< 2e-16
VQEAHLTEDQIFYFPK_655.66_391.2	-2.02E+01	1.77E-09	2.45E+00	-8.22	2.20E-16
VEIDTK_352.7_476.3	7.06E+00	1.17E+03	1.45E+00	4.86	1.20E-06
AVLTIDEK_444.76_605.3	7.85E+00	2.56E+03	9.46E-01	8.29	< 2e-16
FSVVYAK_407.23_579.4	-2.44E+01	2.42E-11	3.08E+00	-7.93	2.20E-15
YYLQGAK_421.72_516.3	-1.82E+01	1.22E-08	2.45E+00	-7.44	1.00E-13
EENFYVDETTVVK_786.88_259.1	-1.90E+01	5.36E-09	2.71E+00	-7.03	2.00E-12
YGFYTHVFR_397.2_421.3	1.90E+01	1.71E+08	2.73E+00	6.93	4.20E-12
HTLNQIDEVK_598.82_951.5	1.03E+01	3.04E+04	2.11E+00	4.89	9.90E-07
AFIQLWAFDAVK_704.89_836.4	1.08E+01	4.72E+04	2.59E+00	4.16	3.20E-05
SGFSFGFK_438.72_585.3	1.35E+01	7.32E+05	2.56E+00	5.27	1.40E-07
GWVTDGFSSLK_598.8_854.4	-3.12E+00	4.42E-02	9.16E-01	-3.4	0.00066
ITENDIQIALDDAK_779.9_632.3	1.91E+00	6.78E+00	1.36E+00	1.4	0.16036

Table 3. Transitions selected by Cox lasso model

Transition	coef	exp(coef)	se(coef)	z	Pr(>|z|)
Collection.Window.GA.in.Days	0.0233	1.02357	0.00928	2.51	0.012
AFTECCVVASQLR_770.87_574.3	1.07568	2.93198	0.84554	1.27	0.203
ELLESYIDGR_597.8_710.3	1.3847	3.99365	0.70784	1.96	0.05
ITLPDFTGDLR_624.34_920.4	0.814	2.25691	0.40652	2	0.045

Table 4. Area under the ROC (AUROC) curve for individual analytes to discriminate pre-term birth subjects from non-pre-term birth subjects. The 77 transitions with the highest AUROC area are shown.

Transition	**AUROC**
ELLESYIDGR_597.8_710.3	0.71

(continued)

Transition	AUROC
AFTECCVVASQLR_770.87_574.3	0.70
ITLPDFTGDLR_624.34_920.4	0.70
IRPFFPQQ_516.79_661.4	0.68
TDAPDLPEENQAR_728.34_613.3	0.67
ITLPDFTGDLR_624.34_288.2	0.67
ELLESYIDGR_597.8_839.4	0.67
SFRPFVPR_335.86_635.3	0.67
ETAASLLQAGYK_626.33_879.5	0.67
TLLPVSKPEIR_418.26_288.2	0.66
ETAASLLQAGYK_626.33_679.4	0.66
SFRPFVPR_335.86_272.2	0.66
LQGTLPVEAR_542.31_571.3	0.66
VEPLYELVTATDFAYSSTVR_754.38_712.4	0.66
DPDQTDGLGLSYLSSHIANVER_796.39_328.1	0.66
VTGWGNLK_437.74_617.3	0.65
ALQDQLVLVAAK_634.88_289.2	0.65
EAQLPVIENK_570.82_329.1	0.65
VRPQQLVK_484.31_609.3	0.65
AFTECCVVASQLR_770.87_673.4	0.65
YEFLNGR_449.72_293.1	0.65
VGEYSLYIGR_578.8_871.5	0.64
EAQLPVIENK_570.82_699.4	0.64
TLLPVSKPEIR_418.26_514.3	0.64
IEEIAAK_387.22_531.3	0.64
LEQGENVFLQATDK_796.4_822.4	0.64
LQGTLPVEAR_542.31_842.5	0.64
FLQEQGHR_338.84_497.3	0.63
ISLLLIESWLEPVR_834.49_371.2	0.63
IITGLLEFEVYLEYLQNR_738.4_530.3	0.63
LSSPAVITDK_515.79_743.4	0.63
VRPQQLVK_484.31_722.4	0.63
SLPVSDSVLSGFEQR_810.92_723.3	0.63
VQEAHLTEDQIFYFPK_655.66_701.4	0.63
NADYSYSVWK_616.78_333.2	0.63
DAQYAPGYDK_564.25_813.4	0.62
FQLPGQK_409.23_276.1	0.62
TASDFITK_441.73_781.4	0.62
YGLVTYATYPK_638.33_334.2	0.62

(continued)

Transition	AUROC
GSFALSFPVESDVAPIAR_931.99_363.2	0.62
TLLIANETLR_572.34_703.4	0.62
VILGAHQEVNLEPHVQEIEVSR_832.78_860.4	0.62
TATSEYQTFFNPR_781.37_386.2	0.62
YEVQGEVFTKPQLWP_910.96_392.2	0.62
DISEVVTPR_508.27_472.3	0.62
GSFALSFPVESDVAPIAR_931.99_456.3	0.62
YGFYTHVFR_397.2_421.3	0.62
TLEAQLTPR_514.79_685.4	0.62
YGFYTHVFR_397.2_659.4	0.62
AVGYLITGYQR_620.84_737.4	0.61
DPDQTDGLGLSYLSSHIANVER_796.39_456.2	0.61
FNAVLTNPQGDYDTSTGK_964.46_262.1	0.61
SPEQQETVLDGNLIIR_906.48_685.4	0.61
ALNHLPLEYNSALYSR_620.99_538.3	0.61
GGEIEGFR_432.71_508.3	0.61
GIVEECCFR_585.26_900.3	0.61
DAQYAPGYDK_564.25_315.1	0.61
FAFNLYR_465.75_712.4	0.61
YTTEIIK_434.25_603.4	0.61
AVLTIDEK_444.76_605.3	0.61
AITPPHPASQANIIFDITEGNLR_825.77_459.3	0.60
EPGLCTWQSLR_673.83_790.4	0.60
AVYEAVLR_460.76_587.4	0.60
ALQDQLVLVAAK_634.88_956.6	0.60
AWVAWR_394.71_531.3	0.60
TNLESILSYPK_632.84_807.5	0.60
HLSLLTTLSNR_418.91_376.2	0.60
FTFTLHLETPKPSISSSNLNPR_829.44_787.4	0.60
AVGYLITGYQR_620.84_523.3	0.60
FQLPGQK_409.23_429.2	0.60
YGLVTYATYPK_638.33_843.4	0.60
TELRPGETLNVNFLLR_624.68_662.4	0.60
LSSPAVITDK_515.79_830.5	0.60
TATSEYQTFFNPR_781.37_272.2	0.60
LPTAVVPLR_483.31_385.3	0.60
APLTKPLK_289.86_260.2	0.60

Table 5. AUROCs for random forest, boosting, lasso, and logistic regression models for a specific number of transitions permitted in the model, as estimated by 100 rounds of bootstrap resampling.

Number of transitions	rf	boosting	logit	lasso
1	0.59	0.67	0.64	0.69
2	0.66	0.70	0.63	0.68
3	0.69	0.70	0.58	0.71
4	0.68	0.72	0.58	0.71
5	0.73	0.71	0.58	0.68
6	0.72	0.72	0.56	0.68
7	0.74	0.70	0.60	0.67
8	0.73	0.72	0.62	0.67
9	0.72	0.72	0.60	0.67
10	0.74	0.71	0.62	0.66
11	0.73	0.69	0.58	0.67
12	0.73	0.69	0.59	0.66
13	0.74	0.71	0.57	0.66
14	0.73	0.70	0.57	0.65
15	0.72	0.70	0.55	0.64

Table 6. Top 15 transitions selected by each multivariate method, ranked by importance for that method.

	rf	boosting	lasso	logit
1	ELLESYIDGR_597.8_710.3	AFTECCVVASQLR_770.87_574.3	AFTECCVVASQLR_770.87_574.3	ALQDQLVLVAAK_634.88_289.2
2	TATSEYQTFFNPR_781.37_386.2	DPDQTDGLGLSYLSSHIANVER_ 796.39_328.1	ISLLLIESWLEPVR_834.49_371.2	AVLTIDEK_444.76_605.3
3	ITLPDFTGDLR_624.34_920.4	ELLESYIDGR_597.8_710.3	LPTAVVPLR_483.31_385.3	Collection.Window.G A.in.Days
4	AFTECCVVASQLR_770.87_574.3	TATSEYQTFFNPR_781.37_386.2	ALQDQLVLVAAK_634.88_289.2	AHYDLR_387.7_566.3
5	VEPLYELVTATDFAYSSTVR_ 754.38_712.4	ITLPDFTGDLR_624.34_920.4	ETAASLLQAGYK_626.33_679.4	AEAQAQYSAAVAK_654.33_908.5
6	GSFALSFPVES DVAPIAR_ 931.99_363.2	GGEIEGFR_432.71_379.2	IITGLLEFEVYLEYLQNR_738.4_530.3	AEAQAQYSAAVAK_654.33_709.4
7	VGEYSLYIGR_578.8_871.5	ALQDQLVLVAAK_634.88_289.2	ADSQAQLLLSTVVGVFTAPGLHLK_ 822.46_983.6	ADSQAQLLLSTVVGVFTAPGLHLK_ 822.46_983.6
8	SFRPFVPR_335.86_635.3	VGEYSLYIGR_578.8_871.5	SLPVSDSVLSGFEQR_810.92_723.3	AITPPHPASQANIIFDITEGNLR_ 825.77_459.3
9	ALQDQLVLVAAK_634.88_289.2	VEPLYELVTATDFAYSSTVR_ 754.38_712.4	SFRPFVPR_335.86_272.2	ADSQAQLLLSTVVGVFTAPGLHLK_ 822.46_664.4
10	EDTPNSVWEPAK_686.82_315.2	SPEQQETVLDGNLIIR_ 906.48_685.4	IIGGSDADIK_494.77_260.2	AYSDLSR_406.2_375.2
11	YGFYTHVFR_397.2_421.3	YEFLNGR_449.72_293.1	NADYSYSVWK_616.78_333.2	DALSSVQESQVAQQAR_ 572.96_672.4
12	DPDQTDGLGLSYLSSHIANVER_ 796.39_328.1	LEQGENVFLQATDK_796.4_822.4	GSFALSFPVESDVAPIAR_ 931.99_456.3	ANRPFLVFIR_411.58_435.3
13	LEQGENVFLQATDK_796.4_822.4	LQGTLPVEAR_542.31_571.3	LSSPAVITDK_515.79_743.4	DALSSVQESQVAQQAR_ 572.96_502.3
14	LQGTLPVEAR_542.31_571.3	ISLLLIESWLEPVR_834.49_371.2	ELPEHTVK_476.76_347.2	ALEQDLPVNIK_620.35_570.4
15	SFRPFVPR_335.86_272.2	TASDFITK_441.73_781.4	EAQLPVIENK_570.82_699.4	AVLTIDEK_444.76_718.4

[0143] Disclosed herein are kits for determining probability of preterm birth, wherein the kits can be used to detect N of the isolated biomarkers listed in Tables 1 through 63. For example, the kits can be used to detect one or more, two or more, or three of the isolated biomarkers selected from the group consisting of AFTECCVVASQLR, ELLESYIDGR, and ITLPDFTGDLR. For example, the kits can be used to detect one or more, two or more, or three of the isolated biomarkers selected from the group consisting of FLNWIK, FGFGGSTDSGPIR, LLELTGPK, VEHSDLSFSK, IEGN-LIFDPNNYLPK, ALVLELAK, TQILEWAAER, DVLLLVHNLPQNLPGYFWYK, SEPRPGVLLR, ITQDAQLK, ALDLSLK, WWGGQPLWITATK, and LSETNR.

[0144] The kits can be used to detect one or more, two or more, three or more, four or more, five or more, six or more, seven or more, or eight of the isolated biomarkers selected from the group consisting of lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0145] The kits can be used to detect one or more, two or more, three or more, four or more, five or more, six or more, seven or more, or eight of the isolated biomarkers selected from the group consisting of Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0146] The kit can include one or more agents for detection of biomarkers, a container for holding a biological sample isolated from a pregnant female; and printed instructions for reacting agents with the biological sample or a portion of the biological sample to detect the presence or amount of the isolated biomarkers in the biological sample. The agents can be packaged in separate containers. The kit can further comprise one or more control reference samples and reagents for performing an immunoassay.

[0147] In one instances, the kit comprises agents for measuring the levels of at least N of the isolated biomarkers listed in Tables 1 through 63. The kit can include antibodies that specifically bind to these biomarkers, for example, the kit can contain at least one of an antibody that specifically binds to lipopolysaccharide-binding protein (LBP), an antibody that specifically binds to prothrombin (THRB), an antibody that specifically binds to complement component C5 (C5 or CO5), an antibody that specifically binds to plasminogen (PLMN), and an antibody that specifically binds to complement component C8 gamma chain (C8G or CO8G).

[0148] In one instance, the kit comprises agents for measuring the levels of at least N of the isolated biomarkers listed in Tables 1 through 63. The kit can include antibodies that specifically bind to these biomarkers, for example, the kit can contain at least one of an antibody that specifically binds to Alpha-1B-glycoprotein (A1BG), Disintegrin and metalloproteinase domain-containing protein 12 (ADA12), Apolipoprotein B-100 (APOB), Beta-2-microglobulin (B2MG), CCAAT/enhancer-binding protein alpha/beta (HP8 Peptide), Corticosteroid-binding globulin (CBG), Complement component C6, Endoglin (EGLN), Ectonucleotide pyrophosphatase/phosphodiesterase family member 2 (ENPP2), Coagulation factor VII (FA7), Hyaluronan-binding protein 2 (HABP2), Pregnancy-specific beta-1-glycoprotein 9 (PSG9), Inhibin beta E chain (INHBE).

[0149] The kit can comprise one or more containers for compositions contained in the kit. Compositions can be in liquid form or can be lyophilized. Suitable containers for the compositions include, for example, bottles, vials, syringes, and test tubes. Containers can be formed from a variety of materials, including glass or plastic. The kit can also comprise a package insert containing written instructions for methods of determining probability of preterm birth.

[0150] The following examples are provided by way of illustration, not limitation.

EXAMPLES

Example 1. Development of Sample Set for Discovery and Validation of Biomarkers for Preterm Birth

[0151] A standard protocol was developed governing conduct of the Proteomic Assessment of Preterm Risk (PAPR) clinical study. This protocol also specified that the samples and clinical information could be used to study other pregnancy complications for some of the subjects. Specimens were obtained from women at 11 Internal Review Board (IRB) approved sites across the United States. After providing informed consent, serum and plasma samples were obtained, as well as pertinent information regarding the patient's demographic characteristics, past medical and pregnancy history, current pregnancy history and concurrent medications. Following delivery, data were collected relating to maternal and infant conditions and complications. Serum and plasma samples were processed according to a protocol that requires standardized refrigerated centrifugation, aliquoting of the samples into 0.5 ml 2-D bar-coded cryovials and subsequent freezing at -80°C.

[0152] Following delivery, preterm birth cases were individually reviewed to determine their status as either a spontaneous preterm birth or a medically indicated preterm birth. Only spontaneous preterm birth cases were used for this analysis. For discovery of biomarkers of preterm birth, 80 samples were analyzed in two gestational age groups: a) a late window composed of samples from 23-28 weeks of gestation which included 13 cases, 13 term controls matched within one week of sample collection and 14 term random controls, and, b) an early window composed of samples from 17-22 weeks of gestation included 15 cases, 15 term controls matched within one week of sample collection and 10 random term controls.

[0153] The samples were subsequently depleted of high abundance proteins using the Human 14 Multiple Affinity Removal System (MARS 14), which removes 14 of the most abundant proteins that are treated as uninformative with regard to the identification for disease-relevant changes in the serum proteome. To this end, equal volumes of each clinical or a pooled human serum sample (HGS) sample were diluted with column buffer and filtered to remove precipitates. Filtered samples were depleted using a MARS-14 column (4.6 x 100 mm, Cat. #5188-6558, Agilent Technologies). Samples were chilled to 4°C in the autosampler, the depletion column was run at room temperature, and collected fractions were kept at 4°C until further analysis. The unbound fractions were collected for further analysis.

[0154] A second aliquot of each clinical serum sample and of each HGS was diluted into ammonium bicarbonate buffer and depleted of the 14 high and approximately 60 additional moderately abundant proteins using an IgY14-SuperMix (Sigma) hand-packed column, comprised of 10 mL of bulk material (50% slurry, Sigma). Shi et al., Methods, 56(2):246-53 (2012). Samples were chilled to 4°C in the autosampler, the depletion column was run at room temperature, and collected fractions were kept at 4°C until further analysis. The unbound fractions were collected for further analysis.

[0155] Depleted serum samples were denatured with trifluorethanol, reduced with dithiotreitol, alkylated using iodoacetamide, and then digested with trypsin at a 1:10 trypsin: protein ratio. Following trypsin digestion, samples were desalted on a C18 column, and the eluate lyophilized to dryness. The desalted samples were resolubilized in a reconstitution solution containing five internal standard peptides.

[0156] Depleted and trypsin digested samples were analyzed using a scheduled Multiple Reaction Monitoring method (sMRM). The peptides were separated on a 150 mm x 0.32 mm Bio-Basic C18 column (ThermoFisher) at a flow rate of 5 μl/min using a Waters Nano Acquity UPLC and eluted using an acetonitrile gradient into a AB SCIEX QTRAP 5500 with a Turbo V source (AB SCIEX, Framingham, MA). The sMRM assay measured 1708 transitions that correspond to 854 peptides and 236 proteins. Chromatographic peaks were integrated using Rosetta Elucidator software (Ceiba Solutions).

[0157] Transitions were excluded from analysis, if their intensity area counts were less than 10000 and if they were missing in more than three samples per batch. Intensity area counts were log transformed and Mass Spectrometry run order trends and depletion batch effects were minimized using a regression analysis.

Example 2. Analysis I of Transitions to Identify Preterm Birth Biomarkers

[0158] The objective of these analyses was to examine the data collected in Example 1 to identify transitions and proteins that predict preterm birth. The specific analyses employed were (i) Cox time-to-event analyses and (ii) models with preterm birth as a binary categorical dependent variable. The dependent variable for all the Cox analyses was Gestational Age of time to event (where event is preterm birth). For the purpose of the Cox analyses, preterm birth subjects have the event on the day of birth. Term subjects are censored on the day of birth. Gestational age on the day of specimen collection is a covariate in all Cox analyses.

[0159] The assay data were previously adjusted for run order and depletion batch, and log transformed. Values for gestational age at time of sample collection were adjusted as follows. Transition values were regressed on gestational age at time of sample collection using only controls (non-pre-term subjects). The residuals from the regression were designated as adjusted values. The adjusted values were used in the models with pre-term birth as a binary categorical dependent variable. Unadjusted values were used in the Cox analyses.

Univariate Cox Proportional Hazards Analyses

[0160] Univariate Cox Proportional Hazards analyses was performed to predict Gestational Age at Birth, including Gestational age on the day of specimen collection as a covariate. Table 1 shows the transitions with p-values less than 0.05. Five proteins have multiple transitions among those with p-value less than 0.05: lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

Multivariate Cox Proportional Hazards Analyses: Stepwise AIC selection

[0161] Cox Proportional Hazards analyses was performed to predict Gestational Age at Birth, including Gestational age on the day of specimen collection as a covariate, using stepwise and lasso models for variable selection. These analyses include a total of n= 80 subjects, with number of PTB events= 28. The stepwise variable selection analysis used the Akaike Information Criterion (AIC) as the stopping criterion. Table 2 shows the transitions selected by the stepwise AIC analysis. The coefficient of determination (R^2) for the stepwise AIC model is 0.86 (not corrected for multiple comparisons).

Multivariate Cox Proportional Hazards Analyses: lasso selection

[0162] Lasso variable selection was used as the second method of multivariate Cox Proportional Hazards analyses to predict Gestational Age at Birth, including Gestational age on the day of specimen collection as a covariate. This analysis uses a lambda penalty for lasso estimated by cross validation. Table 3 shows the results. The lasso variable selection method is considerably more stringent than the stepwise AIC, and selects only 3 transitions for the final model, representing 3 different proteins. These 3 proteins give the top 4 transitions from the univariate analysis; 2 of the top 4 univariate are from the same protein, and hence are not both selected by the lasso method. Lasso tends to select a relatively small number of variables with low mutual correlation. The coefficient of determination (R^2) for the lasso model is 0.21 (not corrected for multiple comparisons).

Univariate AUROC analysis of preterm birth as a binary categorical dependent variable

[0163] Univariate analyses was performed to discriminate pre-term subjects from non-pre-term subjects (pre-term as a binary categorical variable) as estimated by area under the receiver operating characteristic (AUROC) curve. These analyses use transition values adjusted for gestational age at time of sample collection, as described above. Table 4 shows the AUROC curve for the 77 transitions with the highest AUROC area of 0.6 or greater.

Multivariate analysis of preterm birth as a binary categorical dependent variable

[0164] Multivariate analyses was performed to predict preterm birth as a binary categorical dependent variable, using random forest, boosting, lasso, and logistic regression models. Random forest and boosting models grow many classification trees. The trees vote on the assignment of each subject to one of the possible classes. The forest chooses the class with the most votes over all the trees.

[0165] For each of the four methods (random forest, boosting, lasso, and logistic regression) each method was allowed to select and rank its own best 15 transitions. We then built models with 1 to 15 transitions. Each method sequentially reduces the number of nodes from 15 to 1 independently. A recursive option was used to reduce the number of nodes at each step: To determine which node to remove, the nodes were ranked at each step based on their importance from a nested cross-validation procedure. The least important node was eliminated. The importance measures for lasso and logistic regression are z-values. For random forest and boosting, the variable importance was calculated from permuting out-of-bag data: for each tree, the classification error rate on the out-of-bag portion of the data was recorded; the error rate was then recalculated after permuting the values of each variable (i.e., transition); if the transition was in fact important, there would have been be a big difference between the two error rates; the difference between the two error rates were then averaged over all trees, and normalized by the standard deviation of the differences. The AUCs for these models are shown in Table 5, as estimated by 100 rounds of bootstrap resampling. Table 6 shows the top 15 transitions selected by each multivariate method, ranked by importance for that method. These multivariate analyses suggest that models that combine 3 or more transitions give AUC greater than 0.7, as estimated by bootstrap.

[0166] In multivariate models, random forest (rf), boosting, and lasso models gave the best area under the AUROC curve. The following transitions were selected by these models, as significant in Cox univariate models, and/or having high univariate ROC's:

AFTECCVVASQLR_770.87_574.3
ELLESYIDGR_597.8_710.3
ITLPDFTGDLR_624.34_920.4
TDAPDLPEENQAR_728.34_613.3
SFRPFVPR_335.86_635.3

[0167] In summary, univariate and multivariate Cox analyses was performed using transitions to predict Gestational Age at Birth (GAB), including Gestational age on the day of specimen collection as a covariate. In the univariate Cox analysis, five proteins were identified that have multiple transitions among those with p-value less than 0.05: lipopolysaccharide-binding protein (LBP), prothrombin (THRB), complement component C5 (C5 or CO5), plasminogen (PLMN), and complement component C8 gamma chain (C8G or CO8G).

[0168] In multivariate Cox analyses, stepwise AIC variable analysis selects 24 transitions, while the lasso model selects 3 transitions, which include the 3 top proteins in the univariate analysis. Univariate (AUROC) and multivariate (random forest, boosting, lasso, and logistic regression) analyses were performed to predict pre-term birth as a binary categorical variable. Univariate analyses identified 63 analytes with AUROC of 0.6 or greater. Multivariate analyses suggest that models that combine 3 or more transitions give AUC greater than 0.7, as estimated by bootstrap.

Example 3. Study II to Identify and Confirm Preterm Birth Biomarkers

[0169] A further study was performed using essentially the same methods described in the preceding Examples unless noted below. In this study, 2 gestational aged matched controls were used for each case of 28 cases and 56 matched controls, all from the early gestational window only (17-22 weeks).

[0170] The samples were processed in 4 batches with each batch composed of 7 cases, 14 matched controls and 3 HGS controls. Serum samples were depleted of the 14 most abundant serum samples by MARS14 as described in Example 1. Depleted serum was then reduced with dithiothreitol, alkylated with iodacetamide, and then digested with trypsin at a 1:20 trypsin to protein ratio overnight at 37°C. Following trypsin digestion, the samples were desalted on an Empore C18 96-well Solid Phase Extraction Plate (3M Company) and lyophilized to dryness. The desalted samples were resolubilized in a reconstitution solution containing five internal standard peptides .

[0171] The LC-MS/MS analysis was performed with an Agilent Poroshell 120 EC-C18 column (2.1x50mm, 2.7 μm) and eluted with an acetonitrile gradient into a Agilent 6490 Triple Quadrapole mass spectrometer.

[0172] Data analysis included the use of conditional logistic regression where each matching triplet (case and 2 matched controls) was a stratum. The p-value reported in the table indicates whether there is a significant difference between cases and matched controls.

Table 7. Results of Study II

Transition	Protein	Annotation	p-value
DFHINLFQVLPWLK	CFAB_HUMAN	Complement factor B	0.006729512
ITLPDFTGDLR	LBP_HUMAN	Lipopolysaccharide-binding protein	0.012907017
WWGGQPLWITATK	ENPP2_HUMAN	Ectonucleotide pyrophosphatase/phosp hodiesterase family member 2	0.013346
TASDFITK	GELS_HUMAN	Gelsolin	0.013841221
AGLLRPDYALLGHR	PGRP2_HUMAN	N-acetylmuramoyl-L-alanine amidase	0.014241979
FLQEQGHR	CO8G_HUMAN	Complement component C8 gamma chain	0.014339596
FLNWIK	HABP2_HUMAN	Hyaluronan -binding protein 2	0.014790418
EKPAGGIPVLGSLVNTVLK	BPIB1_HUMAN	BPI fold-containing family B member 1	0.019027746
ITGFLKPGK	LBP_HUMAN	Lipopolysaccharide-binding protein	0.019836986
YGLVTYATYPK	CFAB_HUMAN	Complement factor B	0.019927774
SLLQPNK	CO8A_HUMAN	Complement component C8 alpha chain	0.020930939
DISEVVTPR	CFAB_HUMAN	Complement factor B	0.021738046
VQEAHLTEDQIFYFPK	CO8G_HUMAN	Complement component C8 gamma chain	0.021924548
SPELQAEAK	APOA2_HUMAN	Apolipoprotein A-II	0.025944285
TYLHTYESEI	ENPP2_HUMAN	Ectonucleotide pyrophosphatase/phosp hodiesterase family member 2	0.026150038
DSPSVWAAVPGK	PROF1_HUMAN	Profilin-1	0.026607371
HYINLITR	NPY_HUMAN	Pro-neuropeptide Y	0.027432804
SLPVSDSVLSGFEQR	CO8G_HUMAN	Complement component C8 gamma chain	0.029647857
IPGIFELGISSQSDR	CO8B_HUMAN	Complement component C8 beta chain	0.030430996
IQTHSTTYR	F13B_HUMAN	Coagulation factor XIII B chain	0.031667664
DGSPDVTTADIGANTPDATK	PGRP2_HUMAN	N-acetylmuramoyl-L-alanine amidase	0.034738338
QLGLPGPPDVPDHAAYHPF	ITIH4_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H4	0.043130591

(continued)

Transition	Protein	Annotation	p-value
FPLGSYTIQNIVAGSTYLFSTK	LCAP_HUMAN	Leucyl-cystinyl aminopeptidase	0.044698045
AHYDLR	FETUA_HUMAN	Alpha-2-HS-glycoprotein	0.046259201
SFRPFVPR	LBP_HUMAN	Lipopolysaccharide-binding protein	0.047948847

Example 4. Study III Shotgun Identification of Preterm Birth Biomarkers

[0173] A further study used a hypothesis-independent shotgun approach to identify and quantify additional biomarkers not present on our multiplexed hypothesis dependent MRM assay. Samples were processed as described in the preceding Examples unless noted below.

[0174] Tryptic digests of MARS depleted patient (preterm birth cases and term controls) samples were fractionated by two-dimensional liquid chromatography and analyzed by tandem mass spectrometry. Aliquots of the samples, equivalent to 3-4 μl of serum, were injected onto a 6 cm x 75 μm self-packed strong cation exchange (Luna SCX, Phenomenex) column. Peptides were eluded from the SCX column with salt (15, 30, 50, 70, and 100% B, where B = 250mM ammonium acetate, 2% acetonitrile, 0.1% formic acid in water) and consecutively for each salt elution, were bound to a 0.5 μl C18 packed stem trap (Optimize Technologies, Inc.) and further fractionated on a 10 cm x 75 μm reversed phase ProteoPep II PicoFrit column (New Objective). Peptides were eluted from the reversed phase column with an acetonitrile gradient containing 0.1% formic acid and directly ionized on an LTQ-Orbitrap (ThermoFisher). For each scan, peptide parent ion masses were obtained in the Orbitrap at 60K resolution and the top seven most abundant ions were fragmented in the LTQ to obtain peptide sequence information.

[0175] Parent and fragment ion data were used to search the Human RefSeq database using the Sequest (Eng et al., J. Am. Soc. Mass Spectrom 1994; 5:976-989) and X!Tandem (Craig and Beavis, Bioinformatics 2004; 20:1466-1467) algorithms. For Sequest, data was searched with a 20 ppm tolerance for the parent ion and 1 AMU for the fragment ion. Two missed trypsin cleavages were allowed, and modifications included static cysteine carboxyamidomethylation and methionine oxidation. After searching the data was filtered by charge state vs. Xcorr scores (charge +1 ≥ 1.5 Xcorr, charge +2 ≥ 2.0, charge +3 ≥ 2.5). Similar search parameters were used for X!tandem, except the mass tolerance for the fragment ion was 0.8 AMU and there is no Xcorr filtering. Instead, the PeptideProphet algorithm (Keller et al., Anal. Chem 2002;74:5383-5392) was used to validate each X!Tandem peptide-spectrum assignment and Protein assignments were validated using ProteinProphet algorithm (Nesvizhskii et al., Anal. Chem 2002; 74:5383-5392). Data was filtered to include only the peptide-spectrum matches that had PeptideProphet probability of 0.9 or more. After compiling peptide and protein identifications, spectral count data for each peptide were imported into DAnTE software (Polpitiya et al., Bioinformatics. 2008; 24:1556-1558). Log transformed data was mean centered and missing values were filtered, by requiring that a peptide had to be identified in at least 4 cases and 4 controls. To determine the significance of an analyte, Receiver Operating Characteristic (ROC) curves for each analyte were created where the true positive rate (Sensitivity) is plotted as a function of the false positive rate (1-Specificity) for different thresholds that separate the SPTB and Term groups. The area under the ROC curve (AUC) is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one. Peptides with AUC greater than or equal to 0.6 found uniquely by Sequest or Xtandem are found in Tables 8 and 9, respectively, and those identified by both approaches are found in Table 10.

Table 8. Significant peptides (AUC>0.6) for Sequest only

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
5'-AM P-activated protein kinase subunit gamma-3	**Q9UGI9** (AAKG3_HUMAN)	K.LVIFDTM*LEIK.K	0.78
afamin precursor	**P43652** (AFAM_ HUMAN)	K.FIEDNIEYITIIAFAQYVQEATFEEMEK.L	0.79
afamin precursor	**P43652** (AFAM_ HUMAN)	K.IAPQLSTEELVSLGEK.M	0.71
afamin precursor	**P43652** (AFAM_ HUMAN)	K.LKHELTDEELQSLFTNFANVVDK.C	0.60
afamin precursor	**P43652** (AFAM_ HUMAN)	K.LPNNVLQEK.I	0.60
afamin precursor	**P43652** (AFAM_ HUMAN)	K.SDVGFLPPFPTLDPEEK.C	0.71
afamin precursor	**P43652** (AFAM_ HUMAN)	K.VMNHICSK.Q	0.68
afamin precursor	**P43652** (AFAM_ HUMAN)	R.ESLLNHFLYEVAR.R	0.69
afamin precursor	**P43652** (AFAM_ HUMAN)	R.LCFFYNKK.S	0.69
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.AVLDVFEEGTEASAATAVK.I	0.72
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.EQLSLLDR.F	0.65
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.EQLSLLDRFTEDAK.R	0.64
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.EQLSLLDRFTEDAKR.L	0.60
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.ITDLIKDLDSQTMM*VLVNYIFFK.A	0.65

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.ITLLSALVETR.T	0.62
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.RLYGSEAFATDFQDSAAAK.K	0.62
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	R.EIGELYLPK.F	0.65
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.CEGPIPDVTFELLR.E	0.67
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.FALVR.E	0.79
alpha-2-antiplasmin isoform a precursor	**P08697** (A2AP_ HUMAN)	K.SPPGVCSR.D	0.81
alpha-2-antiplasmin isoform a precursor	**P08697** (A2AP_ HUMAN)	R.DSFHLDEQFTVPVEMMQAR.T	0.69
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	K.CNLLAEK.Q	0.67
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	K.EHAVEGDCDFQLLK.L	0.67
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	K. HTLNQI DEVKVWPQQPSGELFEIEIDTLETTCHVLDPTPVAR.C	0.64
alpha-2-macroglobulin precursor	**P01023** (A2MG_ HUMAN)	K.MVSGFIPLKPTVK.M	0.73
alpha-2-macroglobulin precursor	**P01023** (A2MG_ HUMAN)	R.AFQPFFVELTM*PYSVIR.G	0.68
alpha-2-macroglobulin precursor	**P01023** (A2MG_ HUMAN)	R.AFQPFFVELTMPYSVIR.G	0.62
alpha-2-macroglobulin precursor	**P01023** (A2MG_ HUMAN)	R.NQGNTWLTAFVLK.T	0.73

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	K.IDRFMQAVTGWK.T	0.81
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	K.LDTEDKLR.A	0.72
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	K.TGCSLMGASVDSTLAFNTYVHFQGK.M	0.64
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	R.AAMVGMLANFLGFR.I	0.62
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	K.NDNDNIFLSPLSISTAFAMTK.L	0.64
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	K.SKLPGIVAEGRDDLYVSDAFHK.A	0.81
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	R.EVPLNTIIFMGR.V	0.61
antithrom bin-III precursor	**P01008** (ANT3_HUMAN)	R.FATTFYQHLADSKNDNDNIFLSPLSISTAFAMTK.L	0.66
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	R.ITDVIPSEAINELTVLVLVNTIYFK.G	0.60
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	R.RVWELSK.A	0.63
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	R.VAEGTQVLELPFKGDDITM*VLILPKPEK.S	0.62
antithrombin-III precursor	**P01008** (ANT3_HUMAN)	R.VAEGTQVLELPFKGDDITMVLILPKPEK.S	0.62
apolipoprotein A-II preproprotein	**P02652** (APOA2_HUMAN)	K.AGTELVNFLSYFVELGTQPATQ.-	0.61
apolipoprotein A-II preproprotein	**P02652** (APOA2_HUMAN)	K.EPCVESLVSQYFQTVTDYGK.D	0.63

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.ALVQQMEQLR.Q	0.61
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.LGPHAGDVEGHLSFLEK.D	0.61
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.SELTQQLNALFQDK.L	0.71
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.SLAELGGHLDQQVEEFRR.R	0.61
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.VKIDQTVEELRR.S	0.75
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.VNSFFSTFK.E	0.63
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.ATFQTPDFIVPLTDLR.I	0.65
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.AVSM*PSFSILGSDVR.V	0.65
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.AVSMPSFSILGSDVR.V	0.67
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.EQHLFLPFSYK.N	0.65
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.KIISDYHQQFR.Y	0.63
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.QVFLYPEKDEPTYILNIK.R	0.64
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.SPAFTDLHLR.Y	0.69
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.TILGTMPAFEVSLQALQK.A	0.62

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.VLADKFIIPGLK.L	0.72
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.YSQPEDSLIPFFEITVPESQLTVSQFTLPK.S	0.61
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.DLKVEDIPLAR.I	0.64
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.GIISALLVPPETEEAK.Q	0.81
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.ILGEELGFASLHDLQLLGK.L	0.62
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.LELELRPTGEIEQYSVSATYELQR.E	0.60
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.NIQEYLSILTDPDGK.G	0.68
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.TFQIPGYTVPVVNVEVSPFTIEMSAF GYVFPK.A	0.75
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.TIDQMLNSELQWPVPDIYLR.D	0.70
apolipoprotein C-I precursor	**P02654** (APOC1_HUMAN)	K.MREWFSETFQK.V	0.61
apolipoprotein C-II precursor	**P02655** (APOC2_HUMAN)	K.STAAMSTYTGIFTDQVLSVLKGEE.-	0.61
apolipoprotein C-III precursor	**P02656** (APOC3_HUMAN)	R.GWVTDGFSSLK.D	0.62
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.AATVGSLAGQPLQER.A	0.61
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.LKSWFEPLVEDMQR.Q	0.65

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.WVQTLSEQVQEELLSSQVTQELR.A	0.64
ATP-binding cassette sub-family D member 4	**014678** (ABCD4_HUMAN)	K.LCGGGRWELM*R.I	0.60
ATP-binding cassette sub-family F member 3	**Q9NUQ8** (ABCF3_HUMAN)	K.LPGLLK.R	0.73
beta-2-glycoprotein 1 precursor	**P02749** (APOH_ HUMAN)	K.EHSSLAFWK.T	0.64
beta-2-glycoprotein 1 precursor	**P02749** (APOH_ HUMAN)	R.TCPKPDDLPFSTVVPLK.T	0.60
beta-2-glycoprotein 1 precursor	**P02749** (APOH_ HUMAN)	R.VCPFAGILENGAVR.Y	0.68
beta-Ala-His dipeptidase precursor	**Q96KN2** (CNDP1_HUMAN)	K.LFAAFFLEMAQLH.-	0.68
biotinidase precursor	**P43251** (BTD_ HUMAN)	K.SHLIIAQVAK.N	0.62
carboxypeptidase B2 preproprotein	**Q961Y4** (CBPB2_HUMAN)	K.NAIWIDCGIHAR.E	0.62
carboxypeptidase N catalytic chain precursor	**P15169** (CBPN_ HUMAN)	R.EALIQFLEQVHQGIK.G	0.69
carboxypeptidase N subunit 2 precursor	**P22792** (CPN2_HUMAN)	R.LLNIQTYCAGPAYLK.G	0.62
catalase	**P04040** (CATA_ HUMAN)	R.LCENIAGHLKDAQIFIQK.K	0.62
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.AETGDKVYVHLK.N	0.61
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.AGLQAFFQVQECNK.S	0.62

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.DIASGLIGPLIICK.K	0.63
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.DIFTGLIGPM*K.I	0.63
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.DIFTGLIGPMK.I	0.68
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.M*YYSAVDPTKDIFTGLIGPMK.I	0.62
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.MYYSAVDPTKDIFTGLIGPM*K.I	0.63
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.PVWLGFLGPIIK.A	0.63
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.ADDKVYPGEQYTYMLLATEEQSPGEGDGNCVTR.I	0.64
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.DTANLFPQTSLTLHM*WPDTEGTFNVECLTTDHYTGGMK.Q	0.71
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.DTANLFPQTSLTLHMWPDTEGTFNVECLTTDHYTGGMK.Q	0.68
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.FNKNNEGTYYSPNYNPQSR.S	0.74
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.IDTINLFPATLFDAYM*VAQNPGEWM*LSCQNLNHLK.A	0.75
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.IDTINLFPATLFDAYM*VAQNPGEWMLSCQNLNHLK.A	0.86
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.IDTINLFPATLFDAYMVAQNPGEWM*LSCQNLNHLK.A	0.60
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.KAEEEHLGILGPQLHADVGDKVK.I	0.71

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.TTIEKPVWLGFLGPIIK.A	0.63
cholinesterase precursor	**P06276** (CHLE_ HUMAN)	R.FWTSFFPK.V	0.76
clusterin preproprotein	**P10909** (CLUS_ HUMAN)	K.LFDSDPITVTVPVEVSR.K	0.78
clusterin preproprotein	**P10909** (CLUS_ HUMAN)	R.ASSIIDELFQDR.F	0.68
coagulation factor IX preproprotein	**P00740** (FA9_HUMAN)	K.WIVTAAHCVETGVK.I	0.60
coagulation factor VII isoform a preproprotein	**P08709** (FA7_HUMAN)	R.FSLVSGWGQLLDR.G	0.78
coagulation factor X preproprotein	**P00742** (FA10_HUMAN)	K.ETYDFDIAVLR.L	0.75
coiled-coil domain-containing protein 13	**Q8IYE1** (CCD13_HUMAN)	K.VRQLEMEIGQLNVHYLR.N	0.67
complement C1q subcomponent subunit A precursor	**P02745** (C1QA_ HUMAN)	R.PAFSAIR.R	0.66
complement C1q subcomponent subunit B precursor	**P02746** (C1QB_ HUMAN)	K.VVTFCDYAYNTFQVTTGGMVLK.L	0.63
complement C1q subcomponent subunit C precursor	**P02747** (C1QC_ HUMAN)	K.FQSVFTVTR.Q	0.63
complement C1r subcomponent precursor	**P00736** (C1R_ HUMAN)	K.TLDEFTIIQNLQPQYQFR.D	0.62
complement C1r subcomponent precursor	**P00736** (C1R_ HUMAN)	R.MDVFSQNMFCAGHPSLK.Q	0.68
complement C1r subcomponent precursor	**P00736** (C1R_ HUMAN)	R.WILTAAHTLYPK.E	0.74

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
complement C1s subcomponent precursor	**P09871** (C1S_ HUMAN)	K.FYAAGLVSWGPQCGTYGLYTR.V	0.68
complement C1s subcomponent precursor	**P09871** (C1S_ HUMAN)	K.GFQVVVTLR.R	0.63
complement C2 isoform 3	**P06681** (CO2_HUMAN)	R.GALISDQWVLTAAHCFR.D	0.61
complement C2 isoform 3	**P06681** (CO2_HUMAN)	R.PICLPCTMEANLALR.R	0.66
complement C3 precursor	**P01024** (CO3_HUMAN)	R.YYGGGYGSTQATFMVFQALAQYQK .D	0.75
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.GLCVATPVQLR.V	0.74
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.M*RPSTDTITVM*VENSHGLR.V	0.83
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.MRPSTDTITVM*VENSHGLR.V	0.72
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.VGLSGM*AIADVTLLSGFHALR.A	0.71
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.VLSLAQEQVGGSPEK.L	0.63
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.EMSGSPASGIPVK.V	0.65
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.GCGEQTM*IYLAPTLAASR.Y	0.75
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.GLQDEDGYR.M	0.75
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.GQIVFMNREPK.R	0.93

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.KKEVYM*PSSIFQDDFVIPDISEPGTWK.I	0.72
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.LPMSVR.R	0.78
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.LTVAAPPSGGPGFLSIER.P	0.84
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.NFLVR.A	0.75
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.NGESVKLHLETDSLALVALGALDTALYAAGSK.S	0.88
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.QGSFQGGFR.S	0.60
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.TLEIPGNSDPNMIPDGDFNSYVR.V	0.69
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.VTASDPLDTLGSEGALSPGGVASLLR .L	0.63
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.YLDKTEQWSTLPPETK.D	0.67
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.ADNFLLENTLPAQSTFTLAISAYALSLGDK.T	0.63
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.ALVEGVDQLFTDYQIK.D	0.63
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.DGHVILQLNSIPSSDFLCVR.F	0.62
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.DVFLEMNIPYSVVR.G	0.63
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.EFPYRIPLDLVPK.T	0.60

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.FQNSAILTIQPK.Q	0.67
complement C5 preproprotein	**P01031** (CO5_HUMAN)	K.VFKDVFLEMNIPYSVVR.G	0.63
complement C5 preproprotein	**P01031** (CO5_HUMAN)	R.VFQFLEK.S	0.61
complement component C6 precursor	**P13671** (CO6_HUMAN)	K.DLHLSDVFLK.A	0.60
complement component C6 precursor	**P13671** (CO6_HUMAN)	R.TECIKPVVQEVLTITPFQR.L	0.62
complement component C7 precursor	**P10643** (CO7_HUMAN)	K.SSGWHFVVK.F	0.61
complement component C7 precursor	**P10643** (CO7_HUMAN)	R.ILPLTVCK.M	0.75
complement component C8 alpha chain precursor	**P07357** (CO8A_ HUMAN)	R.ALDQYLMEFNACR.C	0.65
complement component C8 gamma chain precursor	**P07360** (CO8G_ HUMAN)	K.YGFCEAADQFHVLDEVR.R	0.60
complement component C9 precursor	**P02748** (CO9_HUMAN)	R.AIEDYINEFSVRK.C	0.69
complement component C9 precursor	**P02748** (CO9_HUMAN)	R.TAGYGINILGMDPLSTPFDNEFYNGLCNR.D	0.69
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.ALFVSEEEKK.L	0.64
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.CLVNLIEK.V	0.70
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.EAGIPEFYDYDVALIK.L	0.66

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.VSEADSSNADWVTK.Q	0.73
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.YGQTIRPICLPCTEGTTR.A	0.67
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.DLEIEVVLFHPNYNINGK.K	0.71
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.FLCTGGVSPYADPNTCR.G	0.64
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.DGWSAQPTCIK.S	0.80
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.EGWIHTVCINGR.W	0.67
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.TDCLSLPSFENAIPMGEK.K	0.61
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	R.DTSCVNPPTVQNAYIVSR.Q	0.60
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	K.CTSTGWIPAPR.C	0.68
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	K.IIYKENER.F	0.76
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	K.IVSSAM*EPDREYHFGQAVR.F	0.75
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	K.IVSSAMEPDREYHFGQAVR.F	0.68
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	R.CTLKPCDYPDIK.H	0.81
complement factor H isoform b precursor	**P08603** (CFAH_ HUMAN)	R.KGEWVALNPLR.K	0.60

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Protein Description	Uniprot ID (name)	Peptide	S_AUC
complement factor H isoform b precursor	**P08603** (CFAH_HUMAN)	R.KGEWVALNPLRK.C	0.69
complement factor H isoform b precursor	**P08603** (CFAH_HUMAN)	R.RPYFPVAVGK.Y	0.68
complement factor H-related protein 1 precursor	**Q03591** (FHR1_HUMAN)	R.EIMENYNIALR.W	0.64
complement factor I preproprotein	**P05156** (CFAI_HUMAN)	K.DASGITCGGIYIGGCWILTAAHCLR.A	0.71
complement factor I preproprotein	**P05156** (CFAI_HUMAN)	K.VANYFDWISYHVGR.P	0.72
complement factor I preproprotein	**P05156** (CFAI_HUMAN)	R.IIFHENYNAGTYQNDIALIEMK.K	0.63
complement factor I preproprotein	**P05156** (CFAI_HUMAN)	R.YQIWTTVVDWIHPDLK.R	0.63
conserved oligomeric Golgi complex subunit 6 isoform	**Q9Y2V7** (COG6_HUMAN)	K.ISNLLK.F	0.65
corticosteroid-binding globulin precursor	**P08185** (CBG_HUMAN)	R.WSAGLTSSQVDLYIPK.V	0.62
C-reactive protein precursor	**P02741** (CRP_HUMAN)	K.YEVQGEVFTKPQLWP.-	0.60
dopamine beta-hydroxylase precursor	**P09172** (DOPO_HUMAN)	R.HVLAAWALGAK.A	0.88
double-stranded RNA-specific editase B2	**Q9NS39** (RED2_HUMAN)	R.AGLRYVCLAEPAER.R	0.75
dual oxidase 2 precursor	**Q9NRD8** (DUOX2_HUMAN)	R.FTQLCVKGGGGGGNGIR.D	0.65
FERM domain-containing protein 8	**Q9BZ67** (FRMD8_HUMAN)	R.VQLGPYQPGRPAACDLR.E	0.65

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Protein Description	**Uniprot ID (name)**	**Peptide**	**S_ AUC**
fetuin-B precursor	**Q9UGM5** (FETUB_ HUMAN)	R.GGLGSLFYLTLDVLETDCHVLR.K	0.83
ficolin-3 isoform 1 precursor	**075636** (FCN3_HUMAN)	R.ELLSQGATLSGWYHLCLPEGR.A	0.69
gastric intrinsic factor precursor	**P27352** (IF_ HUMAN)	K.KTTDM*ILNEIKQGK.F	0.60
gelsolin isoform d	**P06396** (GELS_ HUMAN)	K.NWRDPDQTDGLGLSYLSSHIANVER.V	0.72
gelsolin isoform d	**P06396** (GELS_ HUMAN)	K.TPSAAYLWVGTGASEAEK.T	0.80
gelsolin isoform d	**P06396** (GELS_ HUMAN)	R.VEKFDLVPVPTNLYGDFFTGDAYVIL K.T	0.60
gelsolin isoform d	**P06396** (GELS_ HUMAN)	R.VPFDAATLHTSTAMAAQHGM DDD GTGQK.Q	0.67
glutathione peroxidase 3 precursor	**P22352** (GPX3_HUMAN)	K.FYTFLK.N	0.63
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.GDKVWVYPPEKK.E	0.65
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.LLQDEFPGIPSPLDAAVECHR.G	0.71
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.SGAQATWTELPWPHEK.V	0.64
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.SGAQATWTELPWPHEKVDGALCMEK.S	0.61
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.VDGALCMEK.S	0.66
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.DYFMPCPGR.G	0.68

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.EWFWDLATGTM*K.E	0.64
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.QGHNSVFLIK.G	0.71
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	K.HQGTITVNEEGTQATTVTTVGFMPLSTQVR.F	0.60
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	K.YEITTIHNLFR.K	0.62
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	R.LNILNAK.F	0.68
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	R.NFGYTLR.S	0.64
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	R.VLKDQVNTFDNIFIAPVGISTAMGM*ISLGLK.G	0.63
hepatocyte cell adhesion molecule precursor	**Q14CZ8** (HECAM_ HUMAN)	K.PLLNDSRMLLSPDQK.V	0.61
hepatocyte growth factor activator preproprotein	**Q04756** (HGFA_ HUMAN)	R.VQLSPDLLATLPEPASPGR.Q	0.82
histidine-rich glycoprotein precursor	**P04196** (HRG_ HUMAN)	R.DGYLFQLLR.I	0.63
hyaluronan-binding protein 2 isoform 1 preproprotein	**Q14520** (HABP2_HUMAN)	K.FLNWIK.A	0.82
hyaluronan-binding protein 2 isoform 1 preproprotein	**Q14520** (HABP2_HUMAN)	K.LKPVDGHCALESK.Y	0.61
hyaluronan-binding protein 2 isoform 1 preproprotein	**Q14520** (HABP2_HUMAN)	K.RPGVYTQVTK.F	0.74
inactive caspase-12	**Q6UXS9** (CASPC_ HUMAN)	K.AGADTHGRLLQGNICNDAVTK.A	0.74

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
insulin-degrading enzyme isoform 1	**P14735** (IDE_ HUMAN)	K.KIIEKM*ATFEIDEK.R	0.85
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	R.SFEGLGQLEVLTLDHNQLQEVK.A	0.62
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.ELAAQTIKK.S	0.81
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.GSLVQASEANLQAAQDFVR.G	0.71
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.QLVHHFEIDVDIFEPQGISK.L	0.70
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.QYYEGSEIVVAGR.I	0.83
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.EVAFDLEIPKTAFISDFAVTADGNAFIGDIK.D	0.70
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.GMADQDGLKPTIDKPSEDSPPLEM*LGPR.R	0.63
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.GMADQDGLKPTIDKPSEDSPPLEMLGPR.R	0.60
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.FDPAKLDQIESVITATSANTQLVLETLAQM*DDLQDFLSK.D	0.80
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.KFYNQVSTPLLR.N	0.76
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.NILFVIDVSGSM*WGVK.M	0.68
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.NILFVIDVSGSMWGVK.M	0.62
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.KLGSYEHR.I	0.72

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.LSNENHGIAQR.I	0.66
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.MATTMIQSK.V	0.60
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.SILQM*SLDHHIVTPLTSLVIENEAGDER.M	0.63
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.SILQMSLDHHIVTPLTSLVIENEAGDER.M	0.65
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.TEVNVLPGAK.V	0.69
inter-a lpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.NVVFVIDK.S	0.68
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.WKETLFSVMPGLK.M	0.65
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.YIFHNFM*ER.L	0.67
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.FAHTVVTSR.V	0.63
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.FKPTLSQQQK.S	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.IHEDSDSALQLQDFYQEVANPLLTAVTFEYPSNAVEEVTQNNFR.L	0.64
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.MNFRPGVLSSR.Q	0.63
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.NVHSAGAAGSR.M	0.62
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.NVHSGSTFFK.Y	0.75

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Protein Description	**Uniprot ID (name)**	**Peptide**	**S_ AUC**
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.RLGVYELLLK.V	0.66
kallistatin precursor	**P29622** (KAIN_ HUMAN)	K.KLELHLPK.F	0.78
kallistatin precursor	**P29622** (KAIN_ HUMAN)	R.EIEEVLTPEMLMR.W	0.60
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.AATGECTATVGKR.S	0.67
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.LGQSLDCNAEVYVVPWEK.K	0.72
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.YNSQNQSNNQFVLYR.I	0.62
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	R.QVVAGLNFR.I	0.64
leucine-rich alpha-2-glycoprotein precursor	**P02750** (A2GL_ HUMAN)	K.DLLLPQPDLR.Y	0.64
leucine-rich alpha-2-glycoprotein precursor	**P02750** (A2GL_ HUMAN)	R.LHLEGNKLQVLGK.D	0.76
leucine-rich alpha-2-glycoprotein precursor	**P02750** (A2GL_ HUMAN)	R.TLDLGENQLETLPPDLLR.G	0.61
lipopolysaccharide-binding protein precursor	**P18428** (LBP_ HUMAN)	K.GLQYAAQEGLLALQSELLR.I	0.82
lipopolysaccharide-binding protein precursor	**P18428** (LBP_ HUMAN)	K.LAEGFPLPLLK.R	0.66
lumican precursor	**P51884** (LUM_ HUMAN)	K.SLEYLDLSFNQIAR.L	0.65
lumican precursor	**P51884** (LUM_ HUMAN)	R.LKEDAVSAAFK.G	0.74

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
m7GpppX diphosphatase	**Q96C86** (DCPS_ HUMAN)	R.IVFENPDPSDGFVLIPDLK.W	0.62
matrix metalloproteinase-19 isoform 1 preproprotein	**Q99542** (MMP19_HUMAN)	R.VYFFK.G	0.63
MBT domain-containing protein 1	**Q05BQ5** (MBTD1_HUMAN)	K.WFDYLR.E	0.65
monocyte differentiation antigen CD14 precursor	**P08571** (CD14_HUMAN)	R.LTVGAAQVPAQLLVGALR.V	0.66
pappalysin-1 preproprotein	**Q13219** (PAPP1_HUMAN)	R.VSFSSPLVAISGVALR.S	0.66
phosphatidylinositol-glycan-specific phospholipase D precursor	**P80108** (PHLD_ HUMAN)	K.GIVAAFYSGPSLSDKEK.L	0.71
phosphatidylinositol-glycan-specific phospholipase D precursor	**P80108** (PHLD_ HUMAN)	R.WYVPVKDLLGIYEK.L	0.71
pigment epithelium-derived factor precursor	**P36955** (PEDF_ HUMAN)	K.LQSLFDSPDFSK.I	0.61
pigment epithelium-derived factor precursor	**P36955** (PEDF_ HUMAN)	R.ALYYDLISSPDIHGTYK.E	0.72
plasma kallikrein preproprotein	**P03952** (KLKB1_HUMAN)	R.CLLFSFLPASSINDMEKR.F	0.60
plasma protease C1 inhibitor precursor	**P05155** (IC1_HUMAN)	K.FQPTLLTLPR.I	0.70
plasma protease C1 inhibitor precursor	**P05155** (IC1_HUMAN)	K.GVTSVSQIFHSPDLAIR.D	0.66
plasminogen isoform 1 precursor	**P00747** (PLMN_ HUMAN)	K.VIPACLPSPNYVVADR.T	0.63
plasminogen isoform 1 precursor	**P00747** (PLMN_ HUMAN)	R.FVTWIEGVMR.N	0.60

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
plasminogen isoform 1 precursor	**P00747** (PLMN_ HUMAN)	R.HSIFTPETNPR.A	0.63
platelet basic protein preproprotein	**P02775** (CXCL7_HUMAN)	K.GKEESLDSDLYAELR.C	0.70
platelet glycoprotein V precursor	**P40197** (GPV_ HUMAN)	K.MVLLEQLFLDHNALR.G	0.66
platelet glycoprotein V precursor	**P40197** (GPV_ HUMAN)	R.LVSLDSGLLNSLGALTELQFHR.N	0.88
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	K.ALLAYAFSLLGK.Q	0.66
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	K.DLFHCVSFTLPR.I	0.86
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	K.MLQITNTGFEMK.L	0.84
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	R.NELIPLIYLENPRR.N	0.65
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	R.SYIFIDEAHITQSLTWLSQMQK.D	0.68
pregnancy-specific beta-1-glycoprotein 2 precursor	**P11465** (PSG2_HUMAN)	R.SDPVTLNLLHGPDLPR.I	0.66
pregnancy-specific beta-1-glycoprotein 3 precursor	**Q16557** (PSG3_HUMAN)	R.TLFLFGVTK.Y	0.62
pregnancy-specific beta-1-glycoprotein 5 precursor	**Q15238** (PSG5_HUMAN)	R.ILILPSVTR.N	0.76
pregnancy-specific beta-1-glycoprotein 6 isoform a	**Q00889** (PSG6_HUMAN)	R.SDPVTLNLLPK.L	0.63
progesterone-induced-blocking factor 1	**Q8WXW3** (PIBF1_HUMAN)	R.VLQLEK.Q	0.71

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
protein AMBP preproprotein	**P02760** (AMBP_ HUMAN)	R.VVAQGVGIPEDSIFTMADR.G	0.60
protein CBFA2T2 isoform MTGR1b	**043439** (MTG8R_ HUMAN)	R.LTEREWADEWKHLDHALNCIMEMVEK.T	0.70
protein FAM98C	**Q17RN3** (FA98C_ HUMAN)	R.ALCGGDGAAALREPGAGLR.L	0.75
protein NLRC3	**Q7RTR2** (NLRC3_HUMAN)	K.ALM*DLLAGKGSQGSQAPQALDR.T	0.92
protein Z-dependent protease inhibitor precursor	**Q9UK55** (ZPI_ HUMAN)	K.MGDHLALEDYLTTDLVETWLR.N	0.60
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	K.SPQELLCGASLISDR.W	0.84
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.LAVTTHGLPCLAWASAQAK.A	0.62
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.SEGSSVNLSPPLEQCVPDR.G	0.70
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.SGIECQLWR.S	0.68
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.TATSEYQTFFNPR.T	0.60
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.VTGWGNLKETWTANVGK.G	0.69
putative hydroxypyruvate isomerase isoform 1	**Q5T013** (HYI_ HUMAN)	R.IHLM*AGR.V	0.69
putative hydroxypyruvate isomerase isoform 1	**Q5T013** (HYI_ HUMAN)	R.IHLMAGR.V	0.66
ras-like protein family member 10A precursor	**Q92737** (RSLAA_ HUMAN)	R.PAHPALR.L	0.71

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Protein Description	**Uniprot ID (name)**	**Peptide**	**S_ AUC**
ras-related GTP-binding protein A	**Q7L523** (RRAGA_ HUMAN)	K.ISNIIK.Q	0.82
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	K.M*KYWGVASFLQK.G	0.73
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	R.FSGTWYAM*AK.K	0.63
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	R.LLNLDGTCADSYSFVFSR.D	0.79
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	R.LLNNWDVCADMVGTFTDTEDPAKFK.M	0.77
sex hormone-binding globulin isoform 1 precursor	**P04278** (SHBG_ HUMAN)	R.LFLGALPGEDSSTSFCLNGLWAQGQR.L	0.66
sex hormone-binding globulin isoform 4 precursor	**P04278** (SHBG_ HUMAN)	K.DDWFMLGLR.D	0.60
sex hormone-binding globulin isoform 4 precursor	**P04278** (SHBG_ HUMAN)	R.SCDVESNPGIFLPPGTQAEFNLR.G	0.64
sex hormone-binding globulin isoform 4 precursor	**P04278** (SHBG_ HUMAN)	R.TWDPEGVIFYGDTNPKDDWFM*LGLR.D	0.65
sex hormone-binding globulin isoform 4 precursor	**P04278** (SHBG_ HUMAN)	R.TWDPEGVIFYGDTNPKDDWFMLGLR.D	0.66
signal transducer and activator of transcription 2	**P52630** (STAT2_HUMAN)	R.KFCRDIQDPTQLAEMIFNLLLEEK.R	0.73
spectrin beta chain, non-erythrocytic 1	**Q13813** (SPTN1_HUMAN)	R.NELIRQEKLEQLAR.R	0.60
stabilin-1 precursor	**Q9NY15** (STAB1_HUMAN)	R.KNLSER.W	0.88
succinate-semialdehyde dehydrogenase, mitochondrial	**P51649** (SSDH_ HUMAN)	R.KWYNLMIQNK.D	0.88

(continued)

Protein Description	Uniprot ID (name)	Peptide	S_ AUC
tetranectin precursor	**P05452** (TETN_ HUMAN)	K.SRLDTLAQEVALLK.E	0.75
THAP domain-containing protein 6	**Q8TBB0** (THAP6_HUMAN)	K.RLDVNAAGIWEPKK.G	0.69
thyroxine- binding globulin precursor	**P05543** (THBG_ HUMAN)	R.SILFLGK.V	0.79
tripartite motif-containing protein 5	**Q9C035** (TRIM5_HUMAN)	R.ELISDLEHRLQGSVM*ELLQGVDGVIK.R	0.60
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.EDFTSLSLVLYSR.K	0.66
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.ELSSFIDKGQELCADYSENTFTEYK.K	0.67
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.ELSSFIDKGQELCADYSENTFTEYKK. K	0.66
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.EVVSLTEACCAEGADPDCYDTR.T	0.65
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.TAMDVFVCTYFMPAAQLPELPDVELPTNKDVCDPGNTK.V	0.84
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	R.RTHLPEVFLSK.V	0.69
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	R.VCSQYAAYGEK.K	0.66
vitronectin precursor	**P04004** (VTNC_ HUMAN)	K.LIRDVWGIEGPIDAAFTR.I	0.61
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.DVWGIEGPIDAAFTR.I	0.63
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.ERVYFFK.G	0.81

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Protein Description	Uniprot ID (name)	Peptide	S_ AUC
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.FEDGVLDPDYPR.N	0.64
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.IYISGM*APRPSLAK.K	0.75
zinc finger protein 142	**P52746** (ZN142_HUMAN)	K.TRFLLR.T	0.66

Table 9. Significant peptides (AUC>0.6) forfor X!Tandem only

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
afamin precursor	**P43652** (AFAM_ HUMAN)	K.HELTDEELQSLFTNFANVVDK.C	0.65
afamin precursor	**P43652** (AFAM_ HUMAN)	R.NPFVFAPTLLTVAVHFEEVAK.S	0.91
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.ADLSGITGAR.N	0.67
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.MEEVEAMLLPETLKR.W	0.60
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	K.WEMPFDPQDTHQSR.F	0.64
alpha-1-antichymotrypsin precursor	**P01011** (AACT_ HUMAN)	R.LYGSEAFATDFQDSAAAK.K	0.62
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	K.HQFLLTGDTQGR.Y	0.72
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	K.NGVAQEPVHLDSPAIK.H	0.63
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	K.SLPAPWLSM*APVSWITPGLK.T	0.72
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	K.VTLTCVAPLSGVDFQLRR.G	0.67
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.C*EGPIPDVTFELLR.E	0.67
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.C*LAPLEGAR.F	0.79
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.CLAPLEGAR.F	0.63
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.GVTFLLR.R	0.69
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.LHDNQNGWSGDSAPVELILSDETLPAPEFSPEPESGR.A	0.60
alpha-1B-glycoprotein precursor	**P04217** (A1BG_ HUMAN)	R.TPGAAANLELIFVGPQHAGNYR.C	0.62

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
alpha-2-antiplasmin isoform a precursor	**P08697** (A2AP_ HUMAN)	K.HQM*DLVATLSQLGLQELFQAPDLR.G	0.61
alpha-2-antiplasmin isoform a precursor	**P08697** (A2AP_ HUMAN)	R.LCQDLGPGAFR.L	0.68
alpha-2-antiplasmin isoform a precursor	**P08697** (A2AP_ HUMAN)	R.WFLLEQPEIQVAHFPFK.N	0.60
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	K.VWPQQPSGELFEIEIDTLETTCHVLDPTPVAR.C	0.61
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	R.HTFMGVVSLGSPSGEVSHPR.K	0.68
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	R.Q*PNCDDPETEEAALVAIDYINQNLPWGYK.H	0.69
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	R.QPNCDDPETEEAALVAIDYINQNLPWGYK.H	0.64
alpha-2-HS-glycoprotein preproprotein	**P02765** (FETUA_ HUMAN)	R.TVVQPSVGAAAGPVVPPCPGR.I	0.64
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	K.QPFVQGLALYTPVVLPR.S	0.73
angiotensinogen preproprotein	**P01019** (ANGT_ HUMAN)	R.AAM*VGM*LANFLGFR.I	0.62
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	K.LVPFATELHER.L	0.64
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	R.LLPHANEVSQK.I	0.61
apolipoprotein A-IV precursor	**P06727** (APOA4_HUMAN)	R.SLAPYAQDTQEKLNHQLEGLTFQMK.K	0.70
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.FPEVDVLTK.Y	0.61
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.HINIDQFVR.K	0.70
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.LLSGGNTLHLVSTTK.T	0.66
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.Q*VFLYPEKDEPTYILNIKR.G	0.81
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.QVFLYPEKDEPTYILNIKR.G	0.77

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.SLHMYANR.L	0.83
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.SVSDGIAALDLNAVANK.I	0.62
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.SVSLPSLDPASAKIEGNLIFDPNNYL PK.E	0.67
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.TEVIPPLIENR.Q	0.63
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	K.VLVDHFGYTK.D	0.76
apolipoprotein B-100 precursor	**P04114** (APOB_ HUMAN)	R.TSSFALNLPTLPEVKFPEVDVLTK.Y	0.62
apolipoprotein C-III precursor	**P02656** (APOC3_HUMAN)	R.GWVTDGFSSLKDYWSTVK.D	0.66
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.GEVQAMLGQSTEELR.V	0.81
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.LAVYQAGAR.E	0.63
apolipoprotein E precursor	**P02649** (APOE_ HUMAN)	R.LGPLVEQGR.V	0.69
attractin isoform 2 preproprotein	**O75882** (ATRN_ HUMAN)	K.LTLTPWVGLR.K	0.69
beta-2-glycoprotein 1 precursor	**P02749** (APOH_ HUMAN)	K.FICPLTGLWPINTLK.C	0.63
beta-2-glycoprotein 1 precursor	**P02749** (APOH_ HUMAN)	K.TFYEPGEEITYSCKPGYVSR.G	0.62
beta-Ala-His dipeptidase precursor	**Q96KN2** (CNDP1_HUMAN)	K.MVVSMTLGLHPWIANIDDTQYLAAK.R	0.81
beta-Ala-His dipeptidase precursor	**Q96KN2** (CNDP1_HUMAN)	K.VFQYIDLHQDEFVQTLK.E	0.65
biotinidase precursor	**P43251** (BTD_ HUMAN)	R.TSIYPFLDFM*PSPQVVR.W	0.79
carboxypeptidase N catalytic chain precursor	**P15169** (CBPN_ HUMAN)	R.ELMLQLSEFLCEEFR.N	0.61
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.AEEEHLGILGPQLHADVGDKVK.I	0.73
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.ALYLQYTDETFR.T	0.64
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.DVDKEFYLFPTVFDENESLLLEDNIR .M	0.62

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Protein description	Uniprot ID (name)	Peptide	XT_ AUC
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	K.HYYIGIIETTWDYASDHGEK.K	0.61
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.EYTDASFTNRK.E	0.67
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.HYYIAAEEIIWNYAPSGIDIFTK.E	0.63
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.IYHSHIDAPK.D	0.62
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.Q*KDVDKEFYLFPTVFDENESLLLEDNIR.M	0.74
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.QKDVDKEFYLFPTVFDENESLLLEDNIR.M	0.65
ceruloplasmin precursor	**P00450** (CERU_ HUMAN)	R.TYYIAAVEVEWDYSPQR.E	0.90
coagulation factor IX preproprotein	**P00740** (FA9_HUMAN)	R.SALVLQYLR.V	0.69
coagulation factor V precursor	**P12259** (FA5_HUMAN)	K.EFNPLVIVGLSK.D	0.61
coagulation factor XII precursor	**P00748** (FA12_HUMAN)	R.NPDNDIRPWCFVLNR.D	0.65
coagulation factor XII precursor	**P00748** (FA12_HUMAN)	R.VVGGLVALR.G	0.61
complement C1q subcomponent subunit B precursor	**P02746** (C1QB_ HUMAN)	K.NSLLGMEGANSIFSGFLLFPDMEA. -	0.64
complement C1q subcomponent subunit B precursor	**P02746** (C1QB_ HUMAN)	K.VPGLYYFTYHASSR.G	0.63
complement C1q subcomponent subunit C precursor	**P02747** (C1QC_ HUMAN)	R.Q*THQPPAPNSLIR.F	0.60
complement C1r subcomponent precursor	**P00736** (C1R_ HUMAN)	R.LPVANPQACENWLR.G	0.72
complement C2 isoform 3	**P06681** (CO2_HUMAN)	K.NQGILEFYGDDIALLK.L	0.74
complement C2 isoform 3	**P06681** (CO2_HUMAN)	K.RNDYLDIYAIGVGK.L	0.61
complement C2 isoform 3	**P06681** (CO2_HUMAN)	R.QPYSYDFPEDVAPALGTSFSHMLGATNPTQK.T	0.78
complement C3 precursor	**P01024** (CO3_HUMAN)	R.IHWESASLLR.S	0.69
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.FACYYPR.V	0.64

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Protein description	Uniprot ID (name)	Peptide	XT_ AUC
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.LHLETDSLALVALGALDTALYAAGSK.S	0.74
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.LVNGQSHISLSK.A	0.64
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.M*RPSTDTITVMVENSHGLR.V	0.60
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.MRPSTDTITVMVENSHGLR.V	0.65
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.SCGLHQLLR.G	0.74
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.VGLSGMAIADVTLLSGFHALR.A	0.61
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	K.YVLPNFEVK.I	0.64
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.ALEILQEEDLIDEDDIPVR.S	0.64
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.ECVGFEAVQEVPVGLVQPASATLYDYYNPER.R	0.62
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.EELVYELNPLDHR.G	0.66
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.STQDTVIALDALSAYWIASHTTEER.G	0.70
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.VGDTLNLNLR.A	0.79
complement C4-A isoform 1	**P0C0L4** (CO4A_ HUMAN)	R.VHYTVCIWR.N	0.65
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	K.GLCVATPVQLR.V	1.00
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	K.KYVLPNFEVK.I	0.60
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	K.VDFTLSSERDFALLSLQVPLKDAK.S	0.74
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	R.EMSGSPASGIPVK.V	0.72
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	R.GCGEQTM*IYLAPTLAASR.Y	0.75
complement C4-B-like preproprotein	**P0C0L5** (CO4B_ HUMAN)	R.NGESVKLHLETDSLALVALGALDTALYAAGSK.S	0.85
complement C5 preproprotein	**P01031** (CO5_HUMAN)	R.IPLDLVPK.T	0.65
complement C5 preproprotein	**P01031** (CO5_HUMAN)	R.SYFPESWLWEVHLVPR.R	0.63
complement C5 preproprotein	**P01031** (CO5_HUMAN)	R.YGGGFYSTQDTINAIEGLTEYSLLVK.Q	0.62

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Protein description	Uniprot ID (name)	Peptide	XT_ AUC
complement component C6 precursor	**P13671** (CO6_HUMAN)	K.ENPAVIDFELAPIVDLVR.N	0.63
complement component C8 alpha chain precursor	**P07357** (CO8A_ HUMAN)	K.YNPVVIDFEMQPIHEVLR.H	0.61
complement component C8 alpha chain precursor	**P07357** (CO8A_ HUMAN)	R.HTSLGPLEAK.R	0.65
complement component C8 beta chain preproprotein	**P07358** (CO8B_ HUMAN)	K.C*QHEMDQYWGIGSLASGINLFTNSFEGPVLDHR.Y	0.61
complement component C8 beta chain preproprotein	**P07358** (CO8B_ HUMAN)	K.SGFSFGFK.I	0.64
complement component C8 beta chain preproprotein	**P07358** (CO8B_ HUMAN)	R.DTMVEDLVVLVR.G	0.77
complement component C8 gamma chain precursor	**P07360** (CO8G_ HUMAN)	K.ANFDAQQFAGTWLLVAVGSACR.F	0.63
complement component C8 gamma chain precursor	**P07360** (CO8G_ HUMAN)	R.AEATTLHVAPQGTAMAVSTFR.K	0.61
complement component C9 precursor	**P02748** (CO9_HUMAN)	R.DVVLTTTFVDDIK.A	0.73
complement component C9 precursor	**P02748** (CO9_HUMAN)	R.RPWNVASLIYETK.G	0.66
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.ISVIRPSK.G	0.70
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	K.VASYGVKPR.Y	0.63
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.DFHINLFQVLPWLK.E	0.68
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.DLLYIGK.D	0.63
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.GDSGGPLIVHK.R	0.63

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.LEDSVTYHCSR.G	0.68
complement factor B preproprotein	**P00751** (CFAB_ HUMAN)	R.LPPTTTCQQQK.E	0.68
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.CLHPCVISR.E	0.62
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.CTSTGWIPAPR.C	0.74
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.IDVHLVPDR.K	0.66
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.IVSSAMEPDREYHFGQAVR.F	0.67
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.SIDVACHPGYALPK.A	0.67
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.VSVLCQENYLIQEGEEITCKDGR.W	0.63
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	K.WSSPPQCEGLPCK.S	0.60
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	R.EIMENYNIALR.W	0.61
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	R.RPYFPVAVGK.Y	0.83
complement factor H isoform a precursor	**P08603** (CFAH_ HUMAN)	R.WQSIPLCVEK.I	0.63
complement factor I preproprotein	**P05156** (CFAI_ HUMAN)	R.YQIWTTVVDWIHPDLKR.I	0.72
corticosteroid-binding globulin precursor	**P08185** (CBG_ HUMAN)	K.AVLQLNEEGVDTAGSTGVTLNLTSKPIILR.F	0.61
corticosteroid-binding globulin precursor	**P08185** (CBG_ HUMAN)	R.GLASANVDFAFSLYK.H	0.66
fibrinogen alpha chain isoform alpha-E preproprotein	**P02671** (FIBA_ HUMAN)	K.TFPGFFSPMLGEFVSETESR.G	0.62

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
gelsolin isoform b	**P06396** (GELS_ HUMAN)	K.FDLVPVPTNLYGDFFTGDAYVILK.T	0.66
gelsolin isoform b	**P06396** (GELS_ HUMAN)	K.QTQVSVLPEGGETPLFK.Q	0.66
gelsolin isoform b	**P06396** (GELS_ HUMAN)	K.TPSAAYLWVGTGASEAEK.T	0.71
gelsolin isoform b	**P06396** (GELS_ HUMAN)	R.AQPVQVAEGSEPDGFWEALGGK.A	0.67
gelsolin isoform b	**P06396** (GELS_ HUMAN)	R.IEGSNKVPVDPATYGQFYGGDSYIILYNYR.H	0.60
gelsolin isoform b	**P06396** (GELS_ HUMAN)	R.VEKFDLVPVPTNLYGDFFTGDAYVILK.T	0.73
gelsolin isoform b	**P06396** (GELS_ HUMAN)	R.VPFDAATLHTSTAMAAQHGMDDDGTGQK.Q	0.63
glutathione peroxidase 3 precursor	**P22352** (GPX3_HUMAN)	K.FLVGPDGIPIMR.W	0.60
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.ALPQPQNVTSLLGCTH.-	0.63
hemopexin precursor	**P02790** (HEMO_ HUMAN)	K.SLGPNSCSANGPGLYLIHGPNLYCYSDVEK.L	0.68
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.DGWHSWPIAHQWPQGPSAVDAAFSWEEK.L	0.63
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.GECQAEGVLFFQGDR.E	0.67
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.GECQAEGVLFFQGDREWFWDLATGTM*K.E	0.67
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.LEKEVGTPHGIILDSVDAAFICPGSSR.L	0.75
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.LWWLDLK.S	0.62
hemopexin precursor	**P02790** (HEMO_ HUMAN)	R.WKNFPSPVDAAFR.Q	0.68
heparin cofactor 2 precursor	**P05546** (HEP2_HUMAN)	K.DQVNTFDNIFIAPVGISTAMGMISLGLK.G	0.60
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	K.ANVFVQLPR.L	0.71
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	R.LEALPNSLLAPLGR.L	0.61

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	R.LFQGLGK.L	0.68
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	R.NLIAAVAPGAFLGLK.A	0.76
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	**P35858** (ALS_ HUMAN)	R.TFTPQPPGLER.L	0.73
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.Q*LVHHFEIDVDIFEPQGISK.L	0.69
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.VTFQLTYEEVLK.R	0.61
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	K.VTFQLTYEEVLKR.N	0.70
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.GIEILNQVQESLPELSNHASILIMLTDGDPTEGVTDR.S	0.62
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.GM*ADQDGLKPTIDKPSEDSPPLEM*LGPR.R	0.79
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	**P19827** (ITIH1_HUMAN)	R.KAAISGENAGLVR.A	0.78
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.AGELEVFNGYFVHFFAPDNLDPIPK.N	0.64
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.FYNQVSTPLLR.N	0.68
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	K.VQFELHYQEVK.W	0.68

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.ETAVDGELVVLYDVK.R	0.63
inter-alpha-trypsin inhibitor heavy chain H2 precursor	**P19823** (ITIH2_HUMAN)	R.IYLQPGR.L	0.75
inter-alpha-trypsin inhibitor heavy chain H3 preproprotein	**Q06033** (ITIH3_HUMAN)	R.LWAYLTIEQLLEK.R	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.ITFELVYEELLK.R	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.LQDRGPDVLTATVSGK.L	0.67
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.TGLLLLSDPDKVTIGLLFWDGRGEGLR.L	0.63
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	K.WKETLFSVM*PGLK.M	0.79
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.AISGGSIQIENGYFVHYFAPEGLTTM*PK.N	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.AISGGSIQIENGYFVHYFAPEGLTTMPK.N	0.65
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.ANTVQEATFQMELPK.K	0.68
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.SFAAGIQALGGTNINDAMLMAVQLLDSSNQEER.L	0.64
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	**Q14624** (ITIH4_HUMAN)	R.VQGNDHSATR.E	0.63

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Protein description	Uniprot ID (name)	Peptide	XT_ AUC
inter-alpha-trypsin inhibitor heavy chain H4 isoform 2 precursor	**Q14624** (ITIH4_HUMAN)	K.ITFELVYEELLKR.R	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 2 precursor	**Q14624** (ITIH4_HUMAN)	K.VTIGLLFWDGR.G	0.65
inter-alpha-trypsin inhibitor heavy chain H4 isoform 2 precursor	**Q14624** (ITIH4_HUMAN)	R.LWAYLTIQQLLEQTVSASDADQQALR.N	0.68
kallistatin precursor	**P29622** (KAIN_ HUMAN)	K.LFHTNFYDTVGTIQLINDHVK.K	0.73
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.ENFLFLTPDCK.S	0.64
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.IYPTVNCQPLGMISLMK.R	0.64
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.KIYPTVNCQPLGMISLMK.R	0.78
kininogen-1 isoform 2 precursor	**P01042** (KNG1_HUMAN)	K.SLWNGDTGECTDNAYIDIQLR.I	0.67
lumican precursor	**P51884** (LUM_ HUMAN)	K.ILGPLSYSK.I	0.60
N-acetylmuramoyl-L-alanine amidase precursor	**Q96PD5** (PGRP2_HUMAN)	K.EYGVVLAPDGSTVAVEPLLAGLEAGLQGR.R	0.61
N-acetylmuramoyl-L-alanine amidase precursor	**Q96PD5** (PGRP2_HUMAN)	R.EGKEYGVVLAPDGSTVAVEPLLAGLEAGLQGR.R	0.69
N-acetylmuramoyl-L-alanine amidase precursor	**Q96PD5** (PGRP2_HUMAN)	R.Q*NGAALTSASILAQQVWGTLVLLQR.L	0.60
pigment epithelium-derived factor precursor	**P36955** (PEDF_ HUMAN)	K.IAQLPLTGSMSIIFFLPLK.V	0.65
pigment epithelium-derived factor precursor	**P36955** (PEDF_ HUMAN)	R.SSTSPTTNVLLSPLSVATALSALSLGAEQR.T	0.79
plasma kallikrein preproprotein	**P03952** (KLKB1_HUMAN)	K.VAEYMDWILEK.T	0.62
plasma kallikrein preproprotein	**P03952** (KLKB1_HUMAN)	R.C*LLFSFLPASSINDMEKR.F	0.60
plasma kallikrein preproprotein	**P03952** (KLKB1_HUMAN)	R.C*QFFSYATQTFHK.A	0.60

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
plasma kallikrein preproprotein	**P03952** (KLKB1_HUMAN)	R.CLLFSFLPASSINDMEK.R	0.76
plasma protease C1 inhibitor precursor	**P05155** (IC1_HUMAN)	R.LVLLNAIYLSAK.W	0.96
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	R.NALFCLESAWNVAK.E	0.67
pregnancy zone protein precursor	**P20742** (PZP_ HUMAN)	R.NQGNTWLTAFVLK.T	0.61
pregna ncy-specific beta-1-glycoprotein 9 precursor	**Q00887** (PSG9_HUMAN)	R.SNPVILNVLYGPDLPR.I	0.62
prenylcysteine oxidase 1 precursor	**Q9UHG3** (PCYOX_HUMAN)	K.IAIIGAGIGGTSAAYYLR.Q	0.71
protein AMBP preproprotein	**P02760** (AMBP_ HUMAN)	K.WYNLAIGSTCPWLK.K	0.77
protein AMBP preproprotein	**P02760** (AMBP_ HUMAN)	R.TVAACNLPIVR.G	0.66
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.IVEGSDAEIGMSPWQVMLFR.K	0.62
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.RQECSIPVCGQDQVTVAMTPR.S	0.69
prothrombin preproprotein	**P00734** (THRB_ HUMAN)	R.TFGSGEADCGLRPLFEK.K	0.61
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	R.FSGTWYAMAK.K	0.60
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	R.LLNNWDVCADMVGTFTDTEDPAK.F	0.64
serum amyloid P-component precursor	**P02743** (SAMP_ HUMAN)	R.GYVIIKPLVWV.-	0.62
sex hormone-binding globulin isoform 1 precursor	**P04278** (SHBG_ HUMAN)	K.VVLSSGSGPGLDLPLVLGLPLQLK.L	0.60
sex hormone-binding globulin isoform 1 precursor	**P04278** (SHBG_ HUMAN)	R.TWDPEGVIFYGDTNPKDDWFM*LGLR.D	0.75
sex hormone-binding globulin isoform 1 precursor	**P04278** (SHBG_ HUMAN)	R.TWDPEGVIFYGDTNPKDDWFMLGLR.D	0.74
thrombospondin-1 precursor	**P07996** (TSP1_HUMAN)	K.GFLLLASLR.Q	0.70

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
thyroxine-binding globulin precursor	**P05543** (THBG_ HUMAN)	K.AVLHIGEK.G	0.85
thyroxine-binding globulin precursor	**P05543** (THBG_ HUMAN)	K.FSISATYDLGATLLK.M	0.65
thyroxine-binding globulin precursor	**P05543** (THBG_ HUMAN)	K.KELELQIGNALFIGK.H	0.61
thyroxine- binding globulin precursor	**P05543** (THBG_ HUMAN)	K.MSSINADFAFNLYR.R	0.67
transforming growth factor-beta-induced protein ig-h3 precursor	**Q15582** (BGH3_HUMAN)	R.LTLLAPLNSVFK.D	0.65
transthyretin precursor	**P02766** (TTHY_ HUMAN)	R.GSPAINVAVHVFR.K	0.67
uncharacterized protein C3orf20 isoform 1	**Q8ND61** (CC020_HUMAN)	K.MPSHLMLAR.K	0.64
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.ELPEHTVK.L	0.75
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.EYANQFMWEYSTNYGQAPLSLLVSYTK.S	0.69
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.HLSLLTTLSNR.V	0.65
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.HQPQEFPTYVEPTNDEICEAFR.K	0.64
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.LAQKVPTADLEDVLPLAEDITNILSK.C	0.73
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.LCDNLSTK.N	0.70
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.LCMAALK.H	0.63
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.SCESNSPFPVHPGTAECCTK.E	0.63
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.SYLSMVGSCCTSASPTVCFLK.E	0.61

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.TAMDVFVCTYFM*PAAQLPELPDVELPTNK.D	0.61
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	K.VLEPTLK.S	0.69
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	R.KFPSGTFEQVSQLVK.E	0.66
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	R.THLPEVFLSK.V	0.62
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_ HUMAN)	R.TSALSAK.S	0.74
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.GQYCYELDEK.A	0.73
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.M*DWLVPATCEPIQSVFFFSGDK.Y	0.64
vitronectin precursor	**P04004** (VTNC_ HUMAN)	R.Q*PQFISR.D	0.63

Table 10. Significant peptides (AUC>0.6) for both X!Tandem and Sequest

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
afamin precursor	P43652 (AFAM_HUMAN)	K.HFQNLGK.D	0.74	0.61
afamin precursor	P43652 (AFAM_HUMAN)	R.RHPDLSIPELLR.I	0.67	0.63
afamin precursor	P43652 (AFAM_HUMAN)	R.TINPAVDHCCK.T	0.66	0.86
alpha- 1 -antichymotrypsin precursor	P01011 (AACT_HUMAN)	K.ITDLIKDLDSQ TMMVLVNYIFFK.A	0.71	0.73
alpha-1-antichymotrypsin precursor	P01011 (AACT_HUMAN)	R.DYNLNDILLQLGIEEAFTSK.A	0.74	0.62
alpha-1-antichymotrypsin precursor	P01011 (AACT_HUMAN)	R.GTHVDLGLASANVDFAFSLYK.Q	0.76	0.61
alpha-1B-glycoprotein precursor	P04217 (A1BG_HUMAN)	K.SLPAPWLSMAPVSWITPGLK.T	0.71	0.65
alpha-2-antiplasmin isoform a precursor	P08697 (A2AP_HUMAN)	K.GFPIKEDFLEQSEQLFGAKPVSLTGK.Q	0.66	0.69
alpha-2-antiplasmin isoform a precursor	P08697 (A2AP_HUMAN)	K.HQMDLVATLSQLGLQELFQAPDLR.G	0.67	0.60
alpha-2-antiplasmin isoform a precursor	P08697 (A2AP_HUMAN)	R.QLTSGPNQEQVSPLTLLK.L	0.66	0.61
alpha-2-HS-glycoprotein preproprotein	P02765 (FETUA_ HUMAN)	R.AQLVPLPPSTYVEFTVSGTDCVAK.E	0.64	0.63
angiotensinogen preproprotein	P01019 (ANGT_HUMAN)	K.DPTFIPAPIQAK.T	0.69	0.69
angiotensinogen preproprotein	P01019 (ANGT_HUMAN)	R.FM*QAVTGWK.T	0.65	0.65
antithrombin-III precursor	P01008 (ANT3_HUMAN)	K.ANRPFLVFIR.E	0.72	0.60
antithrombin-III precursor	P01008 (ANT3_HUMAN)	K.GDDITMVLILPKPEK.S	0.69	0.68
antithrombin-III precursor	P01008 (ANT3_HUMAN)	R.DIPMNPMCIYR.S	0.63	0.78
apolipoprotein A-IV precursor	P06727 (APOA4_HUMAN)	K.KLVPFATELHER.L	0.65	0.77
apolipoprotein A-IV precursor	P06727 (APOA4_HUMAN)	K.SLAELGGHLDQQVEEFR.R	0.60	0.75
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.ALYWVNGQVPDGVSK.V	0.61	0.63
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.FIIPGLK.L	0.64	0.68
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.FSVPAGIVIPSFQALTAR.F	0.63	0.63
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.IEGNLIFDPNNYLPK.E	0.63	0.65

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.LNDLNSVLVMPTFHVPFTDLQVPSCK.L	0.91	0.88
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.VELEVPQLCSFILK.T	0.60	0.61
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	K.VNWEEEAASGLLTSLK.D	0.60	0.73
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	R.ATLYALSHAVNNYHK.T	0.78	0.80
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	R.TGISPLALIK.G	0.64	0.77
apolipoprotein B-100 precursor	P04114 (APOB_HUMAN)	R.TLQGIPQMIGEVIR.K	0.65	0.66
apolipoprotein C-III precursor	P02656 (APOC3_HUMAN)	K.DALSSVQESQVAQQAR.G	0.80	0.69
apolipoprotein C-IV precursor	P55056 (APOC4_HUMAN)	R.DGWQWFWSPSTFR.G	0.63	0.67
apolipoprotein E precursor	P02649 (APOE_HUMAN)	K.VQAAVGTSAAPVPSDNH.-	0.70	0.72
apolipoprotein E precursor	P02649 (APOE_HUMAN)	R.WELALGR.F	0.88	0.60
beta-2-microglobulin precursor	P61769 (B2MG_HUMAN)	K.SNFLNCYVSGFHPSDIEVDLLK.N	0.60	0.70
bone marrow proteoglycan isoform 1 preproprotein	P13727 (PRG2_HUMAN)	R.GGHCVALCTR.G	0.83	0.86
carboxypeptidase B2 preproprotein	Q96IY4 (CBPB2_HUMAN)	R.LVDFYVMPVVNVDGYDYSWK.K	0.61	0.65
carboxypeptidase B2 preproprotein	Q96IY4 (CBPB2_HUMAN)	R.YTHGHGSETLYLAPGGGDDWIYDLGIK.Y	0.60	0.68
carboxypeptidase N subunit 2 precursor	P22792 (CPN2_HUMAN)	K.LSNNALSGLPQGVFGK.L	0.65	0.67
carboxypeptidase N subunit 2 precursor	P22792 (CPN2_HUMAN)	K.TLNLAQNLLAQLPEELFHPLTSLQTLK.L	0.67	0.69
carboxypeptidase N subunit 2 precursor	P22792 (CPN2_HUMAN)	R.WLNVQLSPR.Q	0.74	0.67
ceruloplasmin precursor	P00450 (CERU_HUMAN)	K.GDSVVWYLFSAGNEADVHGIYFSGNTYLWR.G	0.90	0.72
ceruloplasmin precursor	P00450 (CERU_HUMAN)	K.MYYSAVDPTK.D	0.70	0.82
ceruloplasmin precursor	P00450 (CERU_HUMAN)	R.GPEEEHLGILGPVIWAEVGDTIR.V	0.60	0.65
ceruloplasmin precursor	P00450 (CERU_HUMAN)	R.IDTINLFPATLFDAYMVAQNPGEWMLSCQNLNHLK.A	0.66	0.70
ceruloplasmin precursor	P00450 (CERU_HUMAN)	R.SGAGTEDSACIPWAYYSTVDQYSGLIGPLIVCR.R	0.88	0.92

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Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
cholinesterase precursor	P06276 (CHLE_HUMAN)	K.IFFPGVSEFGK.E	0.70	0.63
cholinesterase precursor	P06276 (CHLE_HUMAN)	R.AILQSGSFNAPWAVTSLYEAR.N	0.75	0.77
chorionic gonadotropin, beta polypeptide 8 precursor	P01233 (CGHB_ HUMAN)	R.VLQGVLPALPQVVCNYR.D	0.60	0.75
chorionic somatomammotropin hormone 2 isoform 2 precursor	P01243 (CSH_HUMAN)	R.ISLLLIESWLEPVR.F	0.83	0.63
coagulation factor XII precursor	P00748 (FA12_HUMAN)	R.LHEAFSPVSYQHDLALLR.L	0.60	0.66
coagulation factor XII precursor	P00748 (FA12_HUMAN)	R.TTLSGAPCQPWASEATYR.N	0.69	0.82
complement C1q subcomponent subunit A precursor	P02745 (C1QA_HUMAN)	K.GLFQVVSGGMVLQLQQGDQVWVEKDPK.K	0.65	0.60
complement C1r subcomponent precursor	P00736 (C1R_HUMAN)	K.VLNYVDWIKK.E	0.80	0.76
complement C1s subcomponent precursor	P09871 (C1S_HUMAN)	K.SNALDIIFQTDLTGQK.K	0.62	0.77
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	K.EGAIHREELVYELNPLDHR.G	0.76	0.75
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	K.ITQVLHFTK.D	0.63	0.62
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	K.SHALQLNNR.Q	0.66	0.71
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.AVGSGATFSHYYYM*ILSR.G	0.65	0.60
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.EPFLSCCQFAESLR.K	0.64	0.72
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.GHLFLQTDQPIYNPGQR.V	0.63	0.76
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.GLEEELQFSLGSK.I	0.68	0.68
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.GSFEFPVGDAVSK.V	0.67	0.70

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.LLATLCSAEVCQCAEGK.C	0.61	0.71
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.VQQPDCREPFLSCCQFAESLRK.K	0.65	0.83
complement C4-A isoform 1	P0C0L4 (CO4A_ HUMAN)	R.YIYGKPVQGVAYVR.F	0.82	0.76
complement C5 preproprotein	P01031 (CO5_HUMAN)	K.ITHYNYLILSK.G	0.66	0.69
complement C5 preproprotein	P01031 (CO5_HUMAN)	R.ENSLYLTAFTVIGIR.K	0.60	0.68
complement C5 preproprotein	P01031 (CO5_HUMAN)	R.KAFDICPLVK.I	0.77	0.65
complement C5 preproprotein	P01031 (CO5_HUMAN)	R.VDDGVASFVLNLPSGVTVLEFNVK.T	0.68	0.61
complement component C6 precursor	P13671 (CO6_HUMAN)	K.TFSEWLESVKENPAVIDFELAPIVDLVR.N	0.94	0.64
complement component C6 precursor	P13671 (CO6_HUMAN)	R.IFDDFGTHYFTSGSLGGVYDLYQFSSEELK.N	0.78	0.75
complement component C7 precursor	P10643 (CO7_HUMAN)	K.ELSHLPSLYDYSAYR.R	0.69	0.71
complement component C7 precursor	P10643 (CO7_HUMAN)	R.RYSAWAESVTNLPQVIK.Q	0.71	0.70
complement component C8 alpha chain precursor	P07357 (CO8A_HUMAN)	K.YNPVVIDFEM*QPIHEVLR.H	0.68	0.73
complement component C8 beta chain preproprotein	P07358 (CO8B_HUMAN)	K.VEPLYELVTATDFAYSSTVR.Q	0.69	0.70
complement component C8 beta chain preproprotein	P07358 (CO8B_HUMAN)	R.SLM*LHYEFLQR.V	0.61	0.65
complement component C8 gamma chain precursor	P07360 (CO8G_HUMAN)	K.YGFCEAADQFHVLDEVRR.-	0.78	0.76
complement component C8 gamma chain precursor	P07360 (CO8G_HUMAN)	R.FLQEQGHR.A	0.63	0.69
complement component C8 gamma chain precursor	P07360 (CO8G_HUMAN)	R.KLDGICWQVR.Q	0.75	0.70
complement component C8 gamma chain precursor	P07360 (CO8G_HUMAN)	R.SLPVSDSVLSGFEQR.V	0.70	0.60
complement component C9 precursor	P02748 (C09_HUMAN)	R.GTVIDVTDFVNWASSINDAPVLISQK.L	0.68	0.69
complement factor B preproprotein	P00751 (CFAB_HUMAN)	K.NPREDYLDVYVFGVGPLVNQVNINALASK.K	0.72	0.77
complement factor B preproprotein	P00751 (CFAB_HUMAN)	R.GDSGGPLIVHKR.S	0.60	0.76
complement factor B preproprotein	P00751 (CFAB_HUMAN)	R.HVIILMTDGLHNM*GGDPITVIDEIR.D	0.60	0.64

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
complement factor B preproprotein	P00751 (CFAB_HUMAN)	R.KNPREDYLDVYVFGVGPLVNQVNINALASK.K	0.63	0.63
complement factor H isoform a precursor	P08603 (CFAH_HUMAN)	K.SCDIPVFMNAR.T	0.62	0.71
complement factor H isoform a precursor	P08603 (CFAH_HUMAN)	K.SPPEISHGVVAHMSDSYQYGEEVTYK.C	0.88	0.88
complement factor H isoform a precursor	P08603 (CFAH_HUMAN)	K.TDCLSLPSFENAIPMGEKK.D	0.61	0.66
complement factor I preproprotein	P05156 (CFAI_HUMAN)	K.RAQLGDLPWQVAIK.D	0.71	0.74
complement factor I preproprotein	P05156 (CFAI_HUMAN)	K.SLECLHPGTK.F	0.64	0.81
complement factor I preproprotein	P05156 (CFAI_HUMAN)	R.TMGYQDFADVVCYTQK.A	0.73	0.75
extracellular matrix protein 1 isoform 3 precursor	Q16610 (ECM1_HUMAN)	R.ELLALIQLER.E	0.69	0.65
gelsolin isoform a precursor	P06396 (GELS_HUMAN)	R.VPEARPNSMVVEHPEFLK.A	0.76	0.62
glutathione peroxidase 3 precursor	P22352 (GPX3_HUMAN)	R.LFWEPMK.V	0.69	0.67
hemopexin precursor	P02790 (HEMO_ HUMAN)	R.DVRDYFMPCPGR.G	0.70	0.72
heparin cofactor 2 precursor	P05546 (HEP2_HUMAN)	K.DALENIDPATQMMILNCIYFK.G	0.61	0.65
heparin cofactor 2 precursor	P05546 (HEP2_HUMAN)	K.GLIKDALENI DPATQMMILNCIYFK.G	0.64	0.64
heparin cofactor 2 precursor	P05546 (HEP2_HUMAN)	K.QFPILLDFK.T	0.61	0.69
heparin cofactor 2 precursor	P05546 (HEP2_HUMAN)	R.VLKDQVNTFDNIFIAPVGISTAMGMISLGLK.G	0.88	0.75
insulin-like growth factor-binding protein complex acid labile subunit isoform 2 precursor	P35858 (ALS_HUMAN)	R.AFWLDVSHNR.L	0.61	0.82
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	K.ADVQAHGEGQEFSITCLVDEEEMKK.L	0.61	0.74
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	K.ILGDM*QPGDYFDLVLFGTR.V	0.71	0.63
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	K.ILGDMQPGDYFDLVLFGTR.V	0.68	0.60

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	K.NVVFVIDISGSMR.G	0.76	0.83
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	K.TAFISDFAVTADGNAFIGDIKDK.V	0.74	0.63
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	R.GHMLENHVER.L	0.78	0.80
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	R.GM*ADQDGLKPTIDKPSEDSPPLEMLGPR.R	0.61	0.62
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	R.LWAYLTIQELLAK.R	0.68	0.62
inter-alpha-trypsin inhibitor heavy chain H1 isoform a precursor	P19827 (ITIH1_HUMAN)	R.NHM*QYEIVIK.V	0.67	0.65
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	K.AHVSFKPTVAQQR.I	0.75	0.61
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	K.ENIQDNISLFSLGM*GFDVDYDFLKR.L	0.80	0.93
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	K.ENIQDNISLFSLGMGFDVDYDFLKR.L	0.63	0.80
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	K.HLEVDVWVIEPQGLR.F	0.61	0.61
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	K.LWAYLTINQLLAER.S	0.69	0.62
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	R.AEDHFSVIDFNQNIR.T	0.65	0.63
inter-alpha-trypsin inhibitor heavy chain H2 precursor	P19823 (ITIH2_HUMAN)	R.FLHVPDTFEGHFDGVPVISK.G	0.66	0.62
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	K.ILDDLSPR.D	0.67	0.65
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	K.IPKPEASFSPR.R	0.69	0.77
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	K.SPEQQETVLDGNLIIR.Y	0.63	0.69
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	K.YIFHNFMER.L	0.66	0.61

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	R.FSSHVGGTLGQFYQEVLWGSPAASDDGRR.T	0.69	0.71
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	R.GPDVLTATVSGK.L	0.63	0.82
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	R.NMEQFQVSVSVAPNAK.I	0.78	0.60
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	Q14624 (ITIH4_HUMAN)	R.RLDYQEGPPGVEISCWSVEL.-	0.68	0.62
kallistatin precursor	P29622 (KAIN_HUMAN)	K.IVDLVSELKK.D	0.75	0.67
kallistatin precursor	P29622 (KAIN_HUMAN)	R.VGSALFLSHNLK.F	0.70	0.74
kininogen-1 isoform 2 precursor	P01042 (KNG1_HUMAN)	K.IYPTVNCQPLGM*ISLM*K.R	0.89	0.62
kininogen-1 isoform 2 precursor	P01042 (KNG1_HUMAN)	K.TVGSDTFYSFK.Y	0.61	0.68
kininogen-1 isoform 2 precursor	P01042 (KNG1_HUMAN)	R.DIPTNSPELEETLTHTITK.L	0.61	0.76
kininogen-1 isoform 2 precursor	P01042 (KNG1_HUMAN)	R.VQVVAGK.K	0.67	0.71
lumican precursor	P51884 (LUM_HUMAN)	R.FNALQYLR.L	0.68	0.76
macrophage colony-stimulating factor 1 receptor precursor	P09603 (CSF1_HUMAN)	K.VIPGPPALTLVPAELVR.I	0.68	0.60
monocyte differentiation antigen CD14 precursor	P08571 (CD14_HUMAN)	K.ITGTMPPLPLEATGLALSSLR.L	0.80	0.67
N-acetylmuramoyl-L-alanine amidase precursor	Q96PD5 (PGRP2_HUMAN)	K.EFTEAFLGCPAIHPR.C	0.62	0.64
N-acetylmuramoyl-L-alanine amidase precursor	Q96PD5 (PGRP2_HUMAN)	R.RVINLPLDSMAAPWETGDTFPDVVAIAPDVR.A	0.63	0.62
phosphatidylinositol-glycan-specific phospholipase D precursor	P80108 (PHLD_HUMAN)	R.GVFFSVNSWTPDSMSFIYK.A	0.67	0.78
pigment epithelium-derived factor precursor	**P36955** (PEDF_HUMAN)	K.EIPDEISILLLGVAHFK.G	0.63	0.61
pigment epithelium-derived factor precursor	**P36955** (PEDF_HUMAN)	K.IAQLPLTGSM*SIIFFLPLK.V	0.79	0.61
pigment epithelium-derived factor precursor	**P36955** (PEDF_HUMAN)	K.TVQAVLTVPK.L	0.75	0.79

(continued)

Protein description	Uniprot ID (name)	Peptide	XT_ AUC	S_ AUC
pigment epithelium-derived factor precursor	**P36955** (PEDF_HUMAN)	R.ALYYDLISSPDIHGTYKELLDTVTAPQK.N	0.60	0.73
pigment epithelium-derived factor precursor	**P36955** (PEDF_HUMAN)	R.DTDTGALLFIGK.I	0.85	0.62
plasminogen isoform 1 precursor	**P00747** (PLMN_HUMAN)	R.ELRPWCFTTDPNKR.W	0.70	0.68
plasminogen isoform 1 precursor	**P00747** (PLMN_HUMAN)	R.TECFITGWGETQGTFGAGLLK.E	0.63	0.68
platelet basic protein preproprotein	**P02775** (CXCL7_HUMAN)	K.GTHCNQVEVIATLK.D	0.60	0.61
pregnancy zone protein precursor	**P20742** (PZP_HUMAN)	K.AVGYLITGYQR.Q	0.87	0.73
pregnancy zone protein precursor	**P20742** (PZP_HUMAN)	R.AVDQSVLLM*KPEAELSVSSVYNLLTVK.D	0.64	0.62
pregnancy zone protein precursor	**P20742** (PZP_HUMAN)	R.IQHPFTVEEFVLPK.F	0.66	0.74
pregnancy zone protein precursor	**P20742** (PZP_HUMAN)	R.NELIPLIYLENPR.R	0.61	0.61
protein AMBP preproprotein	**P02760** (AMBP_HUMAN)	R.AFIQLWAFDAVK.G	0.72	0.67
proteoglycan 4 isoform B precursor	**Q92954** (PRG4_HUMAN)	K.GFGGLTGQIVAALSTAK.Y	0.70	0.72
prothrombin preproprotein	**P00734** (THRB_HUMAN)	K.YGFYTHVFR.L	0.70	0.63
prothrombin preproprotein	**P00734** (THRB_HUMAN)	R.IVEGSDAEIGM*SPWQVMLFR.K	0.63	0.71
retinol-binding protein 4 precursor	**P02753** (RET4_HUMAN)	K.KDPEGLFLQDNIVAEFSVDETGQMSATAK.G	0.67	0.67
thyroxine-binding globulin precursor	**P05543** (THBG_HUMAN)	K.AQWANPFDPSKTEDSSSFLIDK.T	0.67	0.80
thyroxine-binding globulin precursor	**P05543** (THBG_HUMAN)	K.GWVDLFVPK.F	0.67	0.64
thyroxine-binding globulin precursor	**P05543** (THBG_HUMAN)	R.SFM*LLILER.S	0.65	0.68
thyroxine-binding globulin precursor	**P05543** (THBG_HUMAN)	R.SFMLLILER.S	0.64	0.62
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.EFSHLGKEDFTSLSLVLYSR.K	0.74	0.61
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.EYANQFM*WEYSTNYGQAPLSLLVSYTK.S	0.73	0.61
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.HQPQEFPTYVEPTNDEICEAFRK.D	0.67	0.69
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.SYLSM*VGSCCTSASPTVCFLK.E	0.63	0.62
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.TAM*DVFVCTYFMPAAQLPELPDVELPTNK.D	0.63	0.60
vitamin D-binding protein isoform 1 precursor	**P02774** (VTDB_HUMAN)	K.VPTADLEDVLPLAEDITNILSK.C	0.70	0.71

(continued)

Protein description	**Uniprot ID (name)**	**Peptide**	**XT_ AUC**	**S_ AUC**
vitronectin precursor	**P04004** (VTNC_HUMAN)	K.AVRPGYPK.L	0.68	0.77
vitronectin precursor	**P04004** (VTNC_HUMAN)	R.MDWLVPATCEPIQSVFFFSGDK.Y	0.67	0.65
zinc-alpha-2-glycoprotein precursor	**P25311** (ZA2G_HUMAN)	K.EIPAWVPFDPAAQITK.Q	0.63	0.67

[0176] The differentially expressed proteins identified by the hypothesis-independent strategy above, not already present in our MRM-MS assay, were candidates for incorporation into the MRM-MS assay. Two additional proteins (AFP, PGH1) of functional interest were also selected for MRM development. Candidates were prioritized by AUC and biological function, with preference give for new pathways. Sequences for each protein of interest, were imported into Skyline software which generated a list of tryptic peptides, m/z values for the parent ions and fragment ions, and an instrument-specific collision energy (McLean et al. Bioinformatics (2010) 26 (7): 966-968; McLean et al. Anal. Chem (2010) 82 (24): 10116-10124).

[0177] The list was refined by eliminating peptides containing cysteines and methionies, and by using the shotgun data to select the charge state(s) and a subset of potential fragment ions for each peptide that had already been observed on a mass spectrometer.

[0178] After prioritizing parent and fragment ions, a list of transitions was exported with a single predicted collision energy. Approximately 100 transitions were added to a single MRM run. For development, MRM data was collected on either a QTRAP 5500 (AB Sciex) or a 6490 QQQ (Agilent). Commercially available human female serum (from pregnant and non-pregnant donors), was depleted and processed to tryptic peptides, as described above, and used to "scan" for peptides of interest. In some cases, purified synthetic peptides were used for further optimization. For development, digested serum or purified synthetic peptides were separated with a 15 min acetonitrile gradient at 100 ul/min on a 2.1 x 50 mM Poroshell 120 EC-C18 column (Agilent) at 40°C.

[0179] The MS/MS data was imported back into Skyline, where all chromatograms for each peptide were overlayed and used to identify a concensus peak corresponding to the peptide of interest and the transitions with the highest intensities and the least noise. Table 11, contains a list of the most intensely observed candidate transitions and peptides for transfer to the MRM assay.

Table 11. Candidate peptides and transitions for transferring to the MRM assay

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
alpha-1-antichymotrypsin	K.ADLSGITGAR.N	480.7591++	S [y7] - 661.3628+[1]	1437602
			G [y6] - 574.3307+[2]	637584
			T [y4] - 404.2252+[3]	350392
			L [y8] - 774.4468+[4]	191870
			G [y3] - 303.1775+[5]	150575
			I [y5] - 517.3093+[6]	97828
alpha-1-antichymotrypsin	K.EQLSLLDR.F	487.2693++	S [y5] - 603.3461+[1]	345602
			L [y6] - 716.4301+[2]	230046
			L [y4] - 516.3140+[3]	143874
			D [y2] - 290.1459+[4]	113381
			D [y2] - 290.1459+[5]	113381
			Q [b2] - 258.1084+[6]	78157
alpha-1-antichymotrypsin	K.ITLLSALVETR.T	608.3690++	S [y7] - 775.4308+[1]	1059034
			L [y8] - 888.5149+[2]	541969

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			T [b2] - 215.1390+[3]	408819
			L [y9] - 1001.5990+ [4]	438441
			V [y4] - 504.2776+[5]	311293
			L [y5] - 617.3617+[6]	262544
			L [b3] - 328.2231+[7]	197526
			T [y2] - 276.1666+[8]	212816
			E [y3] - 405.2092+[9]	207163
alpha-1-antichymotrypsin	R.EIGELYLPK.F	531.2975++	G [y7] - 819.4611+[2]	977307
			L [y5] - 633.3970+[3]	820582
			Y [y4] - 520.3130+[4]	400762
			L [y3] - 357.2496+[5]	498958
			P [y2] - 244.1656+[1]	1320591
			I [b2] - 243.1339+[6]	303268
			G [b3] - 300.1554+[7]	305120
alpha-1-antichymotrypsin	R.GTHVDLGLASANVDFAFSLYK.Q	742.3794+++	D [y8] - 990.4931+[1]	154927
			L [b8] - 793.4203+[2]	51068
			D [b5] - 510.2307+[3]	45310
			F [y7] - 875.4662+[4]	42630
			A [b9] - 864.4574+[5]	43355
			S [y4] - 510.2922+[6]	45310
			F [y5] - 657.3606+[7]	37330
			V [y9] - 1089.5615+ [8]	32491
			G [b7] - 680.3362+[9]	38185

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			Y [y2] - 310.1761+ [10]	36336
			N [b12] - 1136.5695+ [11]	16389
			S [b10] - 951.4894+ [12]	16365
			L [b6] - 623.3148+ [13]	13687
			L [y3] - 423.2602+ [14]	17156
			V [b4] - 395.2037+ [15]	10964
alpha-1-antichymotrypsin	R.NLAVSQVVHK.A	547.8195++	A [y8] - 867.5047+[1]	266203
			L [b2] - 228.1343+[2]	314232
			V [y7] - 796.4676+[3]	165231
			A [b3] - 299.1714+[4]	173694
			S [y6] - 697.3991+[5]	158512
			H [y2] - 284.1717+[6]	136431
			V [b4] - 398.2398+[7]	36099
			S [b5] - 485.2718+[8]	23836
		365.5487+++	S [y6] - 697.3991+[1]	223443
			V [y3] - 383.2401+[2]	112952
			V [y4] - 482.3085+[3]	84872
			Q [y5] - 610.3671+[4]	30835
inter-alpha-trypsin inhibitor heavy chain H1	K.AAISGENAGLVR.A	579.3173++	S [y9] - 902.4690+[1]	518001
			G [y8] - 815.4370+[2]	326256
			N [y6] - 629.3729+[3]	296670

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			S [b4] - 343.1976+[4]	258172
inter-alpha-trypsin inhibitor heavy chain H1	K.GSLVQASEANLQAAQDFVR.G	668.6763+++	A [y7] - 806.4155+[1]	304374
			A [y6] - 735.3784+[2]	193844
			V [b4] - 357.2132+[3]	294094
			F [y3] - 421.2558+[4]	167816
			A [b6] - 556.3089+[5]	149216
			L [b11] - 535.7775++ [6]	156882
			A [b13] - 635.3253++ [7]	249287
			A [y14] - 760.3786++ [8]	123723
			F [b17] - 865.9208++ [9]	23057
inter-alpha-trypsin	K.TAFISDFAVTAD	1087.0442++	G [y4] - 432.2453+[1]	22362
inhibitor heavy chain H1	GNAFIGDIK.D		I [y5] - 545.3293+[2]	8319
			A [b8] - 853.4090+[3]	7006
			G [y9] - 934.4993+[4]	6755
			F [y6] - 692.3978+[5]	6193
			V [b9] - 952.4775+[6]	9508
inter-alpha-trypsin inhibitor heavy chain H1	K.VTYDVSR.D	420.2165++	Y [y5] - 639.3097+[1]	609348
			T [b2] - 201.1234+[2]	792556
			D [y4] - 476.2463+[3]	169546
			V [y3] - 361.2194+[4]	256946
			Y [y5] - 320.1585++ [5]	110608
			S [y2] - 262.1510+[6]	50268

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			Y [b3] - 182.5970++ [7]	10947
			D [b4] - 479.2136+[8]	13662
inter-alpha-trypsin inhibitor heavy chain H1	R.EVAFDLEIPK.T	580.8135++	P [y2] - 244.1656+[1]	2032509
			D [y6] - 714.4032+[2]	672749
			A [y8] - 932.5088+[3]	390837
			L [y5] - 599.3763+[4]	255527
			F [y7] - 861.4716+[5]	305087
inter-alpha-trypsin inhibitor heavy chain H1	R.LWAYLTIQELLAK.R	781.4531++	W [b2] - 300.1707+[1]	602601
			A [b3] - 371.2078+[2]	356967
			T [y8] - 915.5510+[3]	150419
			Y [b4] - 534.2711+[4]	103449
			I [y7] - 814.5033+[5]	72044
			Q [y6] - 701.4192+[6]	66989
			L [b5] - 647.3552+[7]	99820
			E [y5] - 573.3606+[8]	44843
inter-alpha-trypsin inhibitor heavy chain H2	K.FYNQVSTPLLR.N	669.3642++	S [y6] - 686.4196+[1]	367330
			V [y7] - 785.4880+[2]	182396
			P [y4] - 498.3398+[3]	103638
			Y [b2] - 311.1390+[4]	52172
			Q [b4] - 553.2405+[5]	54270
			N [b3] - 425.1819+[6]	34567
inter-alpha-trypsin inhibitor heavy chain H2	K.HLEVDVWVIEPQGLR.F	597.3247+++	I [y7] - 812.4625+[1]	206996
			P [y5] - 570.3358+[2]	303693
			E [y6] - 699.3784+[3]	126752

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			P [y5] - 285.6715++ [4]	79841
inter-alpha-trypsin inhibitor heavy chain H2	K.TAGLVR.S	308.6925++	A [b2] - 173.0921+[1]	460019
			G [y4] - 444.2929+[2]	789068
			V [y2] - 274.1874+[3]	34333
			G [b3] - 230.1135+[4]	15169
			L [y3] - 387.2714+[5]	29020
inter-alpha-trypsin inhibitor heavy chain H2	R.IYLQPGR.L	423.7452++	L [y5] - 570.3358+[1]	638209
			P [y3] - 329.1932+[2]	235194
			Y [b2] - 277.1547+[3]	266889
			Q [y4] - 457.2518+[4]	171389
inter-alpha-trypsin inhibitor heavy chain H2	R.LSNENHGIAQR.I	413.5461+++	N [y9] - 519.7574++ [1]	325409
			N [y7] - 398.2146++ [2]	39521
			G [y5] - 544.3202+[3]	139598
			S [b2] - 201.1234+[4]	54786
			E [y8] - 462.7359++ [5]	30623
inter-alpha-trypsin inhibitor heavy chain H2	R.SLAPTAAAKR.R	415.2425++	A [y7] - 629.3617+[1]	582421
			L [b2] - 201.1234+[2]	430584
			P [y6] - 558.3246+[3]	463815
			A [b3] - 272.1605+[4]	204183
			T [y5] - 461.2718+[5]	47301
inter-alpha-trypsin inhibitor heavy chain H3	K.EVSFDVELPK.T	581.8032++	P [y2] - 244.1656+[1]	132304
			V [b2] - 229.1183+[2]	48895

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			L [y3] - 357.2496+[3]	20685
inter-alpha-trypsin inhibitor heavy chain H3	K.IQENVR.N	379.7114++	E [y4] - 517.2729+[1]	190296
			E [b3] - 371.1925+[2]	51697
			Q [b2] - 242.1499+[3]	54241
			N [y3] - 388.2303+[4]	21156
			V [y2] - 274.1874+[5]	8309
inter-alpha-trypsin inhibitor heavy chain H3	R.ALDLSLK.Y	380.2342++	D [y5] - 575.3399+[1]	687902
			L [b2] - 185.1285+[2]	241010
			L [y2] - 260.1969+[3]	29365
inter-alpha-trypsin inhibitor heavy chain H3	R.LIQDAVTGLTVNGQITGDK.R	972.0258++	V [b6] - 640.3665+[1]	139259
			G [b8] - 798.4356+[2]	53886
			G [y7] - 718.3730+[3]	12518
pigment epithelium-derived factor precursor	K.SSFVAPLEK.S	489.2687++	A [y5] - 557.3293+[1]	13436
			V [y6] - 656.3978+[2]	9350
			F [y7] - 803.4662+[3]	6672
			P [y4] - 486.2922+[4]	6753
pigment epithelium-derived factor precursor	K.TVQAVLTVPK.L	528.3266++	Q [y8] - 855.5298+[1]	26719
			V [b2] - 201.1234+[2]	21239
			Q [y8] - 428.2686++ [3]	16900
			A [y7] - 727.4713+[4]	9518
			L [y5] - 557.3657+[5]	5108
			Q [b3] - 329.1819+[6]	5450
			V [y6] - 656.4341+[7]	4391

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
pigment epithelium-derived factor precursor	R.ALYYDLISSPDIHGTYK.E	652.6632+++	Y [y15] - 886.4305++ [1]	78073
			Y [y14] - 804.8988++ [2]	26148
pigment epithelium-derived factor precursor	R.DTDTGALLFIGK.I	625.8350++	G [y8] - 818.5135+[1]	25553
			T [b2] - 217.0819+[2]	22716
			T [b4] - 217.0819++ [3]	22716
			L [y5] - 577.3708+[4]	11600
			I [y3] - 317.2183+[5]	11089
			A [b6] - 561.2151+[6]	6956
pigment epithelium-derived factor precursor	K.ELLDTVTAPQK.N	607.8350++	T [y5] - 544.3089+[1]	17139
			D [y8] - 859.4520+[2]	17440
			L [y9] - 972.5360+[3]	14344
			A [y4] - 443.2613+[4]	11474
			T [y7] - 744.4250+[5]	10808
			V [y6] - 643.3774+[6]	9064
pregnancy-specific beta-1-glycoprotein 1	K.FQLPGQK.L	409.2320++	L [y5] - 542.3297+[1]	116611
			P [y4] - 429.2456+[2]	91769
			Q [b2] - 276.1343+[3]	93301
pregnancy-specific beta-1-glycoprotein 1	R.DLYHYITSYVVDGEIIIYGPAYSGR.E	955.4762+++	G [y7] - 707.3471+[1]	5376
			Y [y8] - 870.4104+[2]	3610
			P [y6] - 650.3257+[3]	2770
			I [y9] - 983.4945+[4]	3361
pregnancy-specific beta-1-glycoprotein 11	K.LFIPQITPK.H	528.8262++	P [y6] - 683.4087+[1]	39754

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			F [b2] - 261.1598+[2]	29966
			I [y7] - 796.4927+[3]	13162
pregnancy-specific beta-1-glycoprotein 11	NSATGEESSTSLTIR	776.8761++	E [b7] - 689.2737+[1]	11009
			T [y6] - 690.4145+[2]	11284
			L [y4] - 502.3348+[3]	2265
			S [y7] - 389.2269++ [4]	1200
			T [y3] - 389.2507+[5]	1200
			I [y2] - 288.2030+[6]	2248
pregnancy-specific beta-1-glycoprotein 2	K.FQQSGQNLFIPQITTK.H	617.3317+++	F [y8] - 474.2817++ [1]	43682
			G [y12] - 680.3852++ [2]	24166
			S [b4] - 491.2249+[3]	23548
			Q [b3] - 404.1928+[4]	17499
			I [y4] - 462.2922+[5]	17304
			F [b9] - 525.7538++ [6]	17206
			I [b10] - 582.2958++ [7]	16718
			L [b8] - 452.2196++ [8]	16490
			P [y6] - 344.2054++ [9]	16198
			G [b5] - 548.2463+ [10]	15320
pregnancy-specific beta-1-glycoprotein 2	IHPSYTNYR	575.7856++	N [b7] - 813.3890+[1]	16879
			Y [b5] - 598.2984+[2]	18087

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			T [y4] - 553.2729+[3]	2682
pregnancy-specific beta-1-glycoprotein 2	FQLSETNR	497.7513++	L [y6] - 719.3682+[1]	358059
			S [y5] - 606.2842+[2]	182330
			Q [b2] - 276.1343+[3]	292482
pregnancy-specific beta-1-glycoprotein 3	VSAPSGTGHLPGLNPL	506.2755+++	T [b7] - 300.6530++ [1]	25346
			H [y8] - 860.4989+[2]	12159
			H [y8] - 430.7531++ [3]	15522
pregnancy-specific beta-1-glycoprotein 3	EDAGSYTLHIVK	666.8433++	Y [b6] - 623.2307+[1]	23965
			Y [y7] - 873.5193+[2]	21686
			L [b8] - 837.3625+[3]	4104
			A [b3] - 316.1139+[4]	1987
pregnancy-specific beta-1-glycoprotein 4	R.TLFIFGVTK.Y	513.3051++	F [y7] - 811.4713+[1]	62145
			L [b2] - 215.1390+[2]	31687
			F [y5] - 551.3188+[3]	972
pregnancy-specific beta-1-glycoprotein 4	NYTYIWWLNGQSLPVSPR	1097.5576++	W [b6] - 841.3879+[1]	25756
			G [y9] - 940.5211+[2]	25018
			Y [b4] - 542.2245+[3]	19778
			Q [y8] - 883.4996+[4]	6642
			P [y2] - 272.1717+[5]	5018
pregnancy-specific beta-1-glycoprotein 5	GVTGYFTFNLYLK	508.2695+++	L [y2] - 260.1969+[1]	176797
			T [y11] - 683.8557++ [2]	136231
			F [b6] - 625.2980+[3]	47523

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			L [y4] - 536.3443+[4]	23513
pregnancy-specific beta-1-glycoprotein 6	SNPVTLNVLYGPDLPR	585.6527+++	Y [y7] - 817.4203+[1]	14118
			G [y6] - 654.3570+[2]	10433
			P [b3] - 299.1350+[3]	87138*
			P [y5] - 299.1714++ [4]	77478*
			P [y5] - 597.3355+[5]	68089*
pregnancy-specific beta-1-glycoprotein 7	DVLLLVHNLPQNLTGHIWYK	791.7741+++	L [y8] - 1017.5516+ [3]	141169
			G [y6] - 803.4199+[5]	115905
			W [y3] - 496.2554+[6]	108565
			P [y11] - 678.8566++ [7]	105493
			V [b2] - 215.1026+[1]	239492
			L [b3] - 328.1867+[2]	204413
			N [b8] - 904.5251+[4]	121880
pregnancy-specific beta-1-glycoprotein 7	YGPAYSGR	435.7089++	A [y5] - 553.2729+[1]	25743*
			Y [y4] - 482.2358+[2]	25580*
			P [y6] - 650.3257+[3]	10831*
			S [y3] - 319.1724+[4]	10559*
			G [b2] - 221.0921+[5]	7837*
pregnancy-specific beta-1-glycoprotein 8	LQLSETNR	480.7591++	S [b4] - 442.2660+[1]	18766
			L [b3] - 355.2340+[2]	12050
			Q [b2] - 242.1499+[3]	1339
			T [b6] - 672.3563+[4]	2489

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
pregnancy-specific beta-1-glycoprotein 9	K.LFIPQITR.N	494.3029++	P [y5] - 614.3620+[1]	53829
			I [y6] - 727.4461+[2]	13731
			I [b3] - 374.2438+[3]	4178
			Q [y4] - 517.3093+[4]	2984
pregnancy-specific beta-1-glycoprotein 9	K.LPIPYITINNLNPR.E	819.4723++	P [b2] - 211.1441+[1]	18814*
			P [b4] - 211.1441++ [2]	18814*
			T [b7] - 798.4760+[3]	17287*
			T [y8] - 941.5163+[4]	10205*
			Y [b5] - 584.3443+[5]	10136*
			N [y6] - 727.3846+[6]	9511*
pregnancy-specific beta-1-glycoprotein 9	R.SNPVILNVLYGPDLPR.I	589.6648+++	P [y5] - 597.3355+[1]	3994
			Y [y7] - 817.4203+[2]	3743
			G [y6] - 654.3570+[3]	3045
pregnancy-specific beta-1-glycoprotein 9	DVLLLVHNLPQNLPGYFWYK	810.4387+++	P [y7] - 960.4614+[1]	120212
			V [b2] - 215.1026+[2]	65494
			L [b3] - 328.1867+[3]	54798
pregnancy-specific beta-1-glycoprotein 9	SENYTYIWWLNGQSLPVSPGVK	846.7603+++	W [y15] - 834.4488++ [1]	14788
			P [y4] - 200.6314++ [2]	19000
			Y [y17] - 972.5225++ [3]	4596
			L [b10] - 678.8166++ [4]	2660
			Y [b6] - 758.2992+[5]	1705

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			P [y4] - 400.2554+[6]	1847
Pan-PSG	ILILPSVTR	506.3317++	P [y5] - 559.3198+[1]	484395
			L [b2] - 227.1754+[2]	102774
			L [b4] - 227.1754++ [3]	102774
			I [y7] - 785.4880+[4]	90153
			I [b3] - 340.2595+[5]	45515
			L [y6] - 672.4039+[6]	40368
thyroxine-binding globulin precursor	K.AQWANPFDPSK.T	630.8040++	A [b4] - 457.2194+[1]	30802
			S [y2] - 234.1448+[2]	28255
			D [y4] - 446.2245+[3]	24933
thyroxine-binding globulin precursor	K.AVLHIGEK.G	289.5080+++	I [y4] - 446.2609+[1]	220841
			H [y5] - 292.1636++ [2]	303815
			H [y5] - 583.3198+[3]	133795
			V [b2] - 171.1128+[4]	166139
			L [y6] - 348.7056++ [5]	823533
thyroxine-binding globulin precursor	K.FLNDVK.T	368.2054++	N [y4] - 475.2511+[1]	296859
			V [y2] - 246.1812+[2]	219597
			L [b2] - 261.1598+[3]	87504
thyroxine-binding globulin precursor	K.FSISATYDLGATLLK.M	800.4351++	Y [y9] - 993.5615+[1]	34111
			G [y6] - 602.3872+[2]	17012
			D [y8] - 830.4982+	45104
			S [b2] - 235.1077+[4]	15480

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
thyroxine-binding globulin precursor	K.GWVDLFVPK.F	530.7949++	W [b2] - 244.1081+[1]	1261810
			P [y2] - 244.1656+[2]	1261810
			V [b7] - 817.4243+[3]	517675
			V [y7] - 817.4818+[4]	517675
			D [y6] - 718.4134+[5]	306994
			F [b6] - 718.3559+[6]	306994
			V [y3] - 343.2340+[7]	112565
			V [b3] - 343.1765+[8]	112565
thyroxine-binding globulin precursor	K.NALALFVLPK.E	543.3395++	A [y7] - 787.5076+[1]	198085
			L [b3] - 299.1714+[2]	199857
			P [y2] - 244.1656+[3]	129799
			L [y8] - 900.5917+[4]	111572
			L [y6] - 716.4705+[5]	88773
			F [y5] - 603.3865+[6]	54020
			L [y3] - 357.2496+[7]	43353
thyroxine-binding globulin precursor	R.SILFLGK.V	389.2471++	L [y5] - 577.3708+[1]	1878736
			I [b2] - 201.1234+[2]	946031
			G [y2] - 204.1343+[3]	424248
			L [y3] - 317.2183+[4]	291162
			F [y4] - 464.2867+[5]	391171
AFP	R.DFNQFSSGEK.N	386.8402+++	N [b3] - 189.0764++ [1]	42543
			S [y4] - 210.6081++ [2]	21340
			G [y3] - 333.1769+[3]	53766

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			N [b3] - 377.1456+[4]	58644
			F [b2] - 263.1026+[5]	5301
AFP	K.GYQELLEK.C	490.2584++	E [y5] - 631.3661+[1]	110518
			L [y4] - 502.3235+[2]	74844
			E [y2] - 276.1554+[3]	42924
			E [b4] - 478.1932+[4]	20953
AFP	K.GEEELQK.Y	416.7060++	E [b2] - 187.0713+[1]	37843
			E [y4] - 517.2980+[2]	56988
AFP	K.FIYEIAR.R	456.2529++	I [y3] - 359.2401+[1]	34880
			I [b2] - 261.1598+[2]	7931
AFP	R.HPFLYAPTILLWAAR.Y	590.3348+++	I [y7] - 421.7660++ [1]	11471
			L [y6] - 365.2239++ [2]	5001
			A [b6] - 365.1896++ [3]	5001
			L [y6] - 729.4406+[4]	3218
			F [b3] - 382.1874+[5]	6536
			A [b6] - 729.3719+[6]	3218
AFP	R.TFQAITVTK.L	504.7898++	T [b6] - 662.3508+[1]	11241
			T [y4] - 448.2766+[2]	7541
			A [b4] - 448.2191+[3]	7541
AFP	K.LTTLER.G	366.7162++	T [y4] - 518.2933+[1]	7836
			L [b4] - 215.1390++ [2]	4205
			T [b2] - 215.1390+[3]	4205

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
AFP	R.HPQLAVSVILR.V		L [y2] - 288.2030+[1]	3781
			I [y3] - 401.2871+[2]	2924
			L [b4] - 476.2616+[3]	2647
AFP	K.LGEYYLQNAFLVAYTK.K	631.6646+++	G [b2] - 171.1128+[1]	10790
			Y [y3] - 411.2238+[2]	2303
			F [b10] - 600.2902++ [3]	1780
			Y [b4] - 463.2187+[4]	2214
			F [y7] - 421.2445++ [6]	3072
PGH1	R.ILPSVPK.D	377.2471++	P [y5] - 527.3188+[1]	5340492
			S [y4] - 430.2660+[5]	419777
			P [y2] - 244.1656+[2]	4198508
			P [y5] - 264.1630++ [3]	2771328
			L [b2] - 227.1754+[4]	2331263
PGH1	K.AEHPTWGDEQLFQTTR.L	639.3026+++	E [b9] - 512.2120++ [1]	64350
			P [b4] - 218.1030++ [2]	38282
			L [b11] - 632.7833++ [3]	129128
			G [y10] - 597.7911++ [4]	19406
			G [b7] - 779.3471+[5]	51467
			T [y3] - 189.1108++ [6]	10590
			D [y9] - 569.2804++ [7]	12460

(continued)

Protein	Peptide	m/z, charge	fragment ion, m/z, charge, rank	area
			L [y6] - 765.4254+[8]	6704
			D [b8] - 447.6907++ [9]	4893
			P [b4] - 435.1987+ [10]	8858
			Q [y7] - 893.4839+ [11]	6101
			T [b5] - 268.6268++ [12]	5456
			T [b5] - 536.2463+ [13]	5549
PGH1	R.LILIGETIK.I	500.3261++	G [y5] - 547.3086+[1]	7649
			T [y3] - 361.2445+[2]	6680
			E [y4] - 490.2871+[3]	5234
			L [y7] - 773.4767+[4]	3342
PGH1	R.LQPFNEYR.K	533.7694++	N [b5] - 600.3140+[1]	25963
			F [b4] - 486.2711+[2]	6915
			E [y3] - 467.2249+[3]	15079
* QTRAP5500 data, all other peak areas are from Agilent 6490				

[0180] Next, the top 2-10 transitions per peptide and up to 7 peptides per protein were selected for collision energy (CE) optimization on the Agilent 6490. Using Skyline or MassHunter Qual software, the optimized CE value for each transition was determined based on the peak area or signal to noise. The two transitions with the largest peak areas per peptide and at least two peptides per protein were chosen for the final MRM method. Substitutions of transitions with lower peak areas were made when a transition with a larger peak area had a high background level or had a low m/z value that has more potential for interference.

[0181] Lastly, the retention times of selected peptides were mapped using the same column and gradient as our established sMRM assay. The newly discovered analytes were subsequently added to the sMRM method and used in a further hypothesis-dependent discovery study described in Example 5 below.

[0182] The above method was typical for most proteins. However, in some cases, the differentially expressed peptide identified in the shotgun method did not uniquely identify a protein, for example, in protein families with high sequence identity. In these cases, a MRM method was developed for each family member. Also, let it be noted that, for any given protein, peptides in addition to those found to be significant and fragment ions not observed on the Orbitrap may have been included in MRM optimization and added to the final sMRM method if those yielded the best signal intensities.

Example 5. Study IV to Identify and Confirm Preterm Birth Biomarkers

[0183] A further hypothesis-dependent discovery study was performed with the scheduled MRM assay used in Examples 3 but now augmented with newly discovered analytes from the Example 4. Less robust transitions (from the original 1708 described in Example 1) were removed to improve analytical performance and make room for the newly discovered analytes. Samples included approximately 30 cases and 60 matched controls from each of three gestational periods (early, 17-22 weeks, middle, 23-25 weeks and late, 26-28 weeks). Log transformed peak areas for each transition were corrected for run order and batch effects by regression. The ability of each analyte to separate cases and controls was determined by calculating univariate AUC values from ROC curves. Ranked univariate AUC values (0.6 or greater) are reported for individual gestational age window sample sets (Tables 12, 13, 15) and a combination of the middle and late window (Table 14). Multivariate classifiers were built using different subsets of analytes (described below) by Lasso and Random Forest methods. Lasso significant transitions correspond to those with non-zero coefficients and Random Forest analye ranking was determined by the Gini importance values (mean decrease in model accuracy if that variable is removed). We report all analytes with non-zero Lasso coefficients (Tables 16-32) and the top 30 analytes from each Random Forest analysis (Tables 33-49). Models were built considering the top univariate 32 or 100 analytes, the single best univariate analyte for the top 50 proteins or all analytes. Lastly 1000 rounds of bootstrap resampling were performed and the nonzero Lasso coefficients or Random Forest Gini importance values were summed for each analyte amongst panels with AUCs of 0.85 or greater.

Table 12. Early Window Individual Stats

Transition	**Protein**	**AUC**
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	0.834
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	0.822
FLNWIK_410.7_560.3	HABP2_HUMAN	0.820
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	0.808
SFRPFVPR_335.9_635.3	LBP_HUMAN	0.800
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	0.800
FSVVYAK_407.2_579.4	FETUA_HUMAN	0.796
ITGFLKPGK_320.9_429.3	LBP_HUMAN	0.796
AHYDLR_387.7_288.2	FETUA_HUMAN	0.796
FSVVYAK_407.2_381.2	FETUA_HUMAN	0.795
SFRPFVPR_335.9_272.2	LBP_HUMAN	0.795
DVLLLVHNLPQNLPGYFWYK_810.4_967.5	PSG9_HUMAN	0.794
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	0.794
QALEEFQK_496.8_680.3	CO8B_HUMAN	0.792
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	0.792
AHYDLR_387.7_566.3	FETUA_HUMAN	0.791
VFQFLEK_455.8_811.4	CO5_HUMAN	0.786
ITGFLKPGK_320.9_301.2	LBP_HUMAN	0.783
VFQFLEK_455.8_276.2	CO5_HUMAN	0.782
SLLQPNK_400.2_599.4	CO8A_HUMAN	0.781
VQTAHFK_277.5_431.2	CO8A_HUMAN	0.780
SDLEVAHYK_531.3_617.3	CO8B_HUMAN	0.777
SLLQPNK_400.2_358.2	CO8A_HUMAN	0.776
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	0.776
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.774

(continued)

Transition	Protein	AUC
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.774
VSEADSSNADWVTK_754.9_533.3	CFAB_HUMAN	0.773
LSSPAVITDK_515.8_743.4	PLMN_HUMAN	0.773
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	0.772
DVLLLVHNLPQNLPGYFWYK_810.4_594.3	PSG9_HUMAN	0.771
ALVLELAK_428.8_672.4	INHBE_HUMAN	0.770
FLNWIK_410.7_561.3	HABP2_HUMAN	0.770
LSSPAVITDK_515.8_830.5	PLMN_HUMAN	0.769
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	0.769
VSEADSSNADWVTK_754.9_347.2	CFAB_HUMAN	0.768
HTLNQIDEVK_598.8_951.5	FETUA_HUMAN	0.767
TTSDGGYSFK_531.7_860.4	INHA_HUMAN	0.761
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.760
HTLNQIDEVK_598.8_958.5	FETUA_HUMAN	0.760
DISEVVTPR_508.3_472.3	CFAB_HUMAN	0.760
LIQDAVTGLTVNGQITGDK_972.0_640.4	ITIH3_HUMAN	0.759
EAQLPVIENK_570.8_699.4	PLMN_HUMAN	0.759
SLPVSDSVLSGFEQR_810.9_836.4	CO8G_HUMAN	0.757
AVLHIGEK_289.5_348.7	THBG_HUMAN	0.755
GLQYAAQEGLLALQSELLR_1037.1_929.5	LBP_HUMAN	0.752
FLQEQGHR_338.8_497.3	CO8G_HUMAN	0.750
LPNNVLQEK_527.8_730.4	AFAM_HUMAN	0.750
AVLHIGEK_289.5_292.2	THBG_HUMAN	0.749
QLYGDTGVLGR_589.8_501.3	CO8G_HUMAN	0.748
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.747
NADYSYSVWK_616.8_769.4	CO5_HUMAN	0.746
GLQYAAQEGLLALQSELLR_1037.1_858.5	LBP_HUMAN	0.746
SLPVSDSVLSGFEQR_810.9_723.3	CO8G_HUMAN	0.745
IEEIAAK_387.2_531.3	CO5_HUMAN	0.743
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.742
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	0.742
FQLSETNR_497.8_605.3	PSG2_HUMAN	0.741
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.741
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.740
LQGTLPVEAR_542.3_571.3	CO5_HUMAN	0.740
SGFSFGFK_438.7_732.4	CO8B_HUMAN	0.740
HELTDEELQSLFTNFANVVDK_817.1_906.5	AFAM_HUMAN	0.740
VQTAHFK_277.5_502.3	CO8A_HUMAN	0.739

(continued)

Transition	Protein	AUC
YENYTSSFFIR_713.8_293.1	IL12B_HUMAN	0.739
AFTECCVVASQLR_770.9_574.3	CO5_HUMAN	0.736
EAQLPVIENK_570.8_329.2	PLMN_HUMAN	0.734
QALEEFQK_496.8_551.3	CO8B_HUMAN	0.734
DAQYAPGYDK_564.3_813.4	CFAB_HUMAN	0.734
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	0.734
IAIDLFK_410.3_635.4	HEP2_HUMAN	0.733
TASDFITK_441.7_781.4	GELS_HUMAN	0.731
YEFLNGR_449.7_606.3	PLMN_HUMAN	0.731
TVQAVLTVPK_528.3_428.3	PEDF_HUMAN	0.731
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	0.730
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	0.730
TVQAVLTVPK_528.3_855.5	PEDF_HUMAN	0.730
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	0.727
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.727
SDLEVAHYK_531.3_746.4	CO8B_HUMAN	0.726
FLPCENK_454.2_550.2	IL10_HUMAN	0.725
HPWIVHWDQLPQYQLNR_744.0_1047.0	KS6A3_HUMAN	0.725
AFTECCVVASQLR_770.9_673.4	CO5_HUMAN	0.725
YGLVTYATYPK_638.3_843.4	CFAB_HUMAN	0.724
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	0.724
DAQYAPGYDK_564.3_315.1	CFAB_HUMAN	0.724
QGHNSVFLIK_381.6_260.2	HEMO_HUMAN	0.722
HELTDEELQSLFTNFANVVDK_817.1_854.4	AFAM_HUMAN	0.722
TLEAQLTPR_514.8_814.4	HEP2_HUMAN	0.721
IEEIAAK_387.2_660.4	CO5_HUMAN	0.721
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.721
IAPQLSTEELVSLGEK_857.5_333.2	AFAM_HUMAN	0.721
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.720
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.719
IAIDLFK_410.3_706.4	HEP2_HUMAN	0.719
FLQEQGHR_338.8_369.2	CO8G_HUMAN	0.719
ALQDQLVLVAAK_634.9_956.6	ANGT_HUMAN	0.718
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN	0.717
YEFLNGR_449.7_293.1	PLMN_HUMAN	0.717
TASDFITK_441.7_710.4	GELS_HUMAN	0.716
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	0.716
TLLPVSKPEIR_418.3_514.3	CO5_HUMAN	0.716

(continued)

Transition	Protein	AUC
NADYSYSVWK_616.8_333.2	CO5_HUMAN	0.715
YGLVTYATYPK_638.3_334.2	CFAB_HUMAN	0.715
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	0.715
HYGGLTGLNK_530.3_759.4	PGAM1_HUMAN	0.714
DFHINLFQVLPWLK_885.5_400.2	CFAB_HUMAN	0.714
NCSFSIIYPVVIK_770.4_555.4	CRHBP_HUMAN	0.714
HPWIVHWDQLPQYQLNR_744.0_918.5	KS6A3_HUMAN	0.712
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.711
ALDLSLK_380.2_185.1	ITIH3_HUMAN	0.711
ALDLSLK_380.2_575.3	ITIH3_HUMAN	0.710
LDFHFSSDR_375.2_611.3	INHBC_HUMAN	0.709
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.707
EVFSKPISWEELLQ_852.9_260.2	FA40A_HUMAN	0.706
IAPQLSTEELVSLGEK_857.5_533.3	AFAM_HUMAN	0.704
LIENGYFHPVK_439.6_343.2	F13B_HUMAN	0.703
NFPSPVDAAFR_610.8_775.4	HEMO_HUMAN	0.703
QLYGDTGVLGR_589.8_345.2	CO8G_HUMAN	0.702
LYYGDDEK_501.7_563.2	CO8A_HUMAN	0.702
FQLSETNR_497.8_476.3	PSG2_HUMAN	0.701
TGVAVNKPAEFTVDAK_549.6_977.5	FLNA_HUMAN	0.700
IPGIFELGISSQSDR_809.9_679.3	CO8B_HUMAN	0.700
TLFIFGVTK_513.3_215.1	PSG4_HUMAN	0.699
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.699
QVFAVQR_424.2_473.3	ELNE_HUMAN	0.699
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	0.699
DFNQFSSGEK_386.8_189.1	FETA_HUMAN	0.699
SVSLPSLDPASAK_636.4_473.3	APOB_HUMAN	0.699
GNGLTWAEK_488.3_634.3	C163B_HUMAN	0.698
LYYGDDEK_501.7_726.3	CO8A_HUMAN	0.698
NFPSPVDAAFR_610.8_959.5	HEMO_HUMAN	0.698
FAFNLYR_465.8_565.3	HEP2_HUMAN	0.697
SGFSFGFK_438.7_585.3	CO8B_HUMAN	0.696
DFHINLFQVLPWLK_885.5_543.3	CFAB_HUMAN	0.696
LQGTLPVEAR_542.3_842.5	CO5_HUMAN	0.694
GAVHVVVAETDYQSFAVLYLER_822.8_863.5	CO8G_HUMAN	0.694
TSESTGSLPSPFLR_739.9_716.4	PSMG1_HUMAN	0.694
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	0.694
ESDTSYVSLK_564.8_347.2	CRP_HUMAN	0.693

(continued)

Transition	Protein	AUC
ILDDLSPR_464.8_587.3	ITIH4_HUMAN	0.693
VQEAHLTEDQIFYFPK_655.7_391.2	CO8G_HUMAN	0.692
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	0.692
DTDTGALLFIGK_625.8_217.1	PEDF_HUMAN	0.692
HFQNLGK_422.2_285.1	AFAM_HUMAN	0.691
NNQLVAGYLQGPNVNLEEK_700.7_999.5	IL1RA_HUMAN	0.691
IPGIFELGISSQSDR_809.9_849.4	CO8B_HUMAN	0.691
ESDTSYVSLK_564.8_696.4	CRP_HUMAN	0.690
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	0.690
DADPDTFFAK_563.8_302.1	AFAM_HUMAN	0.690
LDFHFSSDR_375.2_464.2	INHBC_HUMAN	0.689
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	0.688
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	0.687
IQTHSTTYR_369.5_627.3	F13B_HUMAN	0.686
HYFIAAVER_553.3_658.4	FA8_HUMAN	0.686
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	0.686
DLHLSDVFLK_396.2_366.2	CO6_HUMAN	0.685
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	0.684
AGITIPR_364.2_272.2	IL17_HUMAN	0.684
IAQYYYTFK_598.8_884.4	F13B_HUMAN	0.684
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	0.683
VEPLYELVTATDFAYSSTVR_754.4_549.3	CO8B_HUMAN	0.682
AGITIPR_364.2_486.3	IL17_HUMAN	0.682
YEVQGEVFTKPQLWP_911.0_293.1	CRP_HUMAN	0.681
APLTKPLK_289.9_357.2	CRP_HUMAN	0.681
YNSQLLSFVR_613.8_508.3	TFR1_HUMAN	0.681
ANDQYLTAAALHNLDEAVK_686.4_301.1	IL1A_HUMAN	0.681
IQTHSTTYR_369.5_540.3	F13B_HUMAN	0.681
IHPSYTNYR_575.8_598.3	PSG2_HUMAN	0.681
TEFLSNYLTNVDDITLVPGTLGR_846.8_699.4	ENPP2_HUMAN	0.681
DPTFIPAPIQAK_433.2_461.2	ANGT_HUMAN	0.679
FQSVFTVTR_542.8_623.4	C1QC_HUMAN	0.679
LQVNTPLVGASLLR_741.0_925.6	BPIA1_HUMAN	0.679
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	0.678
HATLSLSIPR_365.6_272.2	VGFR3_HUMAN	0.678
EDTPNSVWEPAK_686.8_315.2	C1S_HUMAN	0.678
TGISPLALIK_506.8_741.5	APOB_HUMAN	0.678
ILPSVPK_377.2_244.2	PGH1_HUMAN	0.676

(continued)

Transition	Protein	AUC
HATLSLSIPR_365.6_472.3	VGFR3_HUMAN	0.676
QGHNSVFLIK_381.6_520.4	HEMO_HUMAN	0.676
LPATEKPVLLSK_432.6_460.3	HYOU1_HUMAN	0.675
APLTKPLK_289.9_398.8	CRP_HUMAN	0.674
GVTGYFTFNLYLK_508.3_683.9	PSG5_HUMAN	0.673
TFLTVYWTPER_706.9_401.2	ICAM1_HUMAN	0.673
GDTYPAELYITGSILR_885.0_274.1	F13B_HUMAN	0.672
EDTPNSVWEPAK_686.8_630.3	C1S_HUMAN	0.672
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.672
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	0.671
GPGEDFR_389.2_322.2	PTGDS_HUMAN	0.670
TDAPDLPEENQAR_728.3_843.4	CO5_HUMAN	0.670
GVTGYFTFNLYLK_508.3_260.2	PSG5_HUMAN	0.669
FAFNLYR_465.8_712.4	HEP2_HUMAN	0.669
ITENDIQJALDDAK_779.9_873.5	APOB_HUMAN	0.669
ILNIFGVIK_508.8_790.5	TFR1_HUMAN	0.669
ISQGEADINIAFYQR_575.6_684.4	MMP8_HUMAN	0.668
GDTYPAELYITGSILR_885.0_1332.8	F13B_HUMAN	0.668
ELLESYIDGR_597.8_710.4	THRB_HUMAN	0.668
FTITAGSK_412.7_576.3	FABPL_HUMAN	0.667
ILDGGNK_358.7_490.2	CXCL5_HUMAN	0.667
GWVTDGFSSLK_598.8_854.4	APOC3_HUMAN	0.667
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.665
IHPSYTNYR_575.8_813.4	PSG2_HUMAN	0.665
ELLESYIDGR_597.8_839.4	THRB_HUMAN	0.665
SDGAKPGPR_442.7_213.6	COLI_HUMAN	0.664
IAQYYYTFK_598.8_395.2	F13B_HUMAN	0.664
SILFLGK_389.2_201.1	THBG_HUMAN	0.664
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	0.664
VSAPSGTGHLPGLNPL_506.3_300.7	PSG3_HUMAN	0.664
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	0.664
YYGYTGAFR_549.3_771.4	TRFL_HUMAN	0.663
TDAPDLPEENQAR_728.3_613.3	CO5_HUMAN	0.663
IEVIITLK_464.8_815.5	CXL11_HUMAN	0.662
ILPSVPK_377.2_227.2	PGH1_HUMAN	0.662
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.661
DYWSTVK_449.7_347.2	APOC3_HUMAN	0.661
IEGNLIFDPNNYLPK_874.0_845.5	APOB_HUMAN	0.661

(continued)

Transition	Protein	AUC
WILTAAHTLYPK_471.9_407.2	C1R_HUMAN	0.661
WNFAYWAAHQPWSR_607.3_545.3	PRG2_HUMAN	0.661
SILFLGK_389.2_577.4	THBG_HUMAN	0.661
FSLVSGWGQLLDR_493.3_516.3	FA7_HUMAN	0.661
DTDTGALLFIGK_625.8_818.5	PEDF_HUMAN	0.661
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.660
LWAYLTIQELLAK_781.5_371.2	ITIH1_HUMAN	0.660
LLEVPEGR_456.8_356.2	C1S_HUMAN	0.659
ITENDIQIALDDAK_779.9_632.3	APOB_HUMAN	0.659
LTTVDIVTLR_565.8_716.4	IL2RB_HUMAN	0.658
IEVIITLK_464.8_587.4	CXL11_HUMAN	0.658
QLGLPGPPDVPDHAAYHPF_676.7_299.2	ITIH4_HUMAN	0.658
TLAFVR_353.7_492.3	FA7_HUMAN	0.656
NSDQEIDFK_548.3_294.2	S10A5_HUMAN	0.656
YHFEALADTGISSEFYDNANDLLSK_940.8_874.5	C08A_HUMAN	0.656
SEPRPGVLLR_375.2_454.3	FA7_HUMAN	0.655
FLPCENK_454.2_390.2	IL10_HUMAN	0.654
NCSFSIIYPVVIK_770.4_831.5	CRHBP_HUMAN	0.654
SLDFTELDVAAEK_719.4_874.5	ANGT_HUMAN	0.654
ILLLGTAVESAWGDEQSAFR_721.7_909.4	CXA1_HUMAN	0.653
SVSLPSLDPASAK_636.4_885.5	APOB_HUMAN	0.653
TGISPLALIK_506.8_654.5	APOB_HUMAN	0.653
YNQLLR_403.7_288.2	ENOA_HUMAN	0.653
YEVQGEVFTKPQLWP_911.0_392.2	CRP_HUMAN	0.652
VPGLYYFTYHASSR_554.3_720.3	C1QB_HUMAN	0.650
SLQNASAIESILK_687.4_589.4	IL3_HUMAN	0.650
WILTAAHTLYPK_471.9_621.4	C1R_HUMAN	0.650
GWVTDGFSSLK_598.8_953.5	APOC3_HUMAN	0.650
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.649
QDLGWK_373.7_503.3	TGFB3_HUMAN	0.649
DYWSTVK_449.7_620.3	APOC3_HUMAN	0.648
ALVLELAK_428.8_331.2	INHBE_HUMAN	0.647
QLGLPGPPDVPDHAAYHPF_676.7_263.1	ITIH4_HUMAN	0.646
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.645
TFLTVYWTPER_706.9_502.3	ICAM1_HUMAN	0.644
FQSVFTVTR_542.8_722.4	C1QC_HUMAN	0.643
DPNGLPPEAQK_583.3_669.4	RET4_HUMAN	0.642
ETLLQDFR_511.3_322.2	AMBP_HUMAN	0.642

(continued)

Transition	Protein	AUC
IIEVEEEQEDPYLNDR_996.0_777.4	FBLN1_HUMAN	0.641
ELCLDPK_437.7_359.2	IL8_HUMAN	0.641
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.641
NQSPVLEPVGR_598.3_866.5	KS6A3_HUMAN	0.641
FNAVLTNPQGDYDTSTGK_964.5_333.2	C1QC_HUMAN	0.641
LLEVPEGR_456.8_686.4	C1S_HUMAN	0.641
FFQYDTWK_567.8_840.4	IGF2_HUMAN	0.640
SPEAEDPLGVER_649.8_670.4	Z512B_HUMAN	0.639
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.639
SGAQATWTELPWPHEK_613.3_793.4	HEMO_HUMAN	0.638
YSHYNER_323.5_581.3	HABP2_HUMAN	0.638
YHFEALADTG!SSEFYDNANDLLSK_940.8_301.1	CO8A_HUMAN	0.637
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.637
YSHYNER_323.5_418.2	HABP2_HUMAN	0.637
YYLQGAK_421.7_327.1	ITIH4_HUMAN	0.636
EVPLSALTNILSAQLISHWK_740.8_996.6	PAI1_HUMAN	0.636
VPGLYYFTYHASSR_554.3_420.2	C1QB_HUMAN	0.636
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	0.636
ETLLQDFR_511.3_565.3	AMBP_HUMAN	0.635
IVLSLDVPIGLLQILLEQAR_735.1_503.3	UCN2_HUMAN	0.635
ENPAVIDFELAPIVDLVR_670.7_811.5	CO6_HUMAN	0.635
LQLSETNR_480.8_355.2	PSG8_HUMAN	0.635
DPDQTDGLGLSYLSSHIANVER_796.4_456.2	GELS_HUMAN	0.635
NVNQSLLELHK_432.2_656.3	FRIH_HUMAN	0.634
EIGELYLPK_531.3_633.4	AACT_HUMAN	0.634
SPEQQETVLDGNLIIR_906.5_699.3	ITIH4_HUMAN	0.634
NKPGVYTDVAYYLAWIR_677.0_545.3	FA12_HUMAN	0.632
QNYHQDSEAAINR_515.9_544.3	FRIH_HUMAN	0.632
EKPAGGIPVLGSLVNTVLK_631.4_930.6	BPIB1_HUMAN	0.632
VTFEYR_407.7_614.3	CRHBP_HUMAN	0.630
DLPHITVDR_533.3_490.3	MMP7_HUMAN	0.630
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	0.630
ENPAVIDFELAPIVDLVR_670.7_601.4	CO6_HUMAN	0.630
YGFYTHVFR_397.2_659.4	THRB_HUMAN	0.629
ILDDLSPR_464.8_702.3	ITIH4_HUMAN	0.629
DPNGLPPEAQK_583.3_497.2	RET4_HUMAN	0.629
GSLVQASEANLQAAQDFVR_668.7_806.4	ITIH1_HUMAN	0.629
FLYHK_354.2_447.2	AMBP_HUMAN	0.627

(continued)

Transition	Protein	AUC
FNAVLTNPQGDYDTSTGK_964.5_262.1	C1QC_HUMAN	0.627
LQDAGVYR_461.2_680.3	PD1L1_HUMAN	0.627
INPASLDK_429.2_630.4	C163A_HUMAN	0.626
LEEHYELR_363.5_580.3	PAI2_HUMAN	0.625
VEHSDLSFSK_383.5_468.2	B2MG_HUMAN	0.624
TSDQIHFFFAK_447.6_659.4	ANT3_HUMAN	0.624
ATLSAAPSNPR_542.8_570.3	CXCL2_HUMAN	0.624
YGFYTHVFR_397.2_421.3	THRB_HUMAN	0.624
EANQSTLENFLER_775.9_678.4	IL4_HUMAN	0.623
GQQPADVTGTALPR_705.9_314.2	CSF1_HUMAN	0.623
VELAPLPSWQPVGK_760.9_400.3	ICAM1_HUMAN	0.622
GEVTYTTSQVSK_650.3_750.4	EGLN_HUMAN	0.622
SLQAFVAVAAR_566.8_487.3	IL23A_HUMAN	0.622
HYGGLTGLNK_530.3_301.1	PGAM1_HUMAN	0.622
GPEDQDISISFAWDK_854.4_753.4	DEF4_HUMAN	0.622
YVVISQGLDKPR_458.9_400.3	LRP1_HUMAN	0.621
LWAYLTIQELLAK_781.5_300.2	ITIH1_HUMAN	0.621
SGAQATWTELPWPHEK_613.3_510.3	HEMO_HUMAN	0.621
GTAEWLSFDVTDTVR_848.9_952.5	TGFB3_HUMAN	0.621
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.621
AHQLAIDTYQEFEETYIPK_766.0_634.4	CSH_HUMAN	0.620
LPATEKPVLLSK_432.6_347.2	HYOU1_HUMAN	0.620
NIQSVNVK_451.3_546.3	GROA_HUMAN	0.620
TAVTANLDIR_537.3_288.2	CHL1_HUMAN	0.619
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.616
QINSYVK_426.2_496.3	CBG_HUMAN	0.616
GFQALGDAADIR_617.3_288.2	TIMP1_HUMAN	0.615
WNFAYWAAHQPWSR_607.3_673.3	PRG2_HUMAN	0.615
NEIWYR_440.7_357.2	FA12_HUMAN	0.615
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.614
YYLQGAK_421.7_516.3	ITIH4_HUMAN	0.614
ALNSIIDVYHK_424.9_774.4	S10A8_HUMAN	0.614
ETPEGAEAKPWYEPIYLGGVFQLEK_951.1_877.5	TNFA_HUMAN	0.614
LNIGYIEDLK_589.3_837.4	PAI2_HUMAN	0.614
NVNQSLLELHK_432.2_543.3	FRIH_HUMAN	0.613
ILLLGTAVESAWGDEQSAFR_721.7_910.6	CXA1_HUMAN	0.613
AALAAFNAQNNGSNFQLEEISR_789.1_633.3	FETUA_HUMAN	0.613
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.613

(continued)

Transition	Protein	AUC
VGEYSLYIGR_578.8_708.4	SAMP_HUMAN	0.613
DIPHWLNPTR_416.9_373.2	PAPP1_HUMAN	0.612
NEIVFPAGILQAPFYTR_968.5_357.2	ECE1_HUMAN	0.612
AEHPTWGDEQLFQTTR_639.3_765.4	PGH1_HUMAN	0.612
VEPLYELVTATDFAYSSTVR_754.4_712.4	CO8B_HUMAN	0.611
DEIPHNDIALLK_459.9_260.2	HABP2_HUMAN	0.611
QINSYVK_426.2_610.3	CBG_HUMAN	0.610
SWNEPLYHLVTEVR_581.6_614.3	PRL_HUMAN	0.610
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.610
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.610
ANDQYLTAAALHNLDEAVK_686.4_317.2	IL1A_HUMAN	0.610
VRPQQLVK_484.3_609.4	ITIH4_HUMAN	0.609
IPKPEASFSPR_410.2_506.3	ITIH4_HUMAN	0.609
SPEQQETVLDGNLIIR_906.5_685.4	ITIH4_HUMAN	0.609
DDLYVSDAFHK_655.3_704.3	ANT3_HUMAN	0.609
ELPEHTVK_476.8_347.2	VTDB_HUMAN	0.609
FLYHK_354.2_284.2	AMBP_HUMAN	0.608
QRPPDLDTSSNAVDLLFFTDESGDSR_961.5_262.2	C1R_HUMAN	0.608
DPDQTDGLGLSYLSSHIANVER_796.4_328.1	GELS_HUMAN	0.608
NEIWYR_440.7_637.4	FA12_HUMAN	0.607
LQLSETN R_480.8_672.4	PSG8_HUMAN	0.606
GQVPENEANVVITTLK_571.3_462.3	CADH1_HUMAN	0.606
FTGSQPFGQGVEHATANK_626.0_521.2	TSP1_HUMAN	0.605
LEPLYSASGPGLRPLVIK_637.4_260.2	CAA60698	0.605
QRPPDLDTSSNAVDLLFFTDESGDSR_961.5_866.3	C1R_HUMAN	0.604
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.604
TSDQ!HFFFAK_447.6_512.3	ANT3_HUMAN	0.604
IQHPFTVEEFVLPK_562.0_861.5	PZP_HUMAN	0.603
NKPGVYTDVAYYLAWIR_677.0_821.5	FA12_HUMAN	0.603
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.603
EIGELYLPK_531.3_819.5	AACT_HUMAN	0.602
LFYADHPFIFLVR_546.6_647.4	SERPH_HUMAN	0.602
AEHPTWGDEQLFQTTR_639.3_569.3	PGH1_HUMAN	0.601
TSYQVYSK_488.2_787.4	C163A_HUMAN	0.601
YTTEIIK_434.2_704.4	C1R_HUMAN	0.601
NVIQISNDLENLR_509.9_402.3	LEP_HUMAN	0.600
AFLEVNEEGSEAAASTAVVIAGR_764.4_685.4	ANT3_HUMAN	0.600

Table 13. Middle Window Individual Stats

Transition	Protein	AUC
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.738
VFQFLEK_455.8_811.4	CO5_HUMAN	0.709
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.705
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.692
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	0.686
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	0.683
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.683
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.681
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.681
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.679
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.677
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	0.675
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.667
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	0.665
IEEIAAK_387.2_660.4	CO5_HUMAN	0.664
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.664
TLLPVSKPEIR_418.3_514.3	CO5_HUMAN	0.662
ALQDQLVLVAAK_634.9_956.6	ANGT_HUMAN	0.661
TLAFVR_353.7_492.3	FA7_HUMAN	0.661
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.658
VEHSDLSFSK_383.5_468.2	B2MG_HUMAN	0.653
DPTFIPAPIQAK_433.2_461.2	ANGT_HUMAN	0.653
QGHNSVFLIK_381.6_260.2	HEMO_HUMAN	0.650
SLDFTELDVAAEK_719.4_874.5	ANGT_HUMAN	0.650
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.649
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.647
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	0.646
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.644
QGHNSVFLIK_381.6_520.4	HEMO_HUMAN	0.644
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	0.643
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.643
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.643
GPITSAAELNDPQSILLR_632.4_826.5	EGLN_HUMAN	0.643
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.642
TEQAAVAR_423.2_487.3	FA12_HUMAN	0.642
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.642
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	0.642

(continued)

Transition	Protein	AUC
DLHLSDVFLK_396.2_366.2	CO6_HUMAN	0.641
AFTECCVVASQLR_770.9_574.3	CO5_HUMAN	0.640
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.639
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	0.639
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.638
HYINLITR_515.3_301.1	NPY_HUMAN	0.637
HFQNLGK_422.2_285.1	AFAM_HUMAN	0.637
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.636
IHPSYTNYR_575.8_813.4	PSG2_HUMAN	0.635
IEEIAAK_387.2_531.3	CO5_HUMAN	0.635
GEVTYTTSQVSK_650.3_750.4	EGLN_HUMAN	0.634
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	0.634
VVGGLVALR_442.3_784.5	FA12_HUMAN	0.634
SDGAKPGPR_442.7_459.2	COLI_HUMAN	0.634
DVLLLVHNLPQNLTGHIWYK_791.8_310.2	PSG7_HUMAN	0.634
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	0.633
NKPGVYTDVAYYLAWIR_677.0_821.5	FA12_HUMAN	0.630
QVFAVQR_424.2_473.3	ELNE_HUMAN	0.630
NHYTESISVAK_624.8_415.2	NEUR1_HUMAN	0.630
IAPQLSTEELVSLGEK_857.5_333.2	AFAM_HUMAN	0.629
IHPSYTNYR_575.8_598.3	PSG2_HUMAN	0.627
EVFSKPISWEELLQ_852.9_260.2	FA40A_HUMAN	0.627
SILFLGK_389.2_201.1	THBG_HUMAN	0.626
IEVIITLK_464.8_587.4	CXL11_HUMAN	0.625
VVGGLVALR_442.3_685.4	FA12_HUMAN	0.624
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4	SHBG_HUMAN	0.624
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.623
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_768.5	SHBG_HUMAN	0.622
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.621
LHEAFSPVSYQHDLALLR_699.4_380.2	FA12_HUMAN	0.621
AHYDLR_387.7_566.3	FETUA_HUMAN	0.620
FSVVYAK_407.2_381.2	FETUA_HUMAN	0.618
ALALPPLGLAPLLNLWAKPQGR_770.5_256.2	SHBG_HUMAN	0.618
YENYTSSFFIR_713.8_293.1	IL12B_HUMAN	0.617
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	0.617
S!LFLGK_389.2_577.4	THBG_HUMAN	0.616
ILPSVPK_377.2_227.2	PGH1_HUMAN	0.615
IPSNPSHR_303.2_496.3	FBLN3_HUMAN	0.615

(continued)

Transition	Protein	AUC
HYFIAAVER_553.3_301.1	FA8_HUMAN	0.615
FSVVYAK_407.2_579.4	FETUA_HUMAN	0.613
VFQFLEK_455.8_276.2	CO5_HUMAN	0.613
IAPQLSTEELVSLGEK_857.5_533.3	AFAM_HUMAN	0.613
ILPSVPK_377.2_244.2	PGH1_HUMAN	0.613
NKPGVYTDVAYYLAWIR_677.0_545.3	FA12_HUMAN	0.613
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.612
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.612
ALALPPLGLAPLLNLWAKPQGR_770.5_457.3	SHBG_HUMAN	0.612
QLGLPGPPDVPDHAAYHPF_676.7_299.2	ITIH4_HUMAN	0.612
ILDDLSPR_464.8_587.3	ITIH4_HUMAN	0.611
VELAPLPSWQPVGK_760.9_400.3	ICAM1_HUMAN	0.611
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	0.611
NHYTESISVAK_624.8_252.1	NEUR1_HUMAN	0.611
SEPRPGVLLR_375.2_454.3	FA7_HUMAN	0.611
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	0.611
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.609
LTTVDIVTLR_565.8_716.4	IL2RB_HUMAN	0.608
TQILEWAAER_608.8_761.4	EGLN_HUMAN	0.608
NEPEETPSIEK_636.8_573.3	SOX5_HUMAN	0.608
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	0.607
LQVNTPLVGASLLR_741.0_925.6	BPIA1_HUMAN	0.607
VPSHAVVAR_312.5_345.2	TRFL_HUMAN	0.607
SLQNASAIESILK_687.4_860.5	IL3_HUMAN	0.607
GVTGYFTFNLYLK_508.3_260.2	PSG5_HUMAN	0.605
DFNQFSSGEK_386.8_189.1	FETA_HUMAN	0.605
QLGLPGPPDVPDHAAYHPF_676.7_263.1	ITIH4_HUMAN	0.605
TLEAQLTPR_514.8_814.4	HEP2_HUMAN	0.604
AFTECCVVASQLR_770.9_673.4	CO5_HUMAN	0.604
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.604
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.603
LWAYLTIQELLAK_781.5_300.2	ITIH1_HUMAN	0.603
GGLFADIASHPWQAAIFAK_667.4_375.2	TPA_HUMAN	0.603
IPSNPSHR_303.2_610.3	FBLN3_HUMAN	0.603
TDAPDLPEENQAR_728.3_843.4	CO5_HUMAN	0.603
SPQAFYR_434.7_684.4	REL3_HUMAN	0.602
SSNNPHSPIVEEFQVPYNK_729.4_261.2	C1S_HUMAN	0.601
AHYDLR_387.7_288.2	FETUA_HUMAN	0.600

(continued)

Transition	Protein	AUC
DGSPDVTTADIGANTPDATK_973.5_844.4	PGRP2_HUMAN	0.600
SPQAFYR_434.7_556.3	REL3_HUMAN	0.600

Table 14. Middle Late Individual Stats

Transition	Protein	AUC
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.656
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.655
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.652
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.649
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.644
VFQFLEK_455.8_811.4	CO5_HUMAN	0.643
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.640
TLAFVR_353.7_492.3	FA7_HUMAN	0.639
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.637
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.637
TEQAAVAR_423.2_487.3	FA12_HUMAN	0.633
QINSYVK_426.2 496.3	CBG_HUMAN	0.633
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.633
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.633
ALQDQLVLVAAK_634.9_956.6	ANGT_HUMAN	0.628
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.628
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	0.628
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.628
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.626
QINSYVK_426.2_610.3	CBG_HUMAN	0.625
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.625
DPTFIPAPIQAK_433.2_461.2	ANGT_HUMAN	0.625
AVYEAVLR_460.8_750.4	PEPD_HUMAN	0.623
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.623
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.623
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.622
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.622
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	0.621
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	0.621
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	0.620
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.619
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.619

(continued)

Transition	Protein	AUC
SLDFTELDVAAEK_719.4_874.5	ANGT_HUMAN	0.618
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.618
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.618
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.615
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.615
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	0.613
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.612
GYQELLEK_490.3_631.4	FETA_HUMAN	0.612
VPLALFALNR_557.3_917.6	PEPD_HUMAN	0.611
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.611
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.608
WSAGLTSSQVDLYIPK_883.0_357.2	CBG_HUMAN	0.608
ITQDAQLK_458.8_702.4	CBG_HUMAN	0.608
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.607
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.607
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.606
LWAYLTIQELLAK_781.5_300.2	ITIH1_HUMAN	0.606
VVGGLVALR_442.3_784.5	FA12_HUMAN	0.605
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	0.603
SVVLIPLGAVDDGEHSQNEK_703.0_798.4	CNDP1_HUMAN	0.603
SETEIHQGFQHLHQLFAK_717.4_318.1	CBG_HUMAN	0.603
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	0.603
IEVIITLK_464.8_587.4	CXL11_HUMAN	0.602
ITQDAQLK_458.8_803.4	CBG_HUMAN	0.602
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	0.601
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.601
LTTVDIVTLR_565.8_716.4	IL2RB_HUMAN	0.600
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.600

Table 15. Late Window Individual Stats

Transition	Protein	AUC
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.724
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	0.703
QJNSYVK_426.2_496.3	CBG_HUMAN	0.695
AVYEAVLR_460.8_750.4	PEPD_HUMAN	0.693
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	0.684
QINSYVK_426.2_610.3	CBG_HUMAN	0.681

(continued)

Transition	Protein	AUC
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.678
VGVISFAQK_474.8_580.3	TFR2_HUMAN	0.674
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.670
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.670
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.660
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	0.660
TSYQVYSK_488.2_787.4	C163A_HUMAN	0.657
ITQDAQLK_458.8_702.4	CBG_HUMAN	0.652
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.650
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	0.650
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	0.650
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	0.648
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.647
VLSSIEQK_452.3_691.4	1433S_HUMAN	0.647
YSHYNER_323.5_418.2	HABP2_HUMAN	0.646
ILDGGNK_358.7_603.3	CXCL5_HUMAN	0.645
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.645
AEIEYLEK_497.8_389.2	LYAM1_HUMAN	0.645
TLPFSR_360.7_506.3	LYAM1_HUMAN	0.645
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	0.644
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.644
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	0.644
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.642
TASDFITK_441.7_781.4	GELS_HUMAN	0.641
SETEIHQGFQHLHQLFAK_717.4_447.2	CBG_HUMAN	0.640
SPQAFYR_434.7_556.3	REL3_HUMAN	0.639
TAVTANLDIR_537.3_288.2	CHL1_HUMAN	0.636
VPLALFALNR_557.3_917.6	PEPD_HUMAN	0.636
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	0.633
SETEIHQGFQHLHQLFAK_717.4_318.1	CBG_HUMAN	0.633
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.633
GYQELLEK_490.3_631.4	FETA_HUMAN	0.633
AYSDLSR_406.2_375.2	SAMP_HUMAN	0.633
SVVLIPLGAVDDGEHSQNEK_703.0_798.4	CNDP1_HUMAN	0.632
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	0.631
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.631
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.628
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.626

(continued)

Transition	Protein	AUC
AGITIPR_364.2_486.3	IL17_HUMAN	0.626
AEVIWTSSDHQVLSGK_586.3_300.2	PD1L1_HUMAN	0.625
TEQAAVAR_423.2_487.3	FA12_HUMAN	0.625
NHYTESISVAK_624.8_415.2	NEUR1_HUMAN	0.625
WSAGLTSSQVDLYIPK_883.0_357.2	CBG_HUMAN	0.623
YSHYNER_323.5_581.3	HABP2_HUMAN	0.623
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	0.621
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.620
SVVLIPLGAVDDGEHSQNEK_703.0_286.2	CNDP1_HUMAN	0.620
TLAFVR_353.7_492.3	FA7_HUMAN	0.619
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	0.619
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	0.618
YWGVASFLQK_599.8_849.5	RET4_HUMAN	0.618
TPSAAYLWVGTGASEAEK_919.5_428.2	GELS_HUMAN	0.618
DPNGLPPEAQK_583.3_669.4	RET4_HUMAN	0.617
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.616
SPQAFYR_434.7_684.4	REL3_HUMAN	0.616
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.615
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.615
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	0.615
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.615
LWAYLTIQELLAK_781.5_371.2	ITIH1_HUMAN	0.613
SYTITGLQPGTDYK_772.4_352.2	FINC_HUMAN	0.612
GAVHVVVAETDYQSFAVLYLER_822.8_863.5	CO8G_HUMAN	0.612
FQLPGQK_409.2_276.1	PSG1_HUMAN	0.612
ILDGGNK_358.7_490.2	CXCL5_HUMAN	0.611
DYWSTVK_449.7_620.3	APOC3_HUMAN	0.611
AGLLRPDYALLGHR_518.0_595.4	PGRP2_HUMAN	0.611
ALNFGGIGVVVGHELTHAFDDQGR_837.1_360.2	ECE1_HUMAN	0.611
GYQELLEK_490.3_502.3	FETA_HUMAN	0.611
HATLSLSIPR_365.6_472.3	VGFR3_HUMAN	0.610
SVPVTKPVPVTKPITVTK_631.1_658.4	Z512B_HUMAN	0.610
FQLPGQK_409.2_429.2	PSG1_HUMAN	0.610
IYLQPGR_423.7_329.2	ITIH2_HUMAN	0.610
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.609
DPNGLPPEAQK_583.3_497.2	RET4_HUMAN	0.609
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.609
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.608

(continued)

Transition	Protein	AUC
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	0.608
VPSHAVVAR_312.5_515.3	TRFL_HUMAN	0.608
YWGVASFLQK_599.8_350.2	RET4_HUMAN	0.608
EWVAIESDSVQPVPR_856.4_468.3	CNDP1_HUMAN	0.607
LQDAGVYR_461.2_680.3	PD1L1_HUMAN	0.607
DLYHYITSYVVDGEIIIYGPAYSGR_955.5_650.3	PSG1_HUMAN	0.607
LWAYLTIQELLAK_781.5_300.2	ITIH1_HUMAN	0.606
ITENDIQIALDDAK_779.9_632.3	APOB_HUMAN	0.606
SYTITGLQPGTDYK_772.4_680.3	FINC_HUMAN	0.606
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.605
IYLQPGR_423.7_570.3	ITIH2_HUMAN	0.605
YNQLLR_403.7_529.4	ENOA_HUMAN	0.605
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.605
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	0.605
TASDFITK_441.7_710.4	GELS_HUMAN	0.605
EWVAIESDSVQPVPR_856.4_486.2	CNDP1_HUMAN	0.605
YEFLNGR_449.7_606.3	PLMN_HUMAN	0.604
SNPVTLNVLYGPDLPR_585.7_654.4	PSG6_HUMAN	0.604
ITQDAQLK_458.8_803.4	CBG_HUMAN	0.603
LTTVDIVTLR_565.8_716.4	IL2RB_HUMAN	0.602
FNAVLTNPQGDYDTSTGK_964.5_262.1	C1QC_HUMAN	0.602
ITGFLKPGK_320.9_301.2	LBP_HUMAN	0.601
DYWSTVK_449.7_347.2	APOC3_HUMAN	0.601
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	0.601
GWVTDGFSSLK_598.8_953.5	APOC3_HUMAN	0.601
YYGYTGAFR_549.3_771.4	TRFL_HUMAN	0.601
ELPEHTVK_476.8_347.2	VTDB_HUMAN	0.601
FTFTLHLETPKPSISSSNLNPR_829.4_874.4	PSG1_HUMAN	0.601
DLYHYITSYVVDGEIIIYGPAYSGR_955.5_707.3	PSG1_HUMAN	0.601
SPQAFYR_434.7_684.4	REL3_HUMAN	0.616
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.615
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.615
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	0.615
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.615
LWAYLTIQELLAK_781.5_371.2	ITIH1_HUMAN	0.613
SYTITGLQPGTDYK_772.4_352.2	FINC_HUMAN	0.612
GAVHVVVAETDYQSFAVLYLER_822.8_863.5	CO8G_HUMAN	0.612
FQLPGQK_409.2_276.1	PSG1_HUMAN	0.612

(continued)

Transition	Protein	AUC
DLYHYITSYVVDGEIIIYGPAYSGR_955.5_707.3	PSG1_HUMAN	0.601

Table 16. Lasso Early 32

Variable	Protein	Coefficient
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	9.53
VQTAHFK_277.5_431.2	CO8A_HUMAN	9.09
FLNWIK_410.7_560.3	HABP2_HUMAN	6.15
ITGFLKPGK_320.9_429.3	LBP_HUMAN	5.29
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	3.83
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	3.41
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.44
AHYDLR_387.7_288.2	FETUA_HUMAN	0.1

Table 17. Lasso Early 100

Variable	Protein	Coefficient
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	6.56
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	6.51
VQTAHFK_277.5_431.2	CO8A_HUMAN	4.51
NIQSVNVK_451.3_674.4	GROA_HUMAN	3.12
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	2.68
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	2.56
AVLHIGEK_289.5_292.2	THBG_HUMAN	2.11
FLNWIK_410.7_560.3	HABP2_HUMAN	1.85
ITGFLKPGK_320.9_429.3	LBP_HUMAN	1.36
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	1.3
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.83
FLPCENK_454.2_550.2	IL10_HUMAN	0.39
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	0.3
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	0.29
VSEADSSNADWVTK_754.9_347.2	CFAB_HUMAN	0.27
ITLPDFTGDLR_624.3_28.2	LBP_HUMAN	0.13
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.04
TASDFITK_41.7_781.4	GELS_HUMAN	-5.91
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	6.56

Table 18. Lasso Protein Early Window

Variable	Protein	Coefficient
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	7.17
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	6.06
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	3.23
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	2.8
QALEEFQK_496.8_680.3	CO8B_HUMAN	2.73
NIQSVNVK_451.3_674.4	GROA_HUMAN	2.53
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	2.51
AVLHIGEK_289.5_348.7	THBG_HUMAN	2.33
FLNWIK_410.7_560.3	HABP2_HUMAN	1.05
FLPCENK_454.2_550.2	IL10_HUMAN	0.74
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	0.7
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.45
EVFSKPISWEELLQ_852.9_260.2	FA40A_HUMAN	0.17
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.06
TASDFITK_441.7_781.4	GELS_HUMAN	-7.65

Table 19. Lasso All Early Window

Variable	Protein	Coefficient
FLNWIK_410.7_560.3	HABP2_HUMAN	3.74
AHYDLR_387.7_288.2	FETUA_HUMAN	0.07
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	6.07
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	8.85
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	2.97
VQTAHFK_277.5_431.2	CO8A_HUMAN	3.36
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	11.24
VSEADSSNADWVTK_754.9_347.2	CFAB_HUMAN	0.63
AVLHIGEK_289.5_292.2	THBG_HUMAN	0.51
TGVAVNKPAEFTVDAK_549.6_977.5	FLNA_HUMAN	0.17
LIENGYFHPVK_439.6_343.2	F13B_HUMAN	1.7
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	-0.93
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	1.4
TASDFITK_441.7_781.4	GELS_HUMAN	-0.07
NIQSVNVK_451.3_674.4	GROA_HUMAN	2.12
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	1.15
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.09
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	2.45
ALDLSLK_380.2_575.3	ITIH3_HUMAN	2.51
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	4.12

(continued)

Variable	Protein	Coefficient
ISQGEADINIAFYQR_575.6_684.4	MMP8_HUMAN	1.29
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	0.55
GPGEDFR_389.2_322.2	PTGDS_HUMAN	0.07
DPNGLPPEAQK_583.3_669.4	RET4_HUMAN	1.36
WNFAYWAAHQPWSR_607.3_545.3	PRG2_HUMAN	-1.27
ELCLDPK_437.7_359.2	IL8_HUMAN	0.3
FFQYDTWK_567.8_840.4	IGF2_HUMAN	1.83
IIEVEEEQEDPYLNDR_996.0_777.4	FBLN1_HUMAN	1.14
ECEELEEK_533.2_405.2	IL15_HUMAN	1.78
LEEHYELR_363.5_580.3	PAI2_HUMAN	0.15
LNIGYIEDLK_589.3_837.4	PAI2_HUMAN	0.32
TAVTANLDIR_537.3_288.2	CHL1_HUMAN	-0.98
SWNEPLYHLVTEVR_581.6_716.4	PRL_HUMAN	1.88
ILNIFGVIK_508.8_790.5	TFR1_HUMAN	0.05
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	-2.69
VGVISFAQK_474.8_693.4	TFR2_HUMAN	-5.68
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	-1.43
GQVPENEANVVITTLK_571.3_462.3	CADH1_HUMAN	-0.55
STPSLTTK_417.7_549.3	IL6RA_HUMAN	-0.59
ALLLGWVPTR_563.3_373.2	PAR4_HUMAN	-0.97

Table 20: Lasso SummedCoef Early Window

Transition	Protein	SumBestCoefs
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	1173.723955
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	811.0150364
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	621.9659363
VQTAHFK_277.5_431.2	CO8A_HUMAN	454.178544
NIQSVNVK_451.3_674.4	GROA_HUMAN	355.9550674
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	331.8629189
GPGEDFR_389.2_322.2	PTGDS_HUMAN	305.9079494
FLPCENK_454.2_550.2	IL10_HUMAN	296.9473975
FLNWIK_410.7_560.3	HABP2_HUMAN	282.9841332
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	237.5320227
ECEELEEK_533.2_405.2	IL15_HUMAN	200.38281
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	194.6252869
QALEEFQK_496.8_680.3	CO8B_HUMAN	179.2518843
IIEVEEEQEDPYLNDR_996.0_777.4	FBLN1_HUMAN	177.7534111

(continued)

Transition	Protein	SumBestCoefs
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	164.9735228
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	162.2414693
LEEHYELR_363.5_580.3	PAI2_HUMAN	152.9262386
ISQGEADINIAFYQR_575.6_684.4	MMP8_HUMAN	144.2445011
HPWIVHWDQLPQYQLNR_744.0_918.5	KS6A3_HUMAN	140.2287926
AHYDLR_387.7_288.2	FETUA_HUMAN	137.9737525
GFQALGDAADIR_617.3_288.2	TIMP1_HUMAN	130.4945567
SWNEPLYHLVTEVR_581.6_716.4	PRL_HUMAN	127.442646
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	120.5149446
YENYTSSFFIR_713.8_293.1	IL12B_HUMAN	117.0947487
FFQYDTWK_567.8_840.4	IGF2_HUMAN	109.8569617
HYFIAAVER_553.3_658.4	FA8_HUMAN	106.9426543
ITGFLKPGK_320.9_429.3	LBP_HUMAN	103.8056505
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	98.50490812
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	97.19989285
ALDLSLK_380.2_575.3	ITIH3_HUMAN	94.84900337
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	92.52335783
HPWIVHWDQLPQYQLNR_744.0_1047.0	KS6A3_HUMAN	91.77547608
LIQDAVTGLTVNGQITGDK_972.0_640.4	ITIH3_HUMAN	83.6483639
LNIGYIEDLK_589.3_837.4	PAI2_HUMAN	83.50221521
IALGGLLFPASNLR_481.3_657.4	SHBG_HUMAN	79.33146741
LPATEKPVLLSK_432.6_460.3	HYOU1_HUMAN	78.89429168
FQLSETNR_497.8_605.3	PSG2_HUMAN	78.13445824
NEIVFPAGILQAPFYTR_968.5_357.2	ECE1_HUMAN	75.12145257
ALDLSLK_380.2_185.1	ITIH3_HUMAN	63.05454715
DLHLSDVFLK_396.2_366.2	CO6_HUMAN	58.26831142
TQILEWAAER_608.8_761.4	EGLN_HUMAN	57.29461621
FSVVYAK_407.2_381.2	FETUA_HUMAN	54.78436389
VSEADSSNADWVTK_754.9_347.2	CFAB_HUMAN	54.40003244
DPNGLPPEAQK_583.3_669.4	RET4_HUMAN	53.89169348
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	53.33747599
LSSPAVITDK_515.8_830.5	PLMN_HUMAN	53.22513181
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	51.5477235
AVLHIGEK_289.5_292.2	THBG_HUMAN	49.73092632
GEVTYTTSQVSK_650.3_750.4	EGLN_HUMAN	45.14743629
GYVIIKPLVWV_643.9_854.6	SAMP_HUMAN	44.05164273
TGVAVNKPAEFTVDAK_549.6_977.5	FLNA_HUMAN	42.99898046
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	42.90897411

(continued)

Transition	Protein	SumBestCoefs
ILDGGNK_358.7_490.2	CXCL5_HUMAN	42.60771281
FLPCENK_454.2_390.2	IL10_HUMAN	42.56799651
GFQALGDAADIR_617.3_717.4	TIMP1_HUMAN	38.68456017
SDGAKPGPR_442.7_213.6	COLI_HUMAN	38.47800265
NTGVISVVTTGLDR_716.4_662.4	CADH1_HUMAN	32.62953675
SERPPIFEIR_415.2_288.2	LRP1_HUMAN	31.48248968
DFHINLFQVLPWLK_885.5_400.2	CFAB_HUMAN	31.27286268
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	31.26972354
ELCLDPK_437.7_359.2	IL8_HUMAN	29.91108737
ILNIFGVIK_508.8_790.5	TFR1_HUMAN	29.88784921
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	29.42327998
GAVHVVVAETDYQSFAVLYLER_822.8_863.5	CO8G_HUMAN	26.70286929
AVLHIGEK_289.5_348.7	THBG_HUMAN	25.78703299
TFLTVYWTPER_706.9_401.2	ICAM1_HUMAN	24.73090242
AGITIPR_364.2_486.3	IL17_HUMAN	23.84580477
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	23.81167843
SLQAFVAVAAR_566.8_487.3	IL23A_HUMAN	23.61468839
SWNEPLYHLVTEVR_581.6_614.3	PRL_HUMAN	23.2538221
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	22.70115313
TAHISGLPPSTDFIVYLSGLAPSIR_871.5_800.5	TENA_HUMAN	22.42695892
QNYHQDSEAAINR_515.9_544.3	FRIH_HUMAN	21.96827269
AHQLAIDTYQEFEETYIPK_766.0_634.4	CSH_HUMAN	21.75765717
GDTYPAELYITGSILR_885.0_274.1	F13B_HUMAN	20.89751398
AHYDLR_387.7_566.3	FETUA_HUMAN	20.67629529
IALGGLLFPASNLR_481.3_412.3	SHBG_HUMAN	19.28973033
ATNATLDPR_479.8_272.2	PAR1_HUMAN	18.77604574
FSVVYAK_407.2_579.4	FETUA_HUMAN	17.81136564
HTLNQIDEVK_598.8_951.5	FETUA_HUMAN	17.29763288
DIPHWLNPTR_416.9_373.2	PAPP1_HUMAN	17.00562521
LYYGDDEK_501.7_563.2	CO8A_HUMAN	16.78897272
AALAAFNAQNNGSNFQLEEISR_789.1_633.3	FETUA_HUMAN	16.41986569
IQTHSTTYR_369.5_627.3	F13B_HUMAN	15.78335174
GPITSAAELNDPQSILLR_632.4_826.5	EGLN_HUMAN	15.3936876
QTLSWTVTPK_580.8_818.4	PZP_HUMAN	14.92509259
AVGYLITGYQR_620.8_737.4	PZP_HUMAN	13.9795325
DIIKPDPPK_511.8_342.2	IL12B_HUMAN	13.76508282
YNQLLR_403.7_288.2	ENOA_HUMAN	12.61733711
GNGLTWAEK_488.3_634.3	C163B_HUMAN	12.5891421

(continued)

Transition	Protein	SumBestCoefs
QVFAVQR_424.2_473.3	ELNE_HUMAN	12.57709327
FLQEQGHR_338.8_497.3	CO8G_HUMAN	12.51843475
HVVQLR_376.2_515.3	IL6RA_HUMAN	11.83747559
DVLLLVHNLPQNLTGHIWYK_791.8_883.0	PSG7_HUMAN	11.69074708
TFLTVYWTPER_706.9_502.3	ICAM1_HUMAN	11.63709776
VELAPLPSWQPVGK_760.9_400.3	ICAM1_HUMAN	10.79897269
TLFIFGVTK_513.3_215.1	PSG4_HUMAN	10.2831751
AYSDLSR_406.2_375.2	SAMP_HUMAN	10.00461148
HATLSLSIPR_365.6_472.3	VGFR3_HUMAN	9.967933028
LQGTLPVEAR_542.3_571.3	CO5_HUMAN	9.963760572
NTVISVNPSTK_580.3_732.4	VCAM1_HUMAN	9.124228658
EVFSKPISWEELLQ_852.9_260.2	FA40A_HUMAN	8.527980294
SLQNASAIESILK_687.4_860.5	IL3_HUMAN	8.429061621
IQHPFTVEEFVLPK_562.0_861.5	PZP_HUMAN	7.996504258
GVTGYFTFNLYLK_508.3_683.9	PSG5_HUMAN	7.94396229
VFQYIDLHQDEFVQTLK_708.4_361.2	CNDP1_HUMAN	7.860590049
ILDDLSPR_464.8_587.3	ITIH4_HUMAN	7.593889262
LIENGYFHPVK_439.6_343.2	F13B_HUMAN	7.05838337
VFQFLEK_455.8_811.4	CO5_HUMAN	6.976884759
AFTECCVVASQLR_770.9_574.3	CO5_HUMAN	6.847474286
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	6.744837357
IQTHSTTYR_369.5_540.3	F13B_HUMAN	6.71464509
IAQYYYTFK_598.8_395.2	F13B_HUMAN	6.540497911
YGFYTHVFR_397.2_421.3	THRB_HUMAN	6.326347548
YHFEALADTGISSEFYDNANDLLSK_940.8_874. 5	CO8A_HUMAN	6.261787525
ANDQYLTAAALHNLDEAVK_686.4_301.1	IL1A_HUMAN	6.217191651
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	6.1038295
GWVTDGFSSLK_598.8_854.4	APOC3_HUMAN	6.053494609
TLEAQLTPR_514.8_814.4	HEP2_HUMAN	5.855967278
VSAPSGTGHLPGLNPL_506.3_300.7	PSG3_HUMAN	5.625944609
EAQLPVIENK_570.8_699.4	PLMN_HUMAN	5.407703773
SPEAEDPLGVER_649.8_670.4	Z512B_HUMAN	5.341420139
IAIDLFK_410.3_635.4	HEP2_HUMAN	4.698739039
YEFLNGR_449.7_293.1	PLMN_HUMAN	4.658286706
VQTAHFK_277.5_502.3	CO8A_HUMAN	4.628247194
IEVIITLK_464.8_815.5	CXL11_HUMAN	4.57198762
ILTPEVR_414.3_601.3	GDF15_HUMAN	4.452884608
LEEHYELR_363.5_288.2	PAI2_HUMAN	4.411983862

(continued)

Transition	Protein	SumBestCoefs
HATLSLSIPR_365.6_272.2	VGFR3_HUMAN	4.334242077
NSDQEIDFK_548.3_294.2	S10A5_HUMAN	4.25302369
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	4.183602548
ELANTIK_394.7_475.3	S10AC_HUMAN	4.13558153
LSIPQITTK_500.8_687.4	PSG5_HUMAN	3.966238797
TLNAYDHR_330.5_312.2	PAR3_HUMAN	3.961140111
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	3.941476057
ELLESYIDGR_597.8_710.4	THRB_HUMAN	3.832723338
ATLSAAPSNPR_542.8_570.3	CXCL2_HUMAN	3.82834767
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4	SHBG_HUMAN	3.80737887
NADYSYSVWK_616.8_333.2	CO5_HUMAN	3.56404167
ILILPSVTR_506.3_559.3	PSGx_HUMAN	3.526998593
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	3.410412424
QVCADPSEEWVQK_788.4_275.2	CCL3_HUMAN	3.30795151
SVQNDSQAIAEVLNQLK_619.7_914.5	DESP_HUMAN	3.259270741
QVFAVQR_424.2_620.4	ELNE_HUMAN	3.211482663
ALPGEQQPLHALTR_511.0_807.5	IBP1_HUMAN	3.211207158
LEPLYSASGPGLRPLVIK_637.4_260.2	CAA60698	3.203088951
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	3.139418139
DAGLSWGSAR_510.2_576.3	NEUR4_HUMAN	3.005197927
YGFYTHVFR_397.2_659.4	THRB_HUMAN	2.985663918
NNQLVAGYLQGPNVNLEEK_700.7_357.2	IL1RA_HUMAN	2.866983196
EKPAGGIPVLGSLVNTVLK_631.4_930.6	BPIB1_HUMAN	2.798965142
FGSDDEGR_441.7_735.3	PTHR_HUMAN	2.743283546
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	2.699725572
FATTFYQHLADSK_510.3_533.3	ANT3_HUMAN	2.615073729
DYWSTVK_449.7_347.2	APOC3_HUMAN	2.525459346
QLGLPGPPDVPDHAAYHPF_676.7_263.1	ITIH4_HUMAN	2.525383799
LSSPAVITDK_515.8_743.4	PLMN_HUMAN	2.522306831
TEFLSNYLTNVDDITLVPGTLGR_846.8_699.4	ENPP2_HUMAN	2.473366805
SILFLGK_389.2_201.1	THBG_HUMAN	2.472413913
VTFEYR_407.7_614.3	CRHBP_HUMAN	2.425338167
SVVLIPLGAVDDGEHSQNEK_703.0_798.4	CNDP1_HUMAN	2.421340244
HTLNQIDEVK_598.8_958.5	FETUA_HUMAN	2.419851187
ALNSIIDVYHK_424.9_661.3	S10A8_HUMAN	2.367904596
ETLALLSTHR_570.8_500.3	IL5_HUMAN	2.230076769
GLQYAAQEGLLALQSELLR_1037.1_858.5	LBP_HUMAN	2.205949216
TYNVDK_370.2_262.1	PPB1_HUMAN	2.11849772

(continued)

Transition	Protein	SumBestCoefs
FTITAGSK_412.7_576.3	FABPL_HUMAN	2.098589805
GIVEECCFR_585.3_900.3	IGF2_HUMAN	2.059942995
YGIEEHGK_311.5_599.3	CXA1_HUMAN	2.033828589
ALVLELAK_428.8_331.2	INHBE_HUMAN	1.993820617
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	1.968753183
HELTDEELQSLFTNFANVVDK_817.1_906.5	AFAM_HUMAN	1.916438806
EANQSTLENFLER_775.9_678.4	IL4_HUMAN	1.902033355
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	1.882254674
LFIPQITR_494.3_727.4	PSG9_HUMAN	1.860649392
DPNGLPPEAQK_583.3_497.2	RET4_HUMAN	1.847702127
VEPLYELVTATDFAYSSTVR_754.4_549.3	CO8B_HUMAN	1.842159131
FQLSETNR_497.8_476.3	PSG2_HUMAN	1.834693717
FSLVSGWGQLLDR_493.3_516.3	FA7_HUMAN	1.790582748
NKPGVYTDVAYYLAWIR_677.0_545.3	FA12_HUMAN	1.777303353
FTGSQPFGQGVEHATANK_626.0_521.2	TSP1_HUMAN	1.736517431
DDLYVSDAFHK_655.3_704.3	ANT3_HUMAN	1.717534082
AFLEVNEEGSEAAASTAVVIAGR_764.4_685.4	ANT3_HUMAN	1.679420475
LPNNVLQEK_527.8_730.4	AFAM_HUMAN	1.66321148
IVLSLDVPIGLLQILLEQAR_735.1_503.3	UCN2_HUMAN	1.644983604
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	1.625411496
SDLEVAHYK_531.3_617.3	CO8B_HUMAN	1.543640117
QLYGDTGVLGR_589.8_501.3	CO8G_HUMAN	1.505242962
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	1.48233058
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	1.439531341
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	1.424401638
YGIEEHGK_311.5_341.2	CXA1_HUMAN	1.379872204
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	1.334272677
AEHPTWGDEQLFQTTR_639.3_569.3	PGH1_HUMAN	1.30549273
FQSVFTVTR_542.8_623.4	C1QC_HUMAN	1.302847429
VPGLYYFTYHASSR_554.3_420.2	C1QB_HUMAN	1.245565877
AYSDLSR_406.2_577.3	SAMP_HUMAN	1.220777002
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	1.216612522
NAVVQGLEQPHGLVVHPLR_688.4_890.6	LRP1_HUMAN	1.212935735
TSDQIHFFFAK_447.6_659.4	ANT3_HUMAN	1.176238265
GTYLYNDCPGPGQDTDCR_697.0_335.2	TNR1A_HUMAN	1.1455649
TSYQVYSK_488.2_787.4	C163A_HUMAN	1.048896429
ALNSIIDVYHK_424.9_774.4	S10A8_HUMAN	1.028522516
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	0.995831393

(continued)

Transition	Protein	SumBestCoefs
LSETNR_360.2_330.2	PSG1_HUMAN	0.976094717
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.956286531
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.947931674
LPATEKPVLLSK_432.6_347.2	HYOU1_HUMAN	0.932537153
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	0.905955419
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	0.9032484
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.884340285
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.881493383
AGFAGDDAPR_488.7_701.3	ACTB_HUMAN	0.814836556
YEFLNGR_449.7_606.3	PLMN_HUMAN	0.767373087
VIAVNEVGR_478.8_284.2	CHL1_HUMAN	0.721519592
SLSQQIENIR_594.3_531.3	CO1A1_HUMAN	0.712051082
EWVAIESDSVQPVPR_856.4_486.2	CNDP1_HUMAN	0.647712421
YGLVTYATYPK_638.3_843.4	CFAB_HUMAN	0.618499569
SVVLIPLGAVDDGEHSQNEK_703.0_286.2	CNDP1_HUMAN	0.606626346
NSDQEIDFK_548.3_409.2	S10A5_HUMAN	0.601928175
NVNQSLLELHK_432.2_543.3	FRIH_HUMAN	0.572008792
IAQYYYTFK_598.8_884.4	F13B_HUMAN	0.495062844
GPITSAAELNDPQSILLR_632.4_601.4	EGLN_HUMAN	0.47565795
YTTEIIK_434.2_704.4	C1R_HUMAN	0.433318952
GYVIIKPLVWV_643.9_304.2	SAMP_HUMAN	0.427905264
LDFHFSSDR_375.2_464.2	INHBC_HUMAN	0.411898116
IPSNPSHR_303.2_496.3	FBLN3_HUMAN	0.390037291
APLTKPLK_289.9_357.2	CRP_HUMAN	0.38859469
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.371359974
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.346336267
SPQAFYR_434.7_556.3	REL3_HUMAN	0.345901234
SVDEALR_395.2_488.3	PRDX2_HUMAN	0.307518869
FVFGTTPEDILR_697.9_742.4	TSP1_HUMAN	0.302313589
FTFTLHLETPKPSISSSNLNPR_829.4_787.4	PSG1_HUMAN	0.269826678
VGEYSLYIGR_578.8_708.4	SAMP_HUMAN	0.226573173
ILPSVPK_377.2_244.2	PGH1_HUMAN	0.225429414
LFIPQITR_494.3_614.4	PSG9_HUMAN	0.18285533
TGYYFDGISR_589.8_857.4	FBLN1_HUMAN	0.182474114
HYGGLTGLNK_530.3_759.4	PGAM1_HUMAN	0.152397007
NQSPVLEPVGR_598.3_866.5	KS6A3_HUMAN	0.128963949
IGKPAPDFK_324.9_294.2	PRDX2_HUMAN	0.113383235
TSESTGSLPSPFLR_739.9_716.4	PSMG1_HUMAN	0.108159874

(continued)

Transition	Protein	SumBestCoefs
ESDTSYVSLK_564.8_347.2	CRP_HUMAN	0.08569303
ETPEGAEAKPWYEPIYLGGVFQLEK_951.1_877.5	TNFA_HUMAN	0.039781728
TSDQIHFFFAK_447.6_512.3	ANT3_HUMAN	0.008064465

Table 21. Lasso32 Middle Window

Variable	UniProt_ID	Coefficient
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	6.99
VFQFLEK_455.8_811.4	CO5_HUMAN	6.43
VLEPTLK_400.3_458.3	VTDB_HUMAN	3.99
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	3.33
TLAFVR_353.7_492.3	FA7_HUMAN	2.44
YGIEEHGK_311.5_599.3	CXA1_HUMAN	2.27
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	2.14
QGHNSVFLIK_381.6_520.4	HEMO_HUMAN	0.25
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-2.81
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	-3.46
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	-6.61

Table 22. Lasso 100 Middle Window

Variable	UniProt_ID	Coefficient
VFQFLEK_455.8_811.4	CO5_HUMAN	6.89
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	4.67
GEVTYTTSQVSK_650.3_750.4	EGLN_HUMAN	3.4
QVFAVQR_424.2_473.3	ELNE_HUMAN	1.94
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	1.91
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	1.8
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	1.67
YGIEEHGK_311.5_599.3	CXA1_HUMAN	1.53
YGIEEHGK_311.5_341.2	CXA1_HUMAN	1.51
HYINLITR_515.3_301.1	NPY_HUMAN	1.47
TLAFVR_353.7_492.3	FA7_HUMAN	1.46
GVTGYFTFNLYLK_508.3_260.2	PSG5_HUMAN	1.28
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.84
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.41
VELAPLPSWQPVGK_760.9_400.3	ICAM1_HUMAN	0.3
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	-0.95
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	-1.54

(continued)

Variable	UniProt_ID	Coefficient
DVLLLVHNLPQNLTGHIWYK_791.8_310.2	PSG7_HUMAN	-1.54
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-1.91
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-2.3
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	-3.6
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	-3.96

Table 23. Lasso Protein Middle Window

Variable	UniProt_ID	Coefficient
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	5.84
VFQFLEK_455.8_811.4	CO5_HUMAN	5.58
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	2.11
TLAFVR_353.7_492.3	FA7_HUMAN	1.83
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	1.62
HYINLITR_515.3_301.1	NPY_HUMAN	1.39
VLEPTLK_400.3_458.3	VTDB_HUMAN	1.37
YGIEEHGK_311.5_599.3	CXA1_HUMAN	1.17
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	1.13
QVFAVQR_424.2_473.3	ELNE_HUMAN	0.79
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.23
DVLLLVHNLPQNLTGHIWYK_791.8_310.2	PSG7_HUMAN	-0.61
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	-0.69
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	-0.85
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-1.45
ELPQSIVYK_538.8- 417.7	FBLN3_HUMAN	-1.9
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-2.07
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	-2.32

Table 24. Lasso All Middle Window

Variable	UniProt_ID	Coefficient
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	2.48
VFQFLEK_455.8_811.4	CO5_HUMAN	2.41
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	1.07
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.64
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.58
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.21
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-0.62
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	-1.28

Table 25. Lasso32 Middle-Late Window

Variable	UniProt_ID	Coefficient
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	4.35
TLAFVR_353.7_492.3	FA7_HUMAN	2.42
YGIEEHGK_311.5_599.3	CXA1_HUMAN	1.46
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	1.37
VFQFLEK_455.8_811.4	CO5_HUMAN	0.89
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.85
QINSYVK_426.2_496.3	CBG_HUMAN	0.56
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.53
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	0.39
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.26
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.24
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	-2.08
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-2.09
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-3.37

Table 26. Lasso 100 Middle-Late Window

Variable	UniProt_ID	Coefficient
VFQFLEK_455.8_811.4	CO5_HUMAN	3.82
SEYGAALAWEK_612.8_845.5	CO6_HUMAN_	2.94
YGIEEHGK_311.5_599.3	CXA1_HUMAN	2.39
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	2.05
TLAFVR_353.7_492.3	FA7_HUMAN	1.9
NQSPVLEPVGR_598.3_866.5	KS6A3_HUMAN	1.87
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	1.4
TQILEWAAER_608.8_761.4	EGLN_HUMAN	1.29
VVGGLVALR_442.3_784.5	FA12_HUMAN	1.24
QINSYVK_426.2_496.3	CBG_HUMAN	1.14
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.84
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.74
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.51
SLQNASAIESILK_687.4_860.5	IL3_HUMAN	0.44
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.38
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.37
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.3
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.19
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.19
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.15

(continued)

Variable	UniProt_ID	Coefficient
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	-0.09
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	-0.52
TSYQVYSK_488.2_787.4	C163A_HUMAN	-0.62
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	-1.29
TAHISGLPPSTDFIVYLSGLAPSIR_871.5_472.3	TENA_HUMAN	-1.53
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-1.73
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-1.95
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-2.9
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-3.04
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	-3.49
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	-3.71

Table 27. Lasso Protein Middle-LateWindow

Variable	UniProt_ID	Coefficient
VFQFLEK_455.8_811.4	CO5_HUMAN	4.25
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	3.06
YGIEEHGK_311.5_599.3	CXA1_HUMAN	2.36
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	2.11
TQILEWAAER_608.8_761.4	EGLN_HUMAN	1.81
NQSPVLEPVGR_598.3_866.5	KS6A3_HUMAN	1.79
TEQAAVAR_423.2_615.4	FA12_HUMAN	1.72
QINSYVK_426.2_496.3	CBG_HUMAN	0.98
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.98
NCSFSIIYPVVIK_770.4_555.4	CRHBP_HUMAN	0.76
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.63
SLQNASAIESILK_687.4_860.5	IL3_HUMAN	0.59
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.55
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.55
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.46
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.22
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.11
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.01
TSYQVYSK_488.2_787.4	C163A_HUMAN	-0.76
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	-1.31
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-1.59
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-1.73
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	-2.02

(continued)

Variable	UniProt_ID	Coefficient
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	-3
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	-3.15
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	-3.49
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	-3.82
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-4.94

Table 28. Lasso All Middle-LateWindow

Variable	UniProt_ID	Coefficient
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	2.38
TLAFVR_353.7_492.3	FA7_HUMAN	0.96
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.34
DPTFIPAPIQAK_433.2_461.2	ANGT_HUMAN	0.33
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	0.13
QINSYVK_426.2_496.3	CBG_HUMAN	0.03
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	-0.02
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-0.05
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	-0.12
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	-0.17
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	-0.31
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	-0.35
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-0.43
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-2.33

Table 29. Lasso 32 LateWindow

Variable	UniProt_ID	Coefficient
QINSYVK_426.2_610.3	CBG_HUMAN	3.24
ILDGGNK_358.7_603.3	CXCL5_HUMAN	2.65
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	2.55
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	2.12
YSHYNER_323.5_418.2	HABP2_HUMAN	1.63
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	1.22
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	0.96
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.86
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.45
TSYQVYSK_488.2_787.4	C163A_HUMAN	-1.73
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA HUMAN	-2.56

(continued)

Variable	UniProt_ID	Coefficient
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	-3.04
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-3.33
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	-4.24
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-5.83
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-6.52
AALAAFNAQNNGSNFQLEE!SR_789.1_746.4	FETUA_HUMAN	-6.55

Table 30: Lasso 100 Late Window

Variable	UniProt_ID	Coefficient
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	4.13
ILDGGNK_358.7_603.3	CXCL5_HUMAN	3.57
QINSYVK_426.2_610.3	CBG_HUMAN	3.41
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	1.64
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	1.57
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	1.45
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.71
YSHYNER_323.5_418.2	HABP2_HUMAN	0.68
FFQYDTWK_567.8_712.3	IGF2_HUMAN	0.42
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	0.36
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.21
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.1
VGVISFAQK_474.8_580.3	TFR2_HUMAN	0.08
TSYQVYSK_488.2_787.4	C163A_HUMAN	-0.36
ALNFGG!GVVVGHELTHAFDDQGR_837.1_360.2	ECE1_HUMAN	-0.65
AYSDLSR_406.2_375.2	SAMP_HUMAN	-1.23
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	-1.63
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	-2.29
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	-2.58
VPLALFALNR_557.3_620.4	PEPD_HUMAN	-2.73
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	-2.87
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	-3.9
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-5.29
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-5.51
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	-6.49

Table 31: Lasso Protein Late Window

Variable	UniProt_ID	Coefficient
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	3.33
ILDGGNK_358.7_603.3	CXCL5_HUMAN	3.25
QINSYVK_426.2_496.3	CBG_HUMAN	2.41
YSHYNER_323.5_418.2	HABP2_HUMAN	1.82
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	1.32
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	1.27
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.26
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	0.18
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.18
TSYQVYSK_488.2_787.4	C163A_HUMAN	-0.11
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	-0.89
AYSDLSR_406.2_375.2	SAMP_HUMAN	-1.47
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	-1.79
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	-2.22
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	-2.41
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	-2.94
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-5.18
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	-5.71
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-7.33

Table 32: Lasso All Late Window

Variable	UniProt_ID	Coefficient
QINSYVK_426.2_496.3	CBG_HUMAN	0.5
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	0.15
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.11
ILDGGNK_358.7_603.3	CXCL5_HUMAN	0.08
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.06
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	-0.39
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	-1.57
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	-2.46
AVYEAVLR_460.8_587.4	PEPD_HUMAN	-2.92

Table 33 : Random Forest 32 Early Window

Variable	Protein	MeanDecreaseGini
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	3.224369171
AHYDLR_387.7_288.2	FETUA_HUMAN	1.869007658
FSVVYAK_407.2_381.2	FETUA_HUMAN	1.770198171

(continued)

Variable	Protein	MeanDecreaseGini
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	1.710936472
ITGFLKPGK_320.9_301.2	LBP_HUMAN	1.623922439
ITGFLKPGK_320.9_429.3	LBP_HUMAN	1.408035272
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	1.345412168
VFQFLEK_455.8_811.4	CO5_HUMAN	1.311332013
VQTAHFK_277.5_431.2	CO8A_HUMAN	1.308902373
FLNWIK_410.7_560.3	HABP2_HUMAN	1.308093745
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	1.297033607
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	1.291280928
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	1.28622301
QALEEFQK_496.8_680.3	CO8B_HUMAN	1.191731825
FSVVYAK_407.2_579.4	FETUA_HUMAN	1.078909138
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	1.072613747
AHYDLR_387.7_566.3	FETUA_HUMAN	1.029562263
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	1.00992071
DVLLLVHNLPQNLPGYFWYK_810.4_967.5	PSG9_HUMAN	1.007095529
SFRPFVPR_335.9_635.3	LBP_HUMAN	0.970312536
SDLEVAHYK_531.3_617.3	CO8B_HUMAN	0.967904893
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	0.960398254
VFQFLEK_455.8_276.2	CO5_HUMAN	0.931652095
SLLQPNK_400.2_599.4	CO8A_HUMAN	0.926470249
SFRPFVPR_335.9_272.2	LBP_HUMAN	0.911599611
FLNWIK_410.7_561.3	HABP2_HUMAN	0.852022868
LSSPAVITDK_515.8_743.4	PLMN_HUMAN	0.825455824
DVLLLVHNLPQNLPGYFWYK_810.4_594.3	PSG9_HUMAN	0.756797142
ALVLELAK_428.8_672.4	INHBE_HUMAN	0.748802555
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.733731518

Table 34. Random Forest 100 Early Window

Variable	Protein	MeanDecreaseGini
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	1.709778508
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	0.961692716
AHYDLR_387.7_288.2	FETUA_HUMAN	0.901586746
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	0.879119498
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN	0.842483095
ITGFLKPGK_320.9_301.2	LBP_HUMAN	0.806905233
FSVVYAK_407.2_381.2	FETUA_HUMAN	0.790429706

(continued)

Variable	Protein	MeanDecreaseGini
ITGFLKPGK_320.9_429.3	LBP_HUMAN	0.710312386
VFQFLEK_455.8_811.4	CO5_HUMAN	0.709531553
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	0.624325189
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	0.618684313
FLNWIK_410.7_560.3	HABP2_HUMAN	0.617501242
TASDFITK_441.7_781.4	GELS_HUMAN	0.609275999
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	0.588718595
VQTAHFK_277.5_431.2	CO8A_HUMAN	0.58669845
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	0.5670608
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	0.555624783
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.537678415
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.535543137
TASDFITK_441.7_710.4	GELS_HUMAN	0.532743323
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	0.51667902
QALEEFQK_496.8_680.3	CO8B_HUMAN	0.511314017
AVLHIGEK_289.5_348.7	THBG_HUMAN	0.510284122
FSVVYAK_407.2_579.4	FETUA_HUMAN	0.503907813
LPNNVLQEK_527.8_730.4	AFAM_HUMAN	0.501281631
AHYDLR_387.7_566.3	FETUA_HUMAN	0.474166711
IAPQLSTEELVSLGEK_857.5_333.2	AFAM_HUMAN	0.459595701
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.44680777
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.434157773
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.432484862

Table 35. Random Forest Protein Early Window

Variable	Protein	MeanDecreaseGini
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	2.881452809
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	1.833987752
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	1.608843881
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN	1.594658208
VFQFLEK_455.8_811.4	CO5_HUMAN	1.290134412
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	1.167981736
TASDFITK_441.7_781.4	GELS_HUMAN	1.152847453
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	1.146752656
FSVVYAK_407.2_579.4	FETUA_HUMAN	1.060168583
AVLHIGEK_289.5_348.7	THBG_HUMAN	1.033625773
FLNWIK_410.7_560.3	HABP2_HUMAN	1.022356789

(continued)

Variable	Protein	MeanDecreaseGini
QALEEFQK_496.8_680.3	CO8B_HUMAN	0.990074129
DVLLLVHNLPQNLPGYFWYK_810.4_967.5	PSG9_HUMAN	0.929633865
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.905895642
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	0.883887371
NNQLVAGYLQGPNVNLEEK_700.7_999.5	IL1RA_HUMAN	0.806472085
SLLQPNK_400.2_599.4	CD8A_HUMAN	0.783623222
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	0.774365756
NIQSVNVK_451.3_674.4	GROA_HUMAN	0.767963386
HPWIVHWDQLPQYQLNR_744.0_1047.0	KS6A3_HUMAN	0.759960139
TTSDGGYSFK_531.7_860.4	INHA_HUMAN	0.732813448
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.718779092
LSSPAVITDK_515.8_743.4	PLMN_HUMAN	0.699547739
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.693159192
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.647300964
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.609165621
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	0.60043345
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	0.596079858
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	0.579034994
ALVLELAK_428.8_672.4	INHBE_HUMAN	0.573458483

Table 36. Random Forest All Early Window

Variable	Protein	MeanDecreaseGini
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	0.730972421
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	0.409808774
AHYDLR_387.7_288.2	FETUA_HUMAN	0.409298983
FSVVYAK_407.2_381.2	FETUA_HUMAN	0.367730833
ITGFLKPGK_320.9_301.2	LBP_HUMAN	0.350485117
VFQFLEK_455.8_811.4	CO5_HUMAN	0.339289475
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	0.334303166
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	0.329800706
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN	0.325596677
ITGFLKPGK_320.9_429.3	LBP_HUMAN	0.31473104
FLNWIK_410.7_560.3	HABP2_HUMAN	0.299810081
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	0.295613448
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	0.292212699
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	0.285812225
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	0.280857718

(continued)

Variable	Protein	MeanDecreaseGini
FSVVYAK_407.2_579.4	FETUA_HUMAN	0.278531322
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	0.258938798
AHYDLR_387.7_566.3	FETUA_HUMAN	0.256160046
QALEEFQK_496.8_680.3	CO8B_HUMAN	0.245543641
HTLNQIDEVK_598.8_951.5	FETUA_HUMAN	0.239528081
TASDFITK_441.7_781.4	GELS_HUMAN	0.227485958
VFQFLEK_455.8_276.2	CO5_HUMAN	0.226172392
DVLLLVHNLPQNLPGYFWYK_810.4_967.5	PSG9_HUMAN	0.218613384
VQTAHFK_277.5_431.2	CO8A_HUMAN	0.217171548
SFRPFVPR_335.9_635.3	LBP_HUMAN	0.214798112
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.211756476
SVSLPSLDPASAK_636.4_473.3	APOB_HUMAN	0.211319422
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.206574494
HFQNLGK_422.2_285.1	AFAM_HUMAN	0.204024196
AVLHIGEK_289.5_348.7	THBG_HUMAN	0.201102917

Table 37. Random Forest SummedGini Early Window

Transition	Protein	SumBestGini
ELIEELVNITQNQK_557.6_517.3	IL13_HUMAN	242.5373659
VFQFLEK_455.8_811.4	CO5_HUMAN	115.1113943
FLNWIK_410.7_560.3	HABP2_HUMAN	107.4572447
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	104.0742727
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN	103.3238077
DAGLSWGSAR_510.3_390.2	NEUR4_HUMAN	70.4151533
AHYDLR_387.7_288.2	FETUA_HUMAN	140.2670822
FSVVYAK_407.2_381.2	FETUA_HUMAN	121.3664352
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	115.5211679
ITGFLKPGK_320.9_429.3	LBP_HUMAN	114.9512704
ITGFLKPGK_320.9_301.2	LBP_HUMAN	112.916627
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN	52.21169288
VQTAHFK_277.5_431.2	CO8A_HUMAN	144.5237215
TLLPVSKPEIR_418.3_288.2	CO5_HUMAN	96.16982897
QALEEFQK_496.8_680.3	CO8B_HUMAN	85.35050759
FSVVYAK_407.2_579.4	FETUA_HUMAN	73.23969945
ELIEELVNITQNQK_557.6_618.3	IL13_HUMAN	61.61450671
TASDFITK_441.7_781.4	GELS_HUMAN	61.32155633
DVLLLVHNLPQNLPGYFWYK_810.4_967.5	PSG9_HUMAN	99.68404123

(continued)

Transition	Protein	SumBestGini
AVLHIGEK_289.5_348.7	THBG_HUMAN	69.96748485
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	56.66810872
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	56.54173176
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	47.92505575
DADPDTFFAK_563.8_825.4	AFAM_HUMAN	40.34147696
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	145.0311483
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	109.4072996
FLPCENK_454.2_550.2	IL10_HUMAN	105.7756691
VQTAHFK_277.5_502.3	CO8A_HUMAN	101.5877845
VFQFLEK_455.8_276.2	CO5_HUMAN	95.71159157
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	94.92157517
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	90.67568777
NKPGVYTDVAYYLAWIR_677.0_545.3	FA12_HUMAN	90.35890105
LEEHYELR_363.5_580.3	PAI2_HUMAN	88.44833508
HPWIVHWDQLPQYQLNR_744.0_1047.0	KS6A3_HUMAN	88.37680942
HTLNQIDEVK_598.8_951.5	FETUA_HUMAN	87.63064143
LPNNVLQEK_527.8_730.4	AFAM_HUMAN	86.64484642
ALDLSLK_380.2_575.3	ITIH3_HUMAN	83.51201287
YGIEEHGK_311.5_599.3	CXA1_HUMAN	82.47620831
LSSPAVITDK_515.8_830.5	PLMN_HUMAN	81.5433587
LEEHYELR_363.5_288.2	PAI2_HUMAN	79.01571985
NVIQISNDLENLR_509.9_402.3	LEP_HUMAN	78.86670236
SGFSFGFK_438.7_732.4	CO8B_HUMAN	78.71961929
SDLEVAHYK_531.3_617.3	CO8B_HUMAN	78.24005567
NADYSYSVWK_616.8_333.2	CO5_HUMAN	76.07974354
AHYDLR_387.7_566.3	FETUA_HUMAN	74.68253347
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	73.75860248
LIENGYFHPVK_439.6_627.4	F13B_HUMAN	73.74965194
ALDLSLK_380.2_185.1	ITIH3_HUMAN	72.760739
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	72.51936706
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	72.49183198
GLQYAAQEGLLALQSELLR_1037.1_929.5	LBP_HUMAN	67.17588648
HFQNLGK_422.2_527.2	AFAM_HUMAN	66.11702719
YSHYNER_323.5_581.3	HABP2_HUMAN	65.56238612
ISQGEADINIAFYQR_575.6_684.4	MMP8_HUMAN	65.50301246
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	64.85259525
NIQSVNVK_451.3_674.4	GROA_HUMAN	64.53010225
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	64.12149927

(continued)

Transition	Protein	SumBestGini
SLLQPNK_400.2_599.4	CO8A_HUMAN	62.68167847
SFRPFVPR_335.9_635.3	LBP_HUMAN	61.90157662
NNQLVAGYLQGPNVNLEEK_700.7_999.5	IL1RA_HUMAN	61.54435815
LYYGDDEK_501.7_563.2	CO8A_HUMAN	60.16700473
SWNEPLYHLVTEVR_581.6_716.4	PRL_HUMAN	59.78209065
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	58.93982896
GTYLYNDCPGPGQDTDCR_697.0_335.2	TNR1A_HUMAN	58.72963941
HATLSLSIPR_365.6_472.3	VGFR3_HUMAN	57.98669834
FIVGFTR_420.2_261.2	CCL20_HUMAN	57.23165578
QNYHQDSEAAINR_515.9_544.3	FRIH_HUMAN	57.21116697
DVLLLVHNLPQNLPGYFWYK_810.4_594.3	PSG9_HUMAN	56.84150484
FLNWIK_410.7_561.3	HABP2_HUMAN	56.37258274
SLQAFVAVAAR_566.8_487.3	IL23A_HUMAN	56.09012981
HFQNLGK_422.2_285.1	AFAM_HUMAN	56.04480022
GPGEDFR_389.2_322.2	PTGDS_HUMAN	55.7583763
NKPGVYTDVAYYLAWIR_677.0_821.5	FA12_HUMAN	55.53857645
LIQDAVTGLTVNGQITGDK_972.0_640.4	ITIH3_HUMAN	55.52577583
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	54.27147366
TLNAYDHR_330.5_312.2	PAR3_HUMAN	54.19190934
IQTHSTTYR_369.5_627.3	F13B_HUMAN	54.18950583
TASDFITK_441.7_710.4	GELS_HUMAN	54.1056456
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	53.8997252
DADPDTFFAK_563.8_302.1	AFAM_HUMAN	53.85914848
SVSLPSLDPASAK_636.4_473.3	APOB_HUMAN	53.41996191
TTSDGGYSFK_531.7_860.4	INHA_HUMAN	52.24655536
AFTECCVVASQLR_770.9_574.3	CO5_HUMAN	51.67853429
ELPQSIVYK_538.8_409.2	FBLN3_HUMAN	51.35853002
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	51.23842124
FQLSETNR_497.8_605.3	PSG2_HUMAN	51.01576848
GSLVQASEANLQAAQDFVR_668.7_806.4	ITIH1_HUMAN	50.81923338
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	50.54425114
ECEELEEK_533.2_405.2	IL15_HUMAN	50.41977421
NADYSYSVWK_616.8_769.4	CO5_HUMAN	50.36434595
SLLQPNK_400.2_358.2	CO8A_HUMAN	49.75593162
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	49.43389721
DISEVVTPR_508.3_787.4	CFAB_HUMAN	49.00234897
AEVIWTSSDHQVLSGK_586.3_300.2	PD1L1_HUMAN	48.79028835
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	48.70665587

(continued)

Transition	Protein	SumBestGini
SILFLGK_389.2_201.1	THBG_HUMAN	48.5997957
AVLHIGEK_289.5_292.2	THBG_HUMAN	48.4605866
QLYGDTGVLGR_589.8_501.3	CO8G_HUMAN	48.11414904
FSLVSGWGQLLDR_493.3_516.3	FA7_HUMAN	47.59635333
DSPVLIDFFEDTER_841.9_399.2	HRG_HUMAN	46.83840473
INPASLDK_429.2_630.4	C163A_HUMAN	46.78947931
GAVHVVVAETDYQSFAVLYLER_822.8_863.5	CO8G_HUMAN	46.66185339
FLQEQGHR_338.8_497.3	CO8G_HUMAN	46.64415952
LNIGYIEDLK_589.3_837.4	PAI2_HUMAN	46.5879123
LSSPAVITDK_515.8_743.4	PLMN_HUMAN	46.2857838
GLQYAAQEGLLALQSELLR_1037.1_858.5	LBP_HUMAN	45.7427767
SDGAKPGPR_442.7_213.6	COLI_HUMAN	45.27828366
GYQELLEK_490.3_502.3	FETA_HUMAN	43.52928868
GGEGTGYFVDFSVR_745.9_869.5	HRG_HUMAN	43.24514327
ADLFYDVEALDLESPK_913.0_447.2	HRG_HUMAN	42.56268679
ADLFYDVEALDLESPK_913.0_331.2	HRG_HUMAN	42.48967422
EAQLPVIENK_570.8_699.4	PLMN_HUMAN	42.21213429
SILFLGK_389.2_577.4	THBG_HUMAN	42.03379581
HTLNQIDEVK_598.8_958.5	FETUA_HUMAN	41.98377176
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	41.89547273
FLPCENK_454.2_390.2	IL10_HUMAN	41.66612478
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	41.50878046
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	41.27830935
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	41.00430596
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	40.90053801
SLPVSDSVLSGFEQR_810.9_836.4	CO8G_HUMAN	40.62020941
DGSPDVTTADIGANTPDATK_973.5_531.3	PGRP2_HUMAN	40.33913091
NTGVISVVTTGLDR_716.4_662.4	CADH1_HUMAN	40.05291612
ALVLELAK_428.8_672.4	INHBE_HUMAN	40.01646465
YEFLNGR_449.7_293.1	PLMN_HUMAN	39.83344278
WGAAPYR_410.7_577.3	PGRP2_HUMAN	39.52766213
TFLTVYWTPER_706.9_401.2	ICAM1_HUMAN	39.13662034
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	38.77511119
VGVISFAQK_474.8_693.4	TFR2_HUMAN	38.5823457
IIEVEEEQEDPYLNDR_996.0_777.4	FBLN1_HUMAN	38.30913304
TGYYFDGISR_589.8_694.4	FBLN1_HUMAN	38.30617106
LQGTLPVEAR_542.3_571.3	CO5_HUMAN	37.93064544
DSPVLIDFFEDTER_841.9_512.3	HRG_HUMAN	37.4447737

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Transition	Protein	SumBestGini
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	37.02483715
DGSPDVTTADIGANTPDATK_973.5_844.4	PGRP2_HUMAN	36.59864788
ILILPSVTR_506.3_785.5	PSGx_HUMAN	36.43814815
SVSLPSLDPASAK_636.4_885.5	APOB_HUMAN	36.27689491
TLAFVR_353.7_492.3	FA7_HUMAN	36.18771771
VAPGVANPGTPLA_582.3_555.3	A6NIT4_HUMAN	35.70677357
HELTDEELQSLFTNFANVVDK_817.1_906.5	AFAM_HUMAN	35.14441609
AGLLRPDYALLGHR_518.0_369.2	PGRP2_HUMAN	35.13047098
GDTYPAELYITGSILR_885.0_1332.8	F13B_HUMAN	34.97832404
LFIPQITR_494.3_727.4	PSG9_HUMAN	34.76811249
GYQELLEK_490.3_631.4	FETA_HUMAN	34.76117605
VSEADSSNADWVTK_754.9_533.3	CFAB_HUMAN	34.49787512
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	34.48448691
SFRPFVPR_335.9_272.2	LBP_HUMAN	34.27529415
ILDGGNK_358.7_490.2	CXCL5_HUMAN	34.2331388
EANQSTLENFLER_775.9_678.4	IL4_HUMAN	34.14295797
DFNQFSSGEK_386.8_189.1	FETA_HUMAN	34.05459951
IEEIAAK_387.2_660.4	CO5_HUMAN	33.93778148
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	33.87864446
LPATEKPVLLSK_432.6_347.2	HYOU1_HUMAN	33.69005522
FLQEQGHR_338.8_369.2	CO8G_HUMAN	33.61179024
APLTKPLK_289.9_357.2	CRP_HUMAN	33.59900279
YSHYNER_323.5_418.2	HABP2_HUMAN	33.50888447
TSYQVYSK_488.2_787.4	C163A_HUMAN	33.11650018
IALGGLLFPASNLR_481.3_657.4	SHBG_HUMAN	33.02974341
TGISPLALIK_506.8_741.5	APOB_HUMAN	32.64471573
LYYGDDEK_501.7_726.3	CO8A_HUMAN	32.60782458
IVLSLDVPIGLLQILLEQAR_735.1_503.3	UCN2_HUMAN	32.37907686
EAQLPVIENK_570.8_329.2	PLMN_HUMAN	32.34049256
TGYYFDGISR_589.8_857.4	FBLN1_HUMAN	32.14526507
VGVISFAQK_474.8_580.3	TFR2_HUMAN	32.11753213
FQSVFTVTR_542.8_623.4	C1QC_HUMAN	32.11360444
TSDQIHFFFAK_447.6_659.4	ANT3_HUMAN	31.95867038
IAPQLSTEELVSLGEK_857.5_333.2	AFAM_HUMAN	31.81531364
EVFSKPISWEELLQ_852.9_260.2	FA40A_HUMAN	31.36698726
DEIPHNDIALLK_459.9_260.2	HABP2_HUMAN	31.1839869
NYFTSVAHPNLFIATK_608.3_319.2	IL1A_HUMAN	31.09867061
ITENDIQIALDDAK_779.9_632.3	APOB_HUMAN	30.77026845

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Transition	Protein	SumBestGini
DTYVSSFPR_357.8_272.2	TCEA1_HUMAN	30.67784731
TDAPDLPEENQAR_728.3_843.4	CO5_HUMAN	30.66251941
LFYADHPFIFLVR_546.6_647.4	SERPH_HUMAN	30.65831566
TEQAAVAR_423.2_487.3	FA12_HUMAN	30.44356842
AVGYLITGYQR_620.8_737.4	PZP_HUMAN	30.36425528
HSHESQDLR_370.2_288.2	HRG_HUMAN	30.34684703
IALGGLLFPASNLR_481.3_412.3	SHBG_HUMAN	30.34101643
IAQYYYTFK_598.8_884.4	F13B_HUMAN	30.23453833
SLPVSDSVLSGFEQR_810.9_723.3	CO8G_HUMAN	30.11396489
IIGGSDADIK_494.8_762.4	C1S_HUMAN	30.06572687
QTLSWTVTPK_580.8_545.3	PZP_HUMAN	30.04139865
HYFIAAVER_553.3_658.4	FA8_HUMAN	29.80239884
QVCADPSEEWVQK_788.4_374.2	CCL3_HUMAN	29.61435573
DLHLSDVFLK_396.2_366.2	CO6_HUMAN	29.60077507
NIQSVNVK_451.3_546.3	GROA_HUMAN	29.47619619
QTLSWTVTPK_580.8_818.4	PZP_HUMAN	29.40047934
HSHESQDLR_370.2_403.2	HRG_HUMAN	29.32242262
LLEVPEGR_456.8_356.2	C1S_HUMAN	29.14169137
LIENGYFHPVK_439.6_343.2	F13B_HUMAN	28.63056809
EDTPNSVWEPAK_686.8_630.3	C1S_HUMAN	28.61352686
AFTECCVVASQLR_770.9_673.4	CO5_HUMAN	28.57830281
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	28.27203693
VSFSSPLVAISGVALR_802.0_715.4	PAPP1_HUMAN	28.13008712
DPDQTDGLGLSYLSSHIANVER_796.4_456.2	GELS_HUMAN	28.06549895
VVGGLVALR_442.3_784.5	FA12_HUMAN	28.00684006
NEIVFPAGILQAPFYTR_968.5_357.2	ECE1_HUMAN	27.97758456
QVCADPSEEWVQK_788.4_275.2	CCL3_HUMAN	27.94276837
LQDAGVYR_461.2_680.3	PD1L1_HUMAN	27.88063261
IQTHSTTYR_369.5_540.3	F13B_HUMAN	27.68873826
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	27.66889639
ALALPPLGLAPLLNLWAKPQGR_770.5_256.2	SHBG_HUMAN	27.63105727
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	27.63097319
IEEIAAK_387.2_531.3	CO5_HUMAN	27.52427934
TAVTANLDIR_537.3_288.2	CHL1_HUMAN	27.44246841
VSEADSSNADWVTK_754.9_347.2	CFAB_HUMAN	27.43976782
ITENDIQIALDDAK_779.9_873.5	APOB_HUMAN	27.39263522
SSNNPHSPIVEEFQVPYNK_729.4_521.3	C1S_HUMAN	27.34493617
HPWIVHWDQLPQYQLNR_744.0_918.5	KS6A3_HUMAN	27.19681613

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Transition	Protein	SumBestGini
TPSAAYLWVGTGASEAEK_919.5_428.2	GELS_HUMAN	27.17319953
AFLEVNEEGSEAAASTAVVIAGR_764.4_614.4	ANT3_HUMAN	27.10487351
WGAAPYR_410.7_634.3	PGRP2_HUMAN	27.09930054
IEVNESGTVASSSTAVIVSAR_693.0_545.3	PAI1_HUMAN	27.02567296
AEAQAQYSAAVAK_654.3_908.5	ITIH4_HUMAN	26.98305259
VPLALFALNR_557.3_917.6	PEPD_HUMAN	26.96988826
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	26.94672621
QALEEFQK_496.8_551.3	CO8B_HUMAN	26.67037155
WNFAYWAAHQPWSR_607.3_545.3	PRG2_HUMAN	26.62600679
IYLQPGR_423.7_570.3	ITIH2_HUMAN	26.58752589
FFQYDTWK_567.8_840.4	IGF2_HUMAN	26.39942037
NEIWYR_440.7_357.2	FA12_HUMAN	26.35177282
GGEGTGYFVDFSVR_745.9_722.4	HRG_HUMAN	26.31688167
VGEYSLYIGR_578.8_708.4	SAMP_HUMAN	26.17367498
TAHISGLPPSTDFIVYLSGLAPSIR_871.5_800.5	TENA_HUMAN	26.13688183
GVTGYFTFNLYLK_508.3_260.2	PSG5_HUMAN	26.06007032
DYWSTVK_449.7_620.3	APOC3_HUMAN	26.03765187
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	25.9096605
YGLVTYATYPK_638.3_334.2	CFAB_HUMAN	25.84440452
LFIPQITR_494.3_614.4	PSG9_HUMAN	25.78081129
YEFLNGR_449.7_606.3	PLMN_HUMAN	25.17159874
SEPRPGVLLR_375.2_454.3	FA7_HUMAN	25.16444381
NSDQEIDFK_548.3_294.2	S10A5_HUMAN	25.12266401
YEVQGEVFTKPQLWP_911.0_293.1	CRP_HUMAN	24.77595195
GVTGYFTFNLYLK_508.3_683.9	PSG5_HUMAN	24.75289081
ISLLLIESWLEPVR_834.5_371.2	CSH_HUMAN	24.72379326
ALLLGWVPTR_563.3_373.2	PAR4_HUMAN	24.68096599
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	24.53420489
SGAQATWTELPWPHEK_613.3_793.4	HEMO_HUMAN	24.25610995
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	24.18769142
DLPHITVDR_533.3_490.3	MMP7_HUMAN	24.02606052
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	24.00163743
AVGYLITGYQR_620.8_523.3	PZP_HUMAN	23.93958524
GFQALGDAADIR_617.3_717.4	TIMP1_HUMAN	23.69249513
YEVQGEVFTKPQLWP_911.0_392.2	CRP_HUMAN	23.67764212
SDGAKPGPR_442.7_459.2	COLI_HUMAN	23.63551614
GFQALGDAADIR_617.3_288.2	TIMP1_HUMAN	23.55832742
IAPQLSTEELVSLGEK_857.5_533.3	AFAM_HUMAN	23.38139357

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Transition	Protein	SumBestGini
DTDTGALLFIGK_625.8_217.1	PEDF_HUMAN	23.33375418
LHEAFSPVSYQHDLALLR_699.4_380.2	FA12_HUMAN	23.27455931
IYLQPGR_423.7_329.2	ITIH2_HUMAN	23.19122626

Table 38. Random Forest 32 Middle Window

Variable	UniProt_ID	MeanDecreaseGini
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	2.27812193
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	2.080133179
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	1.952233942
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	1.518833357
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	1.482593086
VFQFLEK_455.8_811.4	CO5_HUMAN	1.448810425
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	1.389922815
YGIEEHGK_311.5_599.3	CXA1_HUMAN	1.386794676
TLAFVR_353.7_492.3	FA7_HUMAN	1.371530925
VLEPTLK_400.3_587.3	VTDB_HUMAN	1.368583173
VLEPTLK_400.3_458.3	VTDB HUMAN	1.336029064
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	1.307024357
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	1.282930911
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	1.25362163
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	1.205539225
VEHSDLSFSK_383.5_468.2	B2MG_HUMAN	1.201047302
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	1.189617326
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	1.120706696
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	1.107036657
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	1.083264902
IEEIAAK_387.2_660.4	CO5_HUMAN	1.043635292
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.962643698
TLLPVSKPEIR_418.3_514.3	CO5_HUMAN	0.933440467
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.878933553
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.816855601
ALQDQLVLVAAK_634.9_289.2	ANGT_HUMAN	0.812620232
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	0.792274782
QGH_NSVFLIK_381.6_260.2	HEMO_HUMAN	0.770830031
ALQDQLVLVAAK_634.9_956.6	ANGT_HUMAN	0.767468246
SLDFTELDVAAEK_719.4_874.5	ANGT_HUMAN	0.745827911

Table 39. Random Forest 100 Middle Window

Variable	UniProt_ID	MeanDecreaseGini
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	1.241568411
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.903126414
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	0.846216563
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.748261193
VFQFLEK_455.8_811.4	CO5_HUMAN	0.717545171
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	0.683219617
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.671091545
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	0.652293621
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.627095631
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	0.625773888
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.613655529
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.576305627
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	0.574056825
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.570270447
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.556087614
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.531461012
VEHSDLSFSK_383.5_468.2	B2MG_HUMAN	0.531214597
TLAFVR_353.7_492.3	FA7_HUMAN	0.53070743
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.521633041
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.514509661
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.50489698
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.4824926
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.48217238
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.472286273
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.470892051
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.465839813
GEVTYTTSQVSK_650.3_750.4	EGLN_HUMAN	0.458736205
VNHVTLSQPK_374.9_459.3	B2MG_HUMAN	0.454348892
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.45127405
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.430641646

Table 40. Random Forest Protein Middle Window

Variable	UniProt_ID	MeanDecreaseGini
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	2.09649626
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	1.27664656
VFQFLEK_455.8_811.4	CO5_HUMAN	1.243884833
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	1.231814882

(continued)

Variable	UniProt_ID	MeanDecreaseGini
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	1.188808078
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	1.185075445
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	1.122351536
VLEPTLK_400.3_458.3	VTDB_HUMAN	1.062664798
VPLALFALNR_557.3_620.4	PEPD_HUMAN	1.019466776
TLAFVR_353.7_492.3	FA7_HUMAN	0.98797064
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	0.980159531
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.960286027
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.947091926
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.946937719
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.916262164
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.891310053
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.884498494
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.869043942
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.865435217
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.844842109
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.792615068
DVLLLVHNLPQNLTGHIWYK_791.8_310.2	PSG7_HUMAN	0.763629346
GPITSAAELNDPQSILLR_632.4_826.5	EGLN_HUMAN	0.762305265
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4	SHBG_HUMAN	0.706312721
SLQNASAIESILK_687.4_860.5	IL3_HUMAN	0.645503581
HYINLITR_515.3_301.1	NPY_HUMAN	0.62631682
VELAPLPSWQPVGK_760.9_342.2	ICAM1_HUMAN	0.608991877
LQVNTPLVGASLLR_741.0_925.6	BPIA1_HUMAN	0.607801279
TLEAQLTPR_514.8_814.4	HEP2_HUMAN	0.597771074
SDGAKPGPR_442.7_459.2	COLI_HUMAN	0.582773073

Table 41. Random Forest All Middle Window

Variable	UniProt_ID	MeanDecreaseGini
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.493373282
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.382180772
VFQFLEK_455.8_811.4	CO5_HUMAN	0.260292083
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	0.243156718
NADYSYSVWK_616.8_769.4	CO5_HUMAN	0.242388196
VLEPTLK_400.3_458.3	VTDB_HUMAN	0.238171849
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	0.236873731
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.224727161

(continued)

Variable	UniProt_ID	MeanDecreaseGini
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.222105614
TLFIFGVTK_513.3_811.5	PSG4_HUMAN	0.210807574
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.208714978
LNIGYIEDLK_589.3_950.5	PAI2_HUMAN	0.208027555
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.197362212
VNHVTLSQPK_374.9_244.2	B2MG_HUMAN	0.195728091
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.189969499
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.189572857
AGITIPR_364.2_486.3	IL17_HUMAN	0.188351054
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.185069517
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	0.173688295
TLAFVR_353.7_492.3	FA7_HUMAN	0.170636045
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.170608352
TLLIANETLR_572.3_703.4	IL5_HUMAN	0.16745571
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.161514946
LHEAFSPVSYQHDLALLR_699.4_251.2	FA12_HUMAN	0.15852146
DGSPDVTTADIGANTPDATK_973.5_844.4	PGRP2_HUMAN	0.154028378
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.153725879
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.150920884
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.150319671
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.144781622
IEEIAAK_387.2_660.4	CO5_HUMAN	0.141983196

Table 42. Random Forest 32 Middle-Late Window

Variable	UniProt_ID	MeanDecreaseGini
VPLALFALNR_557.3_620.4	PEPD_HUMAN	4.566619475
VFQFLEK_455.8_811.4	CO5_HUMAN	3.062474666
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	3.033740627
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	2.825082394
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	2.787777983
TLAFVR_353.7_492.3	FA7_HUMAN	2.730532075
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	2.671290375
AVYEAVLR_460.8_587.4	PEPD_HUMAN	2.621357053
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	2.57568964
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	2.516708906
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	2.497348374
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	2.457401462

(continued)

Variable	UniProt_ID	MeanDecreaseGini
YGIEEHGK_311.5_599.3	CXA1_HUMAN	2.396824268
VLEPTLK_400.3_587.3	VTDB_HUMAN	2.388105564
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	2.340473883
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	2.332007976
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	2.325669514
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	2.31761671
QINSYVK_426.2_496.3	CBG_HUMAN	2.245221163
QINSYVK_426.2_610.3	CBG_HUMAN	2.212307699
TEQAAVAR_423.2_615.4	FA12_HUMAN	2.105860336
AVYEAVLR_460.8_750.4	PEPD_HUMAN	2.098321893
TEQAAVAR_423.2_487.3	FA12_HUMAN	2.062684763
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	2.05160689
SLQAFVAVAAR_566.8_804.5	IL23A_HUMAN	1.989521006
SLDFTELDVAAEK_719.4_316.2	ANGT_HUMAN	1.820628782
DPTFIPAPIQAK_433.2_556.3	ANGT_HUMAN	1.763514326
DPTFIPAPIQAK_433.2_461.2	ANGT_HUMAN	1.760870392
VLEPTLK_400.3_458.3	VTDB_HUMAN	1.723389354
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	1.63355187

Table 43. Random Forest 100 Middle-Late Window

Variable	UniProt_ID	MeanDecreaseGini
VPLALFALNR_557.3_620.4	PEPD_HUMAN	1.995805024
VFQFLEK_455.8_811.4	CO5_HUMAN	1.235926416
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	1.187464899
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	1.166642578
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	1.146077071
TLAFVR_353.7_492.3	FA7_HUMAN	1.143038275
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	1.130656591
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	1.098305298
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	1.096715712
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	1.086171713
YGIEEHGK_311.5_341.2	CXA1_HUMAN	1.071880823
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	1.062278869
TQILEWAAER_608.8_761.4	EGLN_HUMAN	1.059019017
AVYEAVLR_460.8_587.4	PEPD_HUMAN	1.057920661
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	1.038388955
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	1.028275728

(continued)

Variable	UniProt_ID	MeanDecreaseGini
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	1.026032369
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	1.015065282
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.98667651
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.970330675
DVLLLVHNLPQNLTGHIWYK_791.8_883.0	PSG7_HUMAN	0.934747674
TAHISGLPPSTDFIVYLSGLAPSIR_871.5_472.3	TENA_HUMAN	0.889111923
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.887605636
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.884305889
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.880889836
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.863585472
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.849232356
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.843334824
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.842319271
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.828959173

Table 44. Random Forest Protein Middle-Late Window

Variable	UniProt_ID	MeanDecreaseGini
VPLALFALNR_557.3_620.4	PEPD_HUMAN	3.202123047
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	2.100447309
VFQ.FLEK_455.8_811.4	CO5_HUMAN	2.096157529
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	2.052960939
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	2.046139797
TQILEWAAER_608.8_761.4	EGLN_HUMAN	1.99287941
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	1.920894959
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	1.917665697
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	1.883557705
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	1.870232155
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	1.869000136
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	1.825457092
VLEPTLK_400.3_587.3	VTDB_HUMAN	1.695327774
TEQAAVAR_423.2_615.4	FA12_HUMAN	1.685013152
LLAPSDSPEWLSFDVTGVVR_730.1_430.3	TGFB1_HUMAN	1.684068039
TLNAYDHR_330.5_312.2	PAR3_HUMAN	1.673758239
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	1.648896853
DVLLLVHNLPQNLTGHIWYK_791.8_883.0	PSG7_HUMAN	1.648146088
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	1.645833005
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	1.639121965

(continued)

Variable	UniProt_ID	MeanDecreaseGini
AGLLRPDYALLGHR_518.0_595.4	PGRP2_HUMAN	1.610227875
YGIEEHGK_311.5_599.3	CXA1_HUMAN	1.606978339
QINSYVK_426.2_496.3	CBG_HUMAN	1.554905578
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	1.484081016
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	1.43173022
AEVIWTSSDHQVLSGK_586.3_300.2	PD1L1_HUMAN	1.394857397
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	1.393464547
DFNQFSSGEK_386.8_333.2	FETA_HUMAN	1.374296237
TSYQVYSK_488.2_787.4	C163A_HUMAN	1.36141387
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	1.311118611

Table 45. Random Forest All Middle-Late Window

Variable	UniProt_ID	MeanDecreaseGini
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.685165163
VFQFLEK_455.8_811.4	CO5_HUMAN	0.426827804
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.409942379
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.406589512
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.402152062
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN	0.374861014
ANLINNIFELAGLGK_793.9_299.2	LCAP_HUMAN	0.367089422
TQILEWAAER_608.8_761.4	EGLN_HUMAN	0.353757524
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.350518668
TLAFVR_353.7_492.3	FA7_HUMAN	0.344669505
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.338752336
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.321850027
ELPQSIVYK_538.8_417.7	FBLN3_HUMAN	0.301819017
EVFSKPISWEELLQ_852.9_376.2	FA40A_HUMAN	0.299561811
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.298253589
VLEPTLK_400.3_587.3	VTDB_HUMAN	0.296206088
YGIEEHGK_311.5_599.3	CXA1_HUMAN	0.295621408
DVLLLVHNLPQNLTGHIWYK_791.8_883.0	PSG7_HUMAN	0.292937475
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.275902848
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.275664578
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.27120436
AVDIPGLEAATPYR_736.9_399.2	TENA_HUMAN	0.266568271
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.262537889
TLNAYDHR_330.5_312.2	PAR3_HUMAN	0.259901193

(continued)

Variable	UniProt_ID	MeanDecreaseGini
IYLQPGR_423.7_329.2	ITIH2_HUMAN	0.259086112
AEVIWTSSDHQVLSGK_586.3_300.2	PD1L1_HUMAN	0.25722354
VPSHAVVAR_312.5_515.3	TRFL_HUMAN	0.256151812
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.251704855
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.249400642
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.245930393

Table 46. Random Forest 32 Late Window

Variable	UniProt_ID	MeanDecreaseGini
AVYEAVLR_460.8_587.4	PEPD_HUMAN	1.889521223
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	1.75233545
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	1.676813493
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	1.600684153
AVYEAVLR_460.8_750.4	PEPD_HUMAN	1.462889662
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	1.364115361
VPLALFALNR_557.3_620.4	PEPD_HUMAN	1.324317148
QINSYVK_426.2_610.3	CBG_HUMAN	1.305932064
ITQDAQLK_458.8_702.4	CBG_HUMAN	1.263533228
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	1.245153376
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	1.236529173
QINSYVK_426.2_496.3	CBG_HUMAN	1.221866266
YSHYNER_323.5_418.2	HABP2_HUMAN	1.169575572
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	1.126684146
VGVISFAQK_474.8_580.3	TFR2_HUMAN	1.075283855
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	1.07279097
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	1.05759256
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	1.028933332
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	1.014443799
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	1.010573267
ILDGGNK_358.7_603.3	CXCL5_HUMAN	0.992175141
TSYQVYSK_488.2_787.4	C163A_HUMAN	0.95649585
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.955085198
SETEIHQGFQHLHQLFAK_717.4_447.2	CBG_HUMAN	0.944726739
TLPFSR_360.7_506.3	LYAM1_HUMAN	0.944426109
VLSSIEQK_452.3_691.4	1433S_HUMAN	0.933902495
AEIEYLEK_497.8_389.2	LYAM1_HUMAN	0.891235263
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.87187037

(continued)

Variable	UniProt_ID	MeanDecreaseGini
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	0.869821307
SGVDLADSNQK_567.3_591.3	VGFR3_HUMAN	0.839946466

Table 47. Random Forest 100 Late Window

Variable	UniProt_ID	MeanDecreaseGini
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.971695767
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	0.920098693
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.786924487
AVYEAVLR_460.8_750.4	PEPD_HUMAN	0.772867983
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	0.744138513
AYSDLSR_406.2_375.2	SAMP_HUMAN	0.736078079
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.681784822
QINSYVK_426.2_610.3	CBG_HUMAN	0.585819307
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.577161158
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.573055613
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.569156128
ITQDAQLK_458.8_702.4	CBG_HUMAN	0.551017844
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.539330047
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.527652175
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	0.484155289
FQLPGQK_409.2_429.2	PSG1_HUMAN	0.480394031
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	0.475252565
QINSYVK_426.2_496.3	CBG_HUMAN	0.4728541
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	0.470079977
TLPFSR_360.7_506.3	LYAM1_HUMAN	0.46881451
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	0.4658941
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	0.463604174
YSHYNER_323.5_418.2	HABP2_HUMAN	0.453076307
VGVISFAQK_474.8_580.3	TFR2_HUMAN	0.437768219
LQDAGVYR_461.2_680.3	PD1L1_HUMAN	0.428524689
AEIEYLEK_497.8_389.2	LYAM1_HUMAN	0.42041448
TSYQVYSK_488.2_787.4	C163A_HUMAN	0.419411932
SVVLIPLGAVDDGEHSQNEK_703.0_798.4	CNDP1_HUMAN	0.415325735
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.407951733
ILDGGNK_358.7_603.3	CXCL5_HUMAN	0.401059572

Table 48. Random Forest Protein Late Window

Variable	UniProt_ID	MeanDecreaseGini
AVYEAVLR_460.8_587.4	PEPD_HUMAN	1.836010146
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	1.739802548
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	1.455337749
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	1.395043941
AYSDLSR_406.2_375.2	SAMP_HUMAN	1.177349958
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	1.14243936
QINSYVK_426.2_496.3	CBG_HUMAN	1.05284482
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	0.971678206
YISPDQLADLYK_713.4_277.2	ENOA_HUMAN	0.902293734
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	0.893163413
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	0.856551531
ILDGGNK_358.7_603.3	CXCL5_HUMAN	0.841485153
VGVISFAQK_474.8_580.3	TFR2_HUMAN	0.835256078
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.831195917
YSHYNER_323.5_418.2	HABP2_HUMAN	0.814479968
FQLPGQK_409.2_276.1	PSG1_HUMAN	0.77635168
YENYTSSFFIR_713.8_756.4	IL12B_HUMAN	0.761241391
TEQAAVAR_423.2_615.4	FA12_HUMAN	0.73195592
SGVDLADSNQK_567.3_662.3	VGFR3_HUMAN	0.72504131
VLSSIEQK_452.3_691.4	1433S_HUMAN	0.713380314
GTYLYNDCPGPGQDTDCR_697.0_666.3	TNR1A_HUMAN	0.704248586
TSYQVYSK_488.2_787.4	C163A_HUMAN	0.69026345
TLEAQLTPR_514.8_685.4	HEP2_HUMAN	0.654641588
AEVIWTSSDHQVLSGK_586.3_300.2	PD1L1_HUMAN	0.634751081
TAVTANLDIR_537.3_288.2	CHL1_HUMAN	0.619871203
ITENDIQIALDDAK_779.9_632.3	APOB_HUMAN	0.606313398
TASDFITK_441.7_781.4	GELS_HUMAN	0.593535076
SPQAFYR_434.7_556.3	REL3_HUMAN	0.592004045
NHYTESISVAK_624.8_415.2	NEUR1_HUMAN	0.588383911
LTTVDIVTLR_565.8_815.5	IL2RB_HUMAN	0.587343951

Table 49. Random Forest All Late Window

Variable	UniProt_ID	MeanDecreaseGini
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.437300283
AEIEYLEK_497.8_552.3	LYAM1_HUMAN	0.371624293
AALAAFNAQNNGSNFQLEEISR_789.1_746.4	FETUA_HUMAN	0.304039734
TGVAVNKPAEFTVDAK_549.6_258.1	FLNA_HUMAN	0.280588526
AVYEAVLR_460.8_750.4	PEPD_HUMAN	0.266788699

(continued)

Variable	UniProt_ID	MeanDecreaseGini
AYSDLSR_406.2_375.2	SAMP_HUMAN	0.247412666
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.229955358
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.218186524
ITQDAQLK_458.8_702.4	CBG_HUMAN	0.217646659
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.213840705
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.212794469
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.208620264
QINSYVK_426.2_610.3	CBG_HUMAN	0.202054546
QINSYVK_426.2_496.3	CBG_HUMAN	0.197235139
FQLPGQK_409.2_429.2	PSG1_HUMAN	0.188311102
VFQYIDLHQDEFVQTLK_708.4_375.2	CNDP1_HUMAN	0.180534913
ALEQDLPVNIK_620.4_798.5	CNDP1_HUMAN	0.178464358
YYGYTGAFR_549.3_450.3	TRFL_HUMAN	0.176050092
ALFLDALGPPAVTR_720.9_640.4	INHA_HUMAN	0.171492975
FQLPGQK_409.2_276.1	PSG1_HUMAN	0.167576198
SETEIHQGFQHLHQLFAK_717.4_447.2	CBG_HUMAN	0.162231844
ALEQDLPVNIK_620.4_570.4	CNDP1_HUMAN	0.162165399
VPSHAVVAR_312.5_515.3	TRFL_HUMAN	0.156742065
AVDIPGLEAATPYR_736.9_286.1	TENA_HUMAN	0.153681405
FTFTLHLETPKPSISSSNLNPR_829.4_874.4	PSG1_HUMAN	0.152042057
VGVISFAQK_474.8_580.3	TFR2_HUMAN	0.149034355
TLPFSR_360.7_506.3	LYAM1_HUMAN	0.143223501
SLDFTELDVAAEK_719.4_874.5	ANGT_HUMAN	0.141216186
SPEAEDPLGVER_649.8_314.1	Z512B_HUMAN	0.139843479
YGIEEHGK_311.5_341.2	CXA1_HUMAN	0.135236953

Table 50. Selected Transitions for Early Window

Transition	Parent Protein
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN
VQTAHFK_277.5_431.2	CO8A_HUMAN
FLNWIK_410.7_560.3	HABP2_HUMAN
ITGFLKPGK_320.9_429.3	LBP_HUMAN
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN
LIENGYFHPVK_439.6_627.4	F13B_HUMAN
AVLHIGEK_289.5_292.2	THBG_HUMAN
QALEEFQK_496.8_680.3	CO8B_HUMAN

(continued)

Transition	Parent Protein
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN
TASDFITK_441.7_781.4	GELS_HUMAN
LPNNVLQEK_527.8_844.5	AFAM_HUMAN
AHYDLR_387.7_288.2	FETUA_HUMAN
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN
IEGNLIFDPNNYLPK_874.0_414.2	APOB_HUMAN
ITGFLKPGK_320.9_301.2	LBP_HUMAN
FSVVYAK_407.2_381.2	FETUA_HUMAN
ITGFLKPGK_320.9_429.3	LBP_HUMAN
VFQFLEK_455.8_811.4	CO5_HUMAN
LIQDAVTGLTVNGQITGDK_972.0_798.4	ITIH3_HUMAN
DADPDTFFAK_563.8_825.4	AFAM_HUMAN

Table 51. Selected Proteins for Early Window

Protein	
complement component C6 precursor	CO6_HUMAN
inter-alpha-trypsin inhibitor heavy chain H3 preproprotein	ITIH3_HUMAN
Coagulation factor XIII B chain	F13B_HUMAN
Ectonucleotide pyrophosphatase/phosphodiesterase family member 2	ENPP2_HUMAN
Complement component C8 beta chain	CO8B_HUMAN
thyroxine-binding globulin precursor	THBG_HUMAN
Hyaluronan-binding protein 2	HABP2_HUMAN
lipopolysaccharide-binding protein	LBP_HUMAN
Complement factor B	CFAB_HUMAN
Gelsolin	GELS_HUMAN
afamin precursor	AFAM_HUMAN
apolipoprotein B-100 precursor	APOB_HUMAN
complement component C5	CO5_HUMAN
Alpha-2-HS-glycoprotein	FETUA_HUMAN
complement component C8 gamma chain	CO8G_HUMAN

Table 52. Selected Transitions for Middle-Late Window

Transition	Patent Protein
VPLALFALNR_557.3_620.4	PEPD_HUMAN
VFQFLEK_455.8_811.4	CO5_HUMAN
AQPVQVAEGSEPDGFWEALGGK_758.0_574.3	GELS_HUMAN
LIEIANHVDK_384.6_498.3	ADA12_HUMAN

(continued)

Transition	Patent Protein
TLAFVR_353.7_492.3	FA7_HUMAN
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN
AVYEAVLR_460.8_587.4	PEPD_HUMAN
SEPRPGVLLR_375.2_654.4	FA7_HUMAN
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN

Table 53. Selected Proteins for Middle-Late Window

Protein	
Xaa-Pro dipeptidase	PEPD_HUMAN
Leucyl-cystinyl aminopeptidase	LCAP_HUMAN
complement component C5	CO5_HUMAN
Gelsolin	GELS_HUMAN
complement component C6 precursor	CO6_HUMAN
Endoglin precursor	EGLN_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1	FBLN3_HUMAN
coagulation factor VII isoform a	FA7_HUMAN
Disintegrin and metalloproteinase domain-containing protein 12	ADA12_HUMAN
vitamin D-binding protein isoform 1 precursor	VTDB_HUMAN
coagulation factor XII precursor	FA12_HUMAN
Corticosteroid-binding globulin	CBG_HUMAN

Example 6. Study V to Further Refine Preterm Birth Biomarkers

[0184] A additional hypothesis-dependent discovery study was performed with a further refined scheduled MRM assay. Less robust transitions were again removed to improve analytical performance and make room for the inclusion of stable-isotope labeled standards (SIS) corresponding to 79 analytes of interest identified in previous studies. SIS peptides have identical amino acid sequence, chromatographic and MS fragmentation behaviour as their endogenous peptide counterparts, but differ in mass. Therefore they can be used to reduce LC-MS analytical variability and confirm analyte identity. Samples included approximately 60 spontaneous PTB cases (delivery at less than 37 weeks, 0 days), and 180 term controls (delivery at greater than or equal to 37 weeks, 0 days). Each case was designated a "matched" control to within one day of blood draw and two "random" controls matched to the same 3 week blood draw window (17-19, 20-22 or 23-25 weeks gestation). For the purposes of analysis these three blood draw windows were combined. Samples were processed essentially as described previously, except that in this study, tryptic digests were reconstituted in a solution containing SIS standards. Raw analyte peak areas were Box-Cox transformed, corrected for run order and batch effects by regression and used for univariate and multivariate statistical analyses. Univariate analysis included determination of p-values for adjusted peak areas for all analytes from t-tests considering cases vs controls defined as either deliveries at >37 weeks (Table 54) or deliveries at >40 weeks (Table 55). Univariate analysis also included the determination of p-values for a linear model that evaluates the dependence of each analyte’s adjusted peak area on the time to birth (gestational age at birth minus the gestational age at blood draw) (Table 56) and the gestational age at birth (Table 57). Additionally raw peak area ratios were calculated for endogenous analytes and their corresponding SIS counterparts, Box-Cox transformed and then used for univariate and multivariate statistical analyses. The above univariate analysis was repeated for analyte/SIS peak area ratio values, summarized in Tables 58-61, respectively.

[0185] Multivariate random forest regression models were built using analyte values and clinical variables (e.g. Maternal age, (MAGE), Body mass index, (BMI)) to predict Gestational Age at Birth (GAB). The accuracy of the random forest was evaluated with respect to correlation of the predicted and actual GAB, and with respect to the mean absolute deviation (MAD) of the predicted from actual GAB. The accuracy was further evaluated by determining the area under the receiver operating characteristic curve (AUC) when using the predicted GAB as a quantitative variable to classify subjects as full term or pre-term. Random Forest Importance Values were fit to an Empirical Cumulative Disribution Function and probabilities (P) were calculated. We report the analytes by importance ranking (P>0.7) in the random forest models, using adjusted analyte peak area values (Table 62) and analyte/SIS peak area ratio values (Table 63).

[0186] The probability of pre-term birth, p(PTB), may be estimated using the predicted gestational age at birth (GAB) as follows. The estimate will be based on women enrolled in the Sera PAPR clinical trial, which provided the subjects used to develop the PTB prediction methods.

[0187] Among women with a predicted GAB of j days plus or minus k days, p(PTB) was estimated as the proportion of women in the PAPR clinical trial with a predicted GAB of j days plus or minus k days who actually deliver before 37 weeks gestational age.

[0188] More generally, for women with a predicted GAB of j days plus or minus k days, the probability that the actual gestational age at birth will be less than a specified gestational age, p(actual GAB < specified GAB), was estimated as the proportion of women in the PAPR clinical trial with a predicted GAB of j days plus or minus k days who actually deliver before the specified gestational age. Figure 1 depicts a scatterplot of actual gestational age at birth versus predicted gestational age from random forest regression model. Firgure 2 shows the distribution of predicted gestational age from random forest regression model versus actual gestational age at birth (GAB), where actual GAB was given in categories of (i) less than 37 weeks, (ii) 37 to 39 weeks, and (iii) 40 weeks or greater.

Table 54. Univariate p-values for Adjusted Peak Areas (<37 vs >37 weeks)

Transition	Protein	pvalue
SPELQAEAK_486.8_659.4	APOA2_HUMAN	0.00246566
ALALPPLGLAPLLNLWAKPQGR_770.5_457.3	SHBG_HUMAN	0.002623332
ALALPPLGLAPLLNLWAKPQGR_770.5_256.2	SHBG_HUMAN	0.002822593
SPELQAEAK_486.8_788.4	APOA2_HUMAN	0.003183869
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_768.5	SHBG_HUMAN	0.004936049
VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4	SHBG_HUMAN	0.005598977
DYWSTVK_449.7_347.2	APOC3_HUMAN	0.005680405
DYWSTVK_449.7_620.3	APOC3_HUMAN	0.006288693
WGAAPYR_410.7_634.3	PGRP2_HUMAN	0.006505238
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.007626246
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	0.008149335
LSIPQITTK_500.8_687.4	PSG5_HUMAN	0.009943955
GWVTDGFSSLK_598.8_854.4	APOC3_HUMAN	0.010175055
IALGGLLFPASNLR_481.3_657.4	SHBG_HUMAN	0.010784167
AKPALEDLR_506.8_813.5	APOA1_HUMAN	0.011331968
WGAAPYR_410.7_577.3	PGRP2_HUMAN	0.011761088
VPLALFALNR_557.3_620.4	PEPD_HUMAN	0.014050395
FSLVSGWGQLLDR_493.3_447.3	FA7_HUMAN	0.014271151
LSIPQITTK_500.8_800.5	PSG5_HUMAN	0.014339942
TLAFVR_353.7_274.2	FA7_HUMAN	0.014459876
DVLLLVHNLPQNLPGYFWYK_810.4_960.5	PSG9_HUMAN	0.016720007
FSVVYAK_407.2_381.2	FETUA_HUMAN	0.016792786
DVLLLVHNLPQNLPGYFWYK_810.4_215.1	PSG9_HUMAN	0.017335929

(continued)

Transition	Protein	pvalue
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.018147773
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.019056484
WNFAYWAAHQPWSR_607.3_545.3	PRG2_HUMAN	0.019190043
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.020218682
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	0.020226218
GWVTDGFSSLK_598.8_953.5	APOC3_HUMAN	0.023192703
IALGGLLFPASNLR_481.3_412.3	SHBG_HUMAN	0.023916911
WNFAYWAAHQPWSR_607.3_673.3	PRG2_HUMAN	0.026026975
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.027731407
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.031865281
DADPDTFFAK_563.8_302.1	AFAM_HUMAN	0.0335897
LFIPQITR_494.3_614.4	PSG9_HUMAN	0.034140767
DVLLLVHNLPQNLPGYFWYK_810.4_328.2	PSG9_HUMAN	0.034653304
TLAFVR_353.7_492.3	FA7_HUMAN	0.036441189
AVLHIGEK_289.5_292.2	THBG_HUMAN	0.038539433
IHPSYTNYR_384.2_452.2	PSG2_HUMAN	0.039733019
AGLLRPDYALLGHR_518.0_369.2	PGRP2_HUMAN	0.040916226
ILILPSVTR_506.3_559.3	PSGx_HUMAN	0.042460036
YYLQGAK_421.7_516.3	ITIH4_HUMAN	0.044511962
TPSAAYLWVGTGASEAEK_919.5_849.4	GELS_HUMAN	0.046362381
AGLLRPDYALLGHR_518.0_595.4	PGRP2_HUMAN	0.046572355
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.04754503
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.048642964
VNFTEIQK_489.8_765.4	FETA_HUMAN	0.04871392
LFIPQITR_494.3_727.4	PSG9_HUMAN	0.049288923
DISEVVTPR_508.3_787.4	CFAB_HUMAN	0.049458374
SEPRPGVLLR_375.2_454.3	FA7_HUMAN	0.049567047

Table 55. Univariate p-values for Adjusted Peak Areas (<37 vs >40 weeks)

Transition	Protein	pvalue
SPELQAEAK_486.8_659.4	APOA2_HUMAN	0.001457796
DYWSTVK_449.7_347.2	APOC3_HUMAN	0.001619622
DYWSTVK_449.7_620.3	APOC3_HUMAN	0.002068704
DALSSVQESQVAQQAR_573.0_502.3	APOC3_HUMAN	0.00250563
GWVTDGFSSLK_598.8_854.4	APOC3_HUMAN	0.002543943
SPELQAEAK_486.8_788.4	APOA2_HUMAN	0.003108814
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.004035832

(continued)

Transition	Protein	pvalue
DALSSVQESQVAQQAR_573.0_672.4	APOC3_HUMAN	0.00434652
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.005306924
GWVTDGFSSLK_598.8_953.5	APOC3_HUMAN	0.005685534
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.005770384
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.005798991
ENPAVIDFELAPIVDLVR_670.7_601.4	CO6_HUMAN	0.006248095
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.006735817
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.007351774
AGLLRPDYALLGHR_518.0_369.2	PGRP2_HUMAN	0.009541521
AKPALEDLR_506.8_813.5	APOA1_HUMAN	0.009780371
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.010085363
FSLVSGWGQLLDR_493.3_447.3	FA7_HUMAN	0.010401836
WGAAPYR_410.7_634.3	PGRP2_HUMAN	0.011233623
ENPAVIDFELAPIVDLVR_670.7_811.5	CO6_HUMAN	0.012029564
DVLLLVHNLPQNLPGYFWYK_810.4_215.1	PSG9_HUMAN	0.014808277
LFIPQITR_494.3_614.4	PSG9_HUMAN	0.015879755
WGAAPYR_410.7_577.3	PGRP2_HUMAN	0.016562435
AGLLRPDYALLGHR_518.0_595.4	PGRP2_HUMAN	0.016793521
TLAFVR_353.7_492.3	FA7_HUMAN	0.016919708
FSLVSGWGQLLDR_493.3_403.2	FA7_HUMAN	0.016937583
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	0.019050115
GYVIIKPLVWV_643.9_304.2	SAMP_HUMAN	0.019675317
DVLLLVHNLPQNLPGYFWYK_810.4_960.5	PSG9_HUMAN	0.020387647
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.020458335
DVLLLVHNLPQNLPGYFWYK_810.4_328.2	PSG9_HUMAN	0.021488084
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.021709354
LDFHFSSDR_375.2_448.2	INHBC_HUMAN	0.022403383
LFIPQITR_494.3_727.4	PSG9_HUMAN	0.025561103
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	0.029344366
LSIPQITTK_500.8_800.5	PSG5_HUMAN	0.031361776
ALVLELAK_428.8_672.4	INHBE_HUMAN	0.031690737
SEPRPGVLLR_375.2_454.3	FA7_HUMAN	0.033067953
LSIPQITTK_500.8_687.4	PSG5_HUMAN	0.033972449
LDFHFSSDR_375.2_611.3	INHBC_HUMAN	0.034500249
LDFHFSSDR_375.2_464.2	INHBC_HUMAN	0.035166664
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	0.037334975
HELTDEELQSLFTNFANVVDK_817.1_854.4	AFAM_HUMAN	0.039258528
AYSDLSR_406.2_375.2	SAMP_HUMAN	0.04036485

(continued)

Transition	Protein	pvalue
YYLQGAK_421.7_516.3	ITIH4_HUMAN	0.042204165
ILPSVPK_377.2_264.2	PGH1_HUMAN	0.042397885
ELLESYIDGR_597.8_710.4	THRB_HUMAN	0.043053589
ALALPPLGLAPLLNLWAKPQGR_770.5_256.2	SHBG_HUMAN	0.045692283
VGEYSLYIGR_578.8_871.5	SAMP_HUMAN	0.04765767
ANDQYLTAAALHNLDEAVK_686.4_317.2	IL1A_HUMAN	0.048928376
YYGYTGAFR_549.3_551.3	TRFL_HUMAN	0.049568351

Table 56. Univariate p-values for Adjusted Peak Areas in Time to Birth Linear Model

Protein	pvalue
ADA12_HUMAN	0.003412707
ENPP2_HUMAN	0.003767393
ADA12_HUMAN	0.004194234
ENPP2_HUMAN	0.004298493
ADA12_HUMAN	0.004627197
ADA12_HUMAN	0.004918852
ENPP2_HUMAN	0.005792374
CO6_HUMAN	0.005858282
ENPP2_HUMAN	0.007123606
CO6_HUMAN	0.007162317
ENPP2_HUMAN	0.008228726
ENPP2_HUMAN	0.009168492
PSG9_HUMAN	0.011531192
PSG9_HUMAN	0.019389627
PSG9_HUMAN	0.023680865
INHBE_HUMAN	0.02581564
B2MG_HUMAN	0.026544689
LBP_HUMAN	0.031068274
PSG9_HUMAN	0.031091843
APOA2_HUMAN	0.033130498
INHBC_HUMAN	0.03395215
CBG_HUMAN	0.034710348
PSGx_HUMAN	0.035719227
CBG_HUMAN	0.036331871
CSH_HUMAN	0.039896611
CSH_HUMAN	0.04244001
SAMP_HUMAN	0.047112128

(continued)

Protein	pvalue
LBP_HUMAN	0.048141371
LBP_HUMAN	0.048433174
CO6_HUMAN	0.04850949
PSGx_HUMAN	0.049640167

Table 57. Univariate p-values for Adjusted Peak Areas in Gestation Age at Birth Linear Model

Transition	Protein	pvalue
ENPAVIDFELAPIVDLVR_670.7_811.5	CO6_HUMAN	0.000117239
ENPAVIDFELAPIVDLVR_670.7_601.4	CO6_HUMAN	0.000130113
TYLHTYESEI_628.3_908.4	ENPP2_HUMAN	0.000160472
TYLHTYESEI_628.3_515.3	ENPP2_HUMAN	0.000175167
TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	ENPP2_HUMAN	0.000219886
TEFLSNYLTNVDDITLVPGTLGR_846.8_699.4	ENPP2_HUMAN	0.000328416
WWGGQPLWITATK_772.4_373.2	ENPP2_HUMAN	0.000354644
WWGGQPLWITATK_772.4_929.5	ENPP2_HUMAN	0.000390821
SEYGAALAWEK_612.8_788.4	CO6_HUMAN	0.000511882
LDFHFSSDR_375.2_448.2	INHBC_HUMAN	0.000600637
ALVLELAK_428.8_672.4	INHBE_HUMAN	0.000732445
GLQYAAQEGLLALQSELLR_1037.1_929.5	LBP_HUMAN	0.000743924
DVLLLVHNLPQNLPGYFWYK_810.4_960.5	PSG9_HUMAN	0.000759173
FGFGGSTDSGPIR_649.3_745.4	ADA12_HUMAN	0.001224347
DVLLLVHNLPQNLPGYFWYK_810.4_328.2	PSG9_HUMAN	0.001241329
GYVIIKPLVWV_643.9_304.2	SAMP_HUMAN	0.001853785
SPELQAEAK_486.8_659.4	APOA2_HUMAN	0.001856303
GLQYAAQEGLLALQSELLR_1037.1_858.5	LBP_HUMAN	0.001978165
LDFHFSSDR_375.2_611.3	INHBC_HUMAN	0.002098948
LIEIANHVDK_384.6_683.4	ADA12_HUMAN	0.002212096
SFRPFVPR_335.9_272.2	LBP_HUMAN	0.002545286
SFRPFVPR_335.9_635.3	LBP_HUMAN	0.002620268
WSAGLTSSQVDLYIPK_883.0_515.3	CBG_HUMAN	0.002787272
DLHLSDVFLK_396.2_260.2	CO6_HUMAN	0.002954612
LIEIANHVDK_384.6_498.3	ADA12_HUMAN	0.002955081
DVLLLVHNLPQNLPGYFWYK_810.4_215.1	PSG9_HUMAN	0.003541011
LFIPQITR_494.3_614.4	PSG9_HUMAN	0.003750666
FGFGGSTDSGPIR_649.3_946.5	ADA12_HUMAN	0.003773696
YYLQGAK_421.7_516.3	ITIH4_HUMAN	0.004064026
SEYGAALAWEK_612.8_845.5	CO6_HUMAN	0.004208136

(continued)

Transition	Protein	pvalue
AITPPHPASQANIIFDITEGNLR_825.8_459.3	FBLN1_HUMAN	0.004709104
LDFHFSSDR_375.2_464.2	INHBC_HUMAN	0.005355741
HELTDEELQSLFTNFANVVDK_817.1_854.4	AFAM_HUMAN	0.005370567
ALNHLPLEYNSALYSR_621.0_696.4	CO6_HUMAN	0.005705922
ITQDAQLK_458.8_702.4	CBG_HUMAN	0.006762484
ITLPDFTGDLR_624.3_920.5	LBP_HUMAN	0.006993268
SILFLGK_389.2_577.4	THBG_HUMAN	0.007134146
WSAGLTSSQVDLYIPK_883.0_357.2	CBG_HUMAN	0.007670388
GVTSVSQIFHSPDLAIR_609.7_472.3	IC1_HUMAN	0.007742729
VGEYSLYIGR_578.8_871.5	SAMP_HUMAN	0.007778691
ITLPDFTGDLR_624.3_288.2	LBP_HUMAN	0.008179918
YYLQGAK_421.7_327.1	ITIH4_HUMAN	0.008404686
ALNHLPLEYNSALYSR_621.0_538.3	CO6_HUMAN	0.008601162
DYWSTVK_449.7_620.3	APOC3_HUMAN	0.008626786
TVQAVLTVPK_528.3_855.5	PEDF_HUMAN	0.008907523
ITGFLKPGK_320.9_301.2	LBP_HUMAN	0.009155417
LFIPQITR_494.3_727.4	PSG9_HUMAN	0.009571006
SPELQAEAK_486.8_788.4	APOA2_HUMAN	0.009776508
DYWSTVK_449.7_347.2	APOC3_HUMAN	0.00998356
ITGFLKPGK_320.9_429.3	LBP_HUMAN	0.010050264
FLNWIK_410.7_560.3	HABP2_HUMAN	0.010372454
DLHLSDVFLK_396.2_366.2	CO6_HUMAN	0.010806378
GVTSVSQIFHSPDLAIR_609.7_908.5	IC1_HUMAN	0.011035991
VEHSDLSFSK_383.5_468.2	B2MG_HUMAN	0.011113172
LLDSLPSDTR_558.8_276.2	IC1_HUMAN	0.011589013
LLDSLPSDTR_558.8_890.4	IC1_HUMAN	0.011629438
QALEEFQK_496.8_551.3	CO8B_HUMAN	0.011693839
LLDSLPSDTR_558.8_575.3	IC1_HUMAN	0.012159314
IIGGSDADIK_494.8_762.4	C1S_HUMAN	0.013080243
AFIQLWAFDAVK_704.9_650.4	AMBP_HUMAN	0.013462234
GFQALGDAADIR_617.3_717.4	TIMP1_HUMAN	0.014370997
LPNNVLQEK_527.8_730.4	AFAM_HUMAN	0.014424891
DTDTGALLFIGK_625.8_217.1	PEDF_HUMAN	0.014967952
VQTAHFK_277.5_502.3	CO8A_HUMAN	0.01524844
ILILPSVTR_506.3_559.3	PSGx_HUMAN	0.015263132
SILFLGK_389.2_201.1	THBG_HUMAN	0.015265233
TVQAVLTVPK_528.3_428.3	PEDF_HUMAN	0.015344052
VEPLYELVTATDFAYSSTVR_754.4_712.4	CO8B_HUMAN	0.015451068

(continued)

Transition	Protein	pvalue
FSLVSGWGQLLDR_493.3_447.3	FA7_HUMAN	0.015510454
GWVTDGFSSLK_598.8_854.4	APOC3_HUMAN	0.01610797
LSETNR_360.2_519.3	PSG1_HUMAN	0.016433362
TQILEWAAER_608.8_632.3	EGLN_HUMAN	0.01644844
SETEIHQGFQHLHQLFAK_717.4_318.1	CBG_HUMAN	0.016720367
TNLESILSYPK_632.8_936.5	IC1_HUMAN	0.017314185
TNLESILSYPK_632.8_807.5	IC1_HUMAN	0.017593786
AYSDLSR_406.2_375.2	SAMP_HUMAN	0.018531348
YEVQGEVFTKPQLWP_911.0_392.2	CRP_HUMAN	0.019111323
AYSDLSR_406.2_577.3	SAMP_HUMAN	0.019271266
QALEEFQK_496.8_680.3	CO8B_HUMAN	0.019429489
APLTKPLK_289.9_398.8	CRP_HUMAN	0.020110081
FQPTLLTLPR_593.4_276.1	IC1_HUMAN	0.020114306
ITQDAQLK_458.8_803.4	CBG_HUMAN	0.020401782
AVLHIGEK_289.5_292.2	THBG_HUMAN	0.02056597
ANDQYLTAAALHNLDEAVK_686.4_317.2	IL1A_HUMAN	0.020770124
VGEYSLYIGR_578.8_708.4	SAMP_HUMAN	0.021126414
TLYSSSPR_455.7_533.3	IC1_HUMAN	0.021306106
VEHSDLSFSK_383.5_234.1	B2MG_HUMAN	0.021640643
HELTDEELQSLFTNFANVVDK_817.1_906.5	AFAM_HUMAN	0.021921609
TLYSSSPR_455.7_696.3	IC1_HUMAN	0.022196181
GYVIIKPLVWV_643.9_854.6	SAMP_HUMAN	0.023126336
DEIPHNDIALLK_459.9_260.2	HABP2_HUMAN	0.023232158
ILILPSVTR_506.3_785.5	PSGx_HUMAN	0.023519909
WNFAYWAAHQPWSR_607.3_545.3	PRG2_HUMAN	0.023697087
FQPTLLTLPR_593.4_712.5	IC1_HUMAN	0.023751959
AQPVQVAEGSEPDGFWEALGGK_758.0_623.4	GELS_HUMAN	0.024262721
DEIPHNDIALLK_459.9_510.8	HABP2_HUMAN	0.024414348
GDSGGAFAVQDPNDK_739.3_716.3	C1S_HUMAN	0.025075028
FLNWIK_410.7_561.3	HABP2_HUMAN	0.025649617
APLTKPLK_289.9_357.2	CRP_HUMAN	0.025961162
ALDLSLK_380.2_185.1	ITIH3_HUMAN	0.026233504
GWVTDGFSSLK_598.8_953.5	APOC3_HUMAN	0.026291884
SETEIHQGFQHLHQLFAK_717.4_447.2	CBG_HUMAN	0.026457136
GDSGGAFAVQDPNDK_739.3_473.2	C1S_HUMAN	0.02727457
YEVQGEVFTKPQLWP_911.0_293.1	CRP_HUMAN	0.028244448
HVVQLR_376.2_614.4	IL6RA_HUMAN	0.028428028
DTDTGALLFIGK_625.8_818.5	PEDF_HUMAN	0.028773557

(continued)

Transition	Protein	pvalue
EVPLSALTNILSAQLISHWK_740.8_996.6	PAI1_HUMAN	0.029150774
AFTECCVVASQLR_770.9_574.3	CO5_HUMAN	0.029993325
TLAFVR_353.7_492.3	FA7_HUMAN	0.030064307
LWAYLTIQELLAK_781.5_300.2	ITIH1_HUMAN	0.030368674
DEIPHNDIALLK_459.9_245.1	HABP2_HUMAN	0.031972082
AGLLRPDYALLGHR_518.0_369.2	PGRP2_HUMAN	0.032057409
AVYEAVLR_460.8_587.4	PEPD_HUMAN	0.032527521
LPNNVLQEK_527.8_844.5	AFAM_HUMAN	0.033807082
GAVHVVVAETDYQSFAVLYLER_822.8_580.3	CO8G_HUMAN	0.034370139
WNFAYWAAHQPWSR_607.3_673.3	PRG2_HUMAN	0.0349737
EAQLPVIENK_570.8_329.2	PLMN_HUMAN	0.035304322
VQEAHLTEDQIFYFPK_655.7_701.4	CO8G_HUMAN	0.035704382
AFIQLWAFDAVK_704.9_836.4	AMBP_HUMAN	0.035914532
SGFSFGFK_438.7_585.3	CO8B_HUMAN	0.037168221
SGFSFGFK_438.7_732.4	CO8B_HUMAN	0.040182596
DADPDTFFAK_563.8_302.1	AFAM_HUMAN	0.041439744
EAQLPVIENK_570.8_699.4	PLMN_HUMAN	0.041447675
IIGGSDADIK_494.8_260.2	C1S_HUMAN	0.041683256
AVLTIDEK_444.8_718.4	A1AT_HUMAN	0.043221658
SEPRPGVLLR_375.2_654.4	FA7_HUMAN	0.044079127
YHFEALADTGISSEFYDNANDLLSK_940.8_874.5	CO8A_HUMAN	0.045313634
HFQNLGK_422.2_527.2	AFAM_HUMAN	0.047118971
LEQGENVFLQATDK_796.4_822.4	C1QB_HUMAN	0.047818928
NTVISVNPSTK_580.3_732.4	VCAM1_HUMAN	0.048102262
YYGYTGAFR_549.3_551.3	TRFL_HUMAN	0.048331316
ISLLLIESWLEPVR_834.5_500.3	CSH_HUMAN	0.049561581
LQVLGK_329.2_416.3	A2GL_HUMAN	0.049738493

Table 58. Univariate p-values for Peak Area Ratios (<37 vs >37 weeks)

UniProt_ID	Transition	pvalue
SHBG_HUMAN	IALGGLLFPASNLR_481.3_657.4	0.006134652
SHBG_HUMAN	IALGGLLFPASNLR_481.3_412.3	0.019049498
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_672.4	0.020688543
THBG_HUMAN	AVLHIGEK_289.5_292.2	0.0291698
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_960.5	0.033518454
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_502.3	0.043103265
PSG9_HUMAN	LFIPQITR_494.3_614.4	0.04655948

Table 59. Univariate p-values for Peak Area Ratios (<37 vs >40 weeks)

UniProt ID	Transition	pvalue
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_672.4	0.011174438
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_502.3	0.015231617
PSG9_HUMAN	LFIPQITR_494.3_614.4	0.018308413
PSG9_HUMAN	LFIPQITR_494.3_727.4	0.027616871
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_960.5	0.028117582
THBG_HUMAN	AVLHIGEK_289.5_292.2	0.038899107
CO6_HUMAN	ALNHLPLEYNSALYSR_621.0_696.4	0.040662269
ENPP2_HUMAN	TYLHTYESEI_628.3_908.4	0.044545826

Table 60. Univariate p-values for Peak Area Ratios in Time to Birth Linear

UniProt_ID	Transition	pvalue
ADA12_HUMAN	FGFGGSTDSGPIR_649.3_946.5	5.85E-27
ADA12_HUMAN	FGFGGSTDSGPIR_649.3_745.4	2.65E-24
PSG4_HUMAN	TLFIFGVTK_513.3_215.1	1.07E-20
PSG4_HUMAN	TLFIFGVTK_513.3_811.5	2.32E-20
PSGx_HUMAN	ILILPSVTR_506.3_785.5	8.25E-16
PSGx_HUMAN	ILILPSVTR_506.3_559.3	9.72E-16
PSG1_HUMAN	FQLPGQK_409.2_429.2	1.29E-12
PSG11_HUMAN	LFIPQITPK_528.8_261.2	2.11E-12
PSG1_HUMAN	FQLPGQK_409.2_276.1	2.33E-12
PSG11_HUMAN	LFIPQITPK_528.8_683.4	3.90E-12
PSG6_HUMAN	SNPVTLNVLYGPDLPR_585.7_817.4	5.71E-12
PSG6_HUMAN	SNPVTLNVLYGPDLPR_585.7_654.4	1.82E-11
VGFR3_HUMAN	SGVDLADSNQK_567.3_662.3	4.57E-11
INHBE_HUMAN	ALVLELAK_428.8_331.2	1.04E-08
PSG2_HUMAN	IHPSYTNYR_384.2_452.2	6.27E-08
PSG9_HUMAN	LFIPQITR_494.3_727.4	1.50E-07
VGFR3_HUMAN	SGVDLADSNQK_567.3_591.3	2.09E-07
PSG9_HUMAN	LFIPQITR_494.3_614.4	2.71E-07
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_960.5	3.10E-07
PSG2_HUMAN	IHPSYTNYR_384.2_338.2	2.55E-06
ITIH3_HUMAN	LIQDAVTGLTVNGQITGDK_972.0_640.4	2.76E-06
ENPP2_HUMAN	TYLHTYESEI_628.3_908.4	2.82E-06
ENPP2_HUMAN	WWGGQPLWITATK_772.4_373.2	3.75E-06
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_328.2	3.94E-06
B2MG_HUMAN	VEHSDLSFSK_383.5_468.2	5.42E-06
ENPP2_HUMAN	WWGGQPLWITATK_772.4_929.5	7.93E-06

(continued)

UniProt_ID	Transition	pvalue
ANGT_HUMAN	ALQDQLVLVAAK_634.9_289.2	1.04E-05
B2MG_HUMAN	VNHVTLSQPK_374.9_244.2	1.46E-05
AFAM_HUMAN	LPNNVLQEK_527.8_730.4	1.50E-05
AFAM_HUMAN	LPNNVLQEK_527.8_844.5	1.98E-05
THBG_HUMAN	AVLHIGEK_289.5_292.2	2.15E-05
ENPP2_HUMAN	TYLHTYESEI_628.3_515.3	2.17E-05
IL12B_HUMAN	DIIKPDPPK_511.8_342.2	3.31E-05
AFAM_HUMAN	DADPDTFFAK_563.8_302.1	6.16E-05
THBG_HUMAN	AVLHIGEK_289.5_348.7	8.34E-05
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_215.1	0.000104442
B2MG_HUMAN	VEHSDLSFSK_383.5_234.1	0.000140786
TRFL_HUMAN	YYGYTGAFR_549.3_450.3	0.000156543
HEMO_HUMAN	QGHNSVFLIK_381.6_260.2	0.000164578
A1BG_HUMAN	LLELTGPK_435.8_227.2	0.000171113
CO6_HUMAN	ALNHLPLEYNSALYSR_621.0_696.4	0.000242116
CO6_HUMAN	ALNHLPLEYNSALYSR_621.0_538.3	0.00024681
ALS_HUMAN	IRPHTFTGLSGLR_485.6_432.3	0.000314359
ITIH2_HUMAN	LSNENHGIAQR_413.5_544.3	0.0004877
PEDF_HUMAN	TVQAVLTVPK_528.3_855.5	0.000508174
AFAM_HUMAN	HFQNLGK_422.2_527.2	0.000522139
FLNA_HUMAN	TGVAVNKPAEFTVDAK_549.6_258.1	0.000594403
ANGT_HUMAN	ALQDQLVLVAAK_634.9_956.6	0.000640673
AFAM_HUMAN	HFQNLGK_422.2_285.1	0.000718763
HGFA_HUMAN	LHKPGVYTR_357.5_692.4	0.000753293
HGFA_HUMAN	LHKPGVYTR_357.5_479.3	0.000909298
HABP2_HUMAN	FLNWIK_410.7_561.3	0.001282014
FETUA_HUMAN	HTLNQIDEVK_598.8_951.5	0.001389792
AFAM_HUMAN	DADPDTFFAK_563.8_825.4	0.001498237
B2MG_HUMAN	VNHVTLSQPK_374.9_459.3	0.001559862
ALS_HUMAN	IRPHTFTGLSGLR_485.6_545.3	0.001612361
A1BG_HUMAN	LLELTGPK_435.8_644.4	0.002012656
F13B_HUMAN	LIENGYFHPVK_439.6_343.2	0.00275216
ITIH2_HUMAN	LSNENHGIAQR_413.5_519.8	0.00356561
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_672.4	0.00392745
F13B_HUMAN	LIENGYFHPVK_439.6_627.4	0.00434836
PEDF_HUMAN	TVQAVLTVPK_528.3_428.3	0.00482765
PLMN_HUMAN	YEFLNGR_449.7_293.1	0.007325436
HEMO_HUMAN	QGHNSVFLIK_381.6_520.4	0.009508516

(continued)

UniProt_ID	Transition	pvalue
FETUA_HUMAN	HTLNQIDEVK_598.8_958.5	0.010018936
CO5_HUMAN	LQGTLPVEAR_542.3_842.5	0.011140661
PLMN_HUMAN	YEFLNGR_449.7_606.3	0.01135322
CO5_HUMAN	TLLPVSKPEIR_418.3_288.2	0.015045275
HABP2_HUMAN	FLNWIK_410.7_560.3	0.01523134
APOC3_HUMAN	DALSSVQESQVAQQAR_573.0_502.3	0.01584708
CO5_HUMAN	LQGTLPVEAR_542.3_571.3	0.017298064
CFAB_HUMAN	DISEVVTPR_508.3_472.3	0.021743221
CERU_HUMAN	TTIEKPVWLGFLGPIIK_638.0_640.4	0.02376225
CO8G_HUMAN	SLPVSDSVLSGFEQR_810.9_723.3	0.041150397
CO8G_HUMAN	FLQEQGHR_338.8_497.3	0.042038143
CO5_HUMAN	VFQFLEK_455.8_811.4	0.043651929
CO8B_HUMAN	QALEEFQK_496.8_680.3	0.04761631

Table 61. Univariate p-values for Peak Area Ratios in Gestation Age at Birth Linear Model

UniProt ID	Transition	pvalue
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_960.5	0.000431547
B2MG_HUMAN	VEHSDLSFSK_383.5_468.2	0.000561148
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_328.2	0.000957509
ENPP2_HUMAN	TYLHTYESEI_628.3_908.4	0.001058809
THBG_HUMAN	AVLHIGEK_289.5_292.2	0.001180484
ENPP2_HUMAN	WWGGQPLWITATK_772.4_373.2	0.001524983
PSG9_HUMAN	LFIPQITR_494.3_614.4	0.001542932
ENPP2_HUMAN	WWGGQPLWITATK_772.4_929.5	0.002047607
ENPP2_HUMAN	TYLHTYESEI_628.3_515.3	0.003087492
PSG9_HUMAN	LFIPQITR_494.3_727.4	0.00477154
PSG9_HUMAN	DVLLLVHNLPQNLPGYFWYK_810.4_215.1	0.004824351
THBG_HUMAN	AVLHIGEK_289.5_348.7	0.006668084
AFAM_HUMAN	LPNNVLQEK_527.8_730.4	0.006877647
ADA12_HUMAN	FGFGGSTDSGPIR_649.3_745.4	0.011738104
PEDF_HUMAN	TVQAVLTVPK_528.3_855.5	0.013349511
A1BG_HUMAN	LLELTGPK_435.8_227.2	0.015793885
ITIH3_HUMAN	ALDLSLK_380.2_185.1	0.016080436
ADA12_HUMAN	FGFGGSTDSGPIR_649.3_946.5	0.017037089
B2MG_HUMAN	VEHSDLSFSK_383.5_234.1	0.017072093
CO6_HUMAN	ALNHLPLEYNSALYSR_621.0_696.4	0.024592775
TRFL_HUMAN	YYGYTGAFR_549.3_450.3	0.030890831

(continued)

UniProt ID	Transition	pvalue
AFAM_HUMAN	DADPDTFFAK_563.8_302.1	0.033791429
CO6_HUMAN	ALNHLPLEYNSALYSR_621.0_538.3	0.034865341
AFAM_HUMAN	LPNNVLQEK_527.8_844.5	0.039880594
PEDF_HUMAN	TVQAVLTVPK_528.3_428.3	0.040854402
PLMN_HUMAN	EAQLPVIENK_570.8_329.2	0.041023812
LBP_HUMAN	ITLPDFTGDLR_624.3_920.5	0.042276813
CO8G_HUMAN	VQEAHLTEDQIFYFPK_655.7_701.4	0.042353851
PLMN_HUMAN	YEFLNGR_449.7_606.3	0.04416504
B2MG_HUMAN	VNHVTLSQPK_374.9_459.3	0.045458409
CFAB_UMAN	DISEVVTPR_508.3_472.3	0.046493405
INHBE_HUMAN	ALVLELAK_428.8_331.2	0.04789353

Table 62. Random Forest Importance Values Using Adjusted Peak Areas

Transition	Rank	Importance
INHBE_ALVLELAK_428.8_672.4	1	2964.951571
EGLN_TQILEWAAER_608.8_761.4	2	1218.3406
FA7_SEPRPGVLLR_375.2_654.4	3	998.92897
CBG_ITQDAQLK_458.8_702.4	4	930.9931102
ITIH3_ALDLSLK_380.2_185.1	5	869.6315408
ENPP2_WWGGQPLWITATK_772.4_929.5	6	768.9182114
CBG_ITQDAQLK_458.8_803.4	7	767.8940452
PSG1_LSETNR_360.2_519.3	8	714.6160065
CAA60698_LEPLYSASGPGLRPLVIK_637.4_834.5	9	713.4086612
INHBC_LDFHFSSDR_375.2_611.3	11	681.2442909
CBG_QINSYVK_426.2_610.3	12	674.3363415
LBP_GLQYAAQEGLLALQSELLR_1037.1_858.5	13	603.197751
A1BG_LLELTGPK_435.8_644.4	14	600.9902818
CO6_DLHLSDVFLK_396.2_366.2	15	598.8214342
VCAM1_TQIDSPLSGK_523.3_816.5	16	597.4038769
LRP1_NAVVQGLEQPHGLVVHPLR_688.4_285.2	17	532.0500081
CBG_QINSYVK_426.2_496.3	18	516.5575201
CO6_ENPAVIDFELAPIVDLVR_670.7_811.5	19	501.4669261
ADA12_FGFGGSTDSGPIR_649.3_745.4	20	473.5510333
CO6_DLHLSDVFLK_396.2_260.2	21	470.5473702
ENPP2_TYLHTYESEI_628.3_908.4	22	444.7580726
A1BG_LLELTGPK_435.8_227.2	23	444.696292
FRIH_QNYHQDSEAAINR_515.9_544.3	24	439.2648872

(continued)

Transition	Rank	Importance
ENPP2_TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3	25	389.3769604
CBG_WSAGLTSSQVDLYIPK_883.0_515.3	26	374.0749768
C1QC_FQSVFTVTR_542.8_623.4	27	370.6957977
GELS_DPDQTDGLGLSYLSSHIANVER_796.4_456.2	28	353.1176588
A1BG_ATWSGAVLAGR_544.8_643.4	29	337.4580124
APOA1_AKPALEDLR_506.8_813.5	30	333.5742035
ENPP2_TYLHTYESEI_628.3_515.3	31	322.6339162
PEPD_AVYEAVLR_460.8_750.4	32	321.4377907
TIMP1_GFQALGDAADIR_617.3_717.4	33	310.0997949
ADA12_LIEIANHVDK_384.6_498.3	34	305.8803542
PGRP2_WGAAPYR_410.7_577.3	35	303.5539874
PSG9_LFIPQITR_494.3_614.4	36	300.7877317
HABP2_FLNWIK_410.7_560.3	37	298.3363186
CBG_WSAGLTSSQVDLYIPK_883.0_357.2	38	297.2474385
PSG2_IHPSYTNYR_384.2_452.2	39	292.6203405
PSG5_LSIPQITTK_500.8_800.5	40	290.2023364
HABP2_FLNWIK_410.7_561.3	41	289.5092933
CO6_SEYGAALAWEK_612.8_788.4	42	287.7634114
ADA12_LIEIANHVDK_384.6_683.4	43	286.5047372
EGLN_TQILEWAAER_608.8_632.3	44	284.5138846
CO6_ENPAVIDFELAPIVDLVR_670.7_601.4	45	273.5146272
FA7_FSLVSGWGQLLDR_493.3_447.3	46	271.7850098
ITIH3_ALDLSLK_380.2_575.3	47	269.9425709
ADA12_FGFGGSTDSGPIR_649.3_946.5	48	264.5698225
FETUA_AALAAFNAQNNGSNFQLEEISR_789.1_746.4	49	247.4728828
FBLN1_AITPPHPASQANIIFDITEGNLR_825.8_459.3	50	246.572102
TSP1_FVFGTTPEDILR_697.9_843.5	51	245.0459575
VCAM1_NTVISVNPSTK_580.3_732.4	52	240.576729
ENPP2_TEFLSNYLTNVDDITLVPGTLGR_846.8_699.4	53	240.1949512
FBLN3_ELPQSIVYK_538.8_409.2	55	233.6825304
ACTB_VAPEEHPVLLTEAPLNPK_652.0_892.5	56	226.9772749
TSP1_FVFGTTPEDILR_697.9_742.4	57	224.4627393
PLMN_EAQLPVIENK_570.8_699.4	58	221.4663735
C1S_IIGGSDADIK_494.8_260.2	59	218.069476
ILIA_ANDQYLTAAALHNLDEAVK_686.4_317.2	60	216.5531949
PGRP2_WGAAPYR_410.7_634.3	61	211.0918302
PSG5_LSIPQITTK_500.8_687.4	62	208.7871461
PSG6_SNPVTLNVLYGPDLPR_585.7_654.4	63	207.9294937

(continued)

Transition	Rank	Importance
PRG2_WNFAYWAAHQPWSR_607.3_545.3	64	202.9494031
CXCL2_CQCLQTLQGIHLK_13p8RT_533.6_567.4	65	202.9051326
CXCL2_CQCLQTLQGIHLK_13p48RT_533.6_695.4	66	202.6561548
G6PE_LLDFEFSSGR_585.8_553.3	67	201.004611
GELS_TASDFITK_441.7_710.4	68	200.2704809
B2MG_VEHSDLSFSK_383.5_468.2	69	199.880987
CO8B_IPGIFELGISSQSDR_809.9_849.4	70	198.7563875
PSG8_LQLSETNR_480.8_606.3	71	197.6739966
LBP_GLQYAAQEGLLALQSELLR_1037.1_929.5	72	197.4094851
AFAM_LPNNVLQEK_527.8_844.5	73	196.8123228
MAGE	74	196.2410502
PSG2_IHPSYTNYR_384.2_338.2	75	196.2410458
PSG9_LFIPQITR_494.3_727.4	76	193.5329266
TFR1_YNSQLLSFVR_613.8_734.5	77	193.2711994
C1R_QRPPDLDTSSNAVDLLFFTDESGDSR_961.5_866.3	78	193.0625419
PGH1_ILPSVPK_377.2_264.2	79	190.0504508
FA7_SEPRPGVLLR_375.2_454.3	80	188.2718422
FA7_TLAFVR_353.7_274.2	81	187.6895294
PGRP2_DGSPDVTTADIGANTPDATK_973.5_844.4	82	185.6017519
C1S_IIGGSDADIK_494.8_762.4	83	184.5985543
PEPD_VPLALFALNR_557.3_620.4	84	184.3962957
C1S_EDTPNSVWEPAK_686.8_630.3	85	179.2043504
CHL1_TAVTANLDIR_537.3_802.4	86	174.9866792
CHL1_VIAVNEVGR_478.8_744.4	88	172.2053147
SDF1_ILNTPNCALQIVAR_791.9_341.2	89	171.4604557
PAI1_EVPLSALTNILSAQLISHWK_740.8_996.6	90	169.5635635
AMBP_AFIQLWAFDAVK_704.9_650.4	91	169.2124477
G6PE_LLDFEFSSGR_585.8_944.4	92	168.2398598
THBG_SILFLGK_389.2_577.4	93	166.3110206
PRDX2_GLFIIDGK_431.8_545.3	94	164.3125132
ENPP2_WWGGQPLWITATK_772.4_373.2	95	163.4011689
VGFR3_SGVDLADSNQK_567.3_662.3	96	162.8822352
C1S_EDTPNSVWEPAK_686.8_315.2	97	161.6140915
AFAM_DADPDTFFAK_563.8_302.1	98	159.5917449
CBG_SETEIHQGFQHLHQLFAK_717.4_447.2	99	156.1357404
C1S_LLEVPEGR_456.8_686.4	100	155.1763293
PTGDS_GPGEDFR_389.2_623.3	101	154.9205208
ITIH2_IYLQPGR_423.7_329.2	102	154.6552717

(continued)

Transition	Rank	Importance
FA7_TLAFVR_353.7_492.3	103	152.5009422
FA7_FSLVSGWGQLLDR_493.3_403.2	104	151.9971204
SAMP_VGEYSLYIGR_578.8_871.5	105	151.4738449
APOH_EHSSLAFWK_552.8_267.1	106	151.0052645
PGRP2_AGLLRPDYALLGHR_518.0_595.4	107	150.4149907
C1QC_FNAVLTNPQGDYDTSTGK_964.5_333.2	108	149.2592827
PGRP2_AGLLRPDYALLGHR_518.0_369.2	109	147.3609354
PGRP2_TFTLLDPK_467.8_686.4	111	145.2145223
CO5_TDAPDLPEENQAR_728.3_843.4	112	144.5213118
THRB_ELLESYIDGR_597.8_839.4	113	143.924639
GELS_DPDQTDGLGLSYLSSHIANVER_796.4_328.1	114	142.8936101
TRFL_YYGYTGAFR_549.3_450.3	115	142.8651352
HEMO_QGHNSVFLIK_381.6_260.2	116	142.703845
C1S_GDSGGAFAVQDPNDK_739.3_716.3	117	142.2799122
B1A4H9_AHQLAIDTYQEFR_531.3_450.3	118	138.196407
C1S_SSNNPHSPIVEEFQVPYNK_729.4_261.2	119	136.7868935
HYOU1_LPATEKPVLLSK_432.6_347.2	120	136.1146437
FETA_GYQELLEK_490.3_502.3	121	135.2890322
LRP1_SERPPIFEIR_415.2_288.2	122	134.6569527
CO6_SEYGAALAWEK_612.8_845.5	124	132.8634704
CERU_TTIEKPVWLGFLGPIIK_638.0_844.5	125	132.1047746
IBP1_AQETSGEEISK_589.8_850.4	126	130.934446
SHBG_VVLSSGSGPGLDLPLVLGLPLQLK_791.5_768.5	127	128.2052287
CBG_SETEIHQGFQHLHQLFAK_717.4_318.1	128	127.9873837
A1AT_LSITGTYDLK_555.8_696.4	129	127.658818
PGRP2_DGSPDVTTADIGANTPDATK_973.5_531.3	130	126.5775806
C1QB_LEQGENVFLQATDK_796.4_675.4	131	126.1762726
EGLN_GPITSAAELNDPQSILLR_632.4_826.5	132	125.7658253
IL12B_YENYTSSFFIR_713.8_293.1	133	125.0476631
B2MG_VEHSDLSFSK_383.5_234.1	134	124.9154706
PGH1_AEHPTWGDEQLFQTTR_639.3_765.4	135	124.8913193
INHBE_ALVLELAK_428.8_331.2	136	124.0109276
HYOU1_LPATEKPVLLSK_432.6_460.3	137	123.1900369
CXCL2_CQCLQTLQGIHLK_13p48RT_533.6_567.4	138	122.8800873
PZP_AVGYLITGYQR_620.8_523.3	139	122.4733204
AFAM_IAPQLSTEELVSLGEK_857.5_333.2	140	122.4707849
ICAM1_VELAPLPSWQPVGK_760.9_400.3	141	121.5494206
CHL1_VIAVNEVGR_478.8_284.2	142	119.0877137

(continued)

Transition	Rank	Importance
APOB_ITENDIQIALDDAK_779.9_632.3	143	118.0222045
SAMP_AYSDLSR_406.2_577.3	144	116.409429
AMBP_AFIQLWAFDAVK_704.9_836.4	145	116.1900846
EGLN_GPITSAAELNDPQSILLR_632.4_601.4	146	115.8438804
LRP1_NAVVQGLEQPHGLVVHPLR_688.4_890.6	147	114.539707
SHBG_VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4	148	113.1931134
IBP1_AQETSGEEISK_589.8_979.5	149	112.9902709
PSG6_SNPVTLNVLYGPDLPR_585.7_817.4	150	112.7910917
APOC3_DYWSTVK_449.7_347.2	151	112.544736
C1R_WILTAAHTLYPK_471.9_621.4	152	112.2199708
ANGT_ADSQAQLLLSTVVGVFTAPGLHLK_822.5_983.6	153	111.9634671
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_328.2	154	111.5743214
A1AT_AVLTIDEK_444.8_605.3	155	111.216651
PSGx_ILILPSVTR_506.3_785.5	156	110.8482935
THRB_ELLESYIDGR_597.8_710.4	157	110.7496103
SHBG_ALALPPLGLAPLLNLWAKPQGR_770.5_256.2	158	110.5091269
PZP_QTLSWTVTPK_580.8_545.3	159	110.4675104
SHBG_ALALPPLGLAPLLNLWAKPQGR_770.5_457.3	160	110.089808
PSG4_TLFIFGVTK_513.3_811.5	161	109.9039967
PLMN_YEFLNGR_449.7_293.1	162	109.6880397
PEPD_AVYEAVLR_460.8_587.4	163	109.3697285
PLMN_LSSPAVITDK_515.8_830.5	164	108.963353
FINC_SYTITGLQPGTDYK_772.4_352.2	165	108.452612
C1R_WILTAAHTLYPK_471.9_407.2	166	107.8348417
CHL1_TAVTANLDIR_537.3_288.2	167	107.7278897
TENA_AVDIPGLEAATPYR_736.9_286.1	168	107.6166195
CRP_YEVQGEVFTKPQLWP_911.0_293.1	169	106.9739589
APOB_SVSLPSLDPASAK_636.4_885.5	170	106.5901668
PRDX2_SVDEALR_395.2_488.3	171	106.2325046
CO8A_YHFEALADTGISSEFYDNANDLLSK_940.8_301.1	172	105.8963287
C1QC_FQSVFTVTR_542.8_722.4	173	105.4338742
PSGx_ILILPSVTR_506.3_559.3	174	105.1942655
VCAM1_TQIDSPLSGK_523.3_703.4	175	105.0091767
VCAM1_NTVISVNPSTK_580.3_845.5	176	104.8754444
CSH_ISLLLIESWLEPVR_834.5_500.3	177	104.6158295
HGFA_EALVPLVADHK_397.9_439.8	178	104.3383142
CGB1_CRPINATLAVEK_457.9_660.4	179	104.3378072
APOB_IEGNLIFDPNNYLPK_874.0_414.2	180	103.9849346

(continued)

Transition	Rank	Importance
C1QB_LEQGENVFLQATDK_796.4_822.4	181	103.9153207
APOH_EHSSLAFWK_552.8_838.4	182	103.9052103
CO5_LQGTLPVEAR_542.3_842.5	183	103.1061869
SHBG_IALGGLLFPASNLR_481.3_412.3	184	102.2490294
B2MG_VNHVTLSQPK_374.9_459.3	185	102.1204362
APOA2_SPELQAEAK_486.8_659.4	186	101.9166647
FLNA_TGVAVNKPAEFTVDAK_549.6_258.1	187	101.5207852
PLMN_YEFLNGR_449.7_606.3	188	101.2531011

Table 63. Random Forest Importance Values Using Peak Area Ratios

Variable	Rank	Importance
HABP2_FLNWIK_410.7_561.3	1	3501.905733
ADA12_FGFGGSTDSGPIR_649.3_946.5	2	3136.589992
A1BG_LLELTGPK_435.8_227.2	3	2387.891934
B2MG_VEHSDLSFSK_383.5_234.1	4	1431.31771
ADA12_FGFGGSTDSGPIR_649.3_745.4	5	1400.917331
B2MG_VEHSDLSFSK_383.5_468.2	6	1374.453629
APOB_IEGNLIFDPNNYLPK_874.0_414.2	7	1357.812445
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_960.5	8	1291.934596
A1BG_LLELTGPK_435.8_644.4	9	1138.712941
ITIH3_ALDLSLK_380.2_185.1	10	1137.127027
ENPP2_TYLHTYESEI_628.3_908.4	11	1041.036693
IL12B_YENYTSSFFIR_713.8_293.1	12	970.1662913
ENPP2_WWGGQPLWITATK_772.4_373.2	13	953.0631062
ENPP2_TYLHTYESEI_628.3_515.3	14	927.3512901
PSG9_LFIPQITR_494.3_614.4	15	813.9965357
MAGE	16	742.2425022
ENPP2_WWGGQPLWITATK_772.4_929.5	17	731.5206413
CERU_TTIEKPVWLGFLGPIIK_638.0_640.4	18	724.7745695
ITIH3_ALDLSLK_380.2_575.3	19	710.1982467
PSG2_IHPSYTNYR_384.2_452.2	20	697.4750893
ITIH1_LWAYLTIQELLAK_781.5_371.2	21	644.7416886
INHBE_ALVLELAK_428.8_331.2	22	643.008853
HGFA_LHKPGVYTR_357.5_692.4	23	630.8698445
TRFL_YYGYTGAFR_549.3_450.3	24	609.5866675
THBG_AVLHIGEK_289.5_348.7	25	573.9320948
GELS_TASDFITK_441.7_710.4	26	564.3288862

(continued)

Variable	Rank	Importance
PSG9_LFIPQITR_494.3_727.4	27	564.1749327
VGFR3_SGVDLADSNQK_567.3_662.3	28	563.8087791
INHA_TTSDGGYSFK_531.7_860.4	29	554.210214
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_328.2	30	545.1743627
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[0189]

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K.YIFHNFM*ER.L
R.FAHTVVTSR.V
R.FKPTLSQQQK.S
R.IHEDSDSALQLQDFYQEVANPLLTAVTFEYPSNAVEEVTQNNFR.L
R.MNFRPGVLSSR.Q
R.NVHSAGAAGSR.M
R.NVHSGSTFFK.Y
R.RLGVYELLLK.V
K.KLELHLPK.F
R.EIEEVLTPEMLMR.W
K.AATGECTATVGKR.S
K.LGQSLDCNAEVYVVPWEK.K
K.YNSQNQSNNQFVLYR.I
R.QVVAGLNFR.I
K.DLLLPQPDLR.Y
R.LHLEGNKLQVLGK.D
R.TLDLGENQLETLPPDLLR.G
K.GLQYAAQEGLLALQSELLR.I
K.LAEGFPLPLLK.R
K.SLEYLDLSFNQIAR.L
R.LKEDAVSAAFK.G
R.IVFENPDPSDGFVLIPDLK.W
R.VYFFK.G
K.WFDYLR.E
R.LTVGAAQVPAQLLVGALR.V
R.VSFSSPLVAISGVALR.S

K.GIVAAFYSGPSLSDKEK.L
R.WYVPVKDLLGIYEK.L
K.LQSLFDSPDFSK.I
R.ALYYDLISSPDIHGTYK.E
R.CLLFSFLPASSINDMEKR.F
K.FQPTLLTLPR.I
K.GVTSVSQIFHSPDLAIR.D
K.VIPACLPSPNYVVADR.T
R.FVTWIEGVMR.N
R.HSIFTPETNPR.A
K.GKEESLDSDLYAELR.C
K.MVLLEQLFLDHNALR.G
R.LVSLDSGLLNSLGALTELQFHR.N
K.ALLAYAFSLLGK.Q
K.DLFHCVSFTLPR.I
K.MLQITNTGFEMK.L
R.NELIPLIYLENPRR.N
R.SYIFIDEAHITQSLTWLSQMQK.D
R.SDPVTLNLLHGPDLPR.I
R.TLFLFGVTK.Y
R.ILILPSVTR.N
R.SDPVTLNLLPK.L
R.VLQLEK.Q
R.WAQGVGIPEDSIFTMADR.G
R.LTEREWADEWKHLDHALNCIMEMVEK.T
R.ALCGGDGAAALREPGAGLR.L
K.ALM*DLLAGKGSQGSQAPQALDR.T
K.MGDHLALEDYLTTDLVETWLR.N
K.SPQELLCGASLISDR.W
R.LAVTTHGLPCLAWASAQAK.A
R.SEGSSVNLSPPLEQCVPDR.G
R. SGIECQLWR. S
R.TATSEYQTFFNPR.T
R.VTGWGNLKETWTANVGK.G
R.IHLM*AGR.V
R.IHLMAGR.V
R.PAHPALR.L
K.ISNIIK.Q
K.M*KYWGVASFLQK.G
R.FSGTWYAM*AK.K
R.LLNLDGTCADSYSFVFSR.D
R.LLNNWDVCADMVGTFTDTEDPAKFK.M
R.LFLGALPGEDSSTSFCLNGLWAQGQR.L
K.DDWFMLGLR.D
R.SCDVESNPGIFLPPGTQAEFNLR.G
R.TWDPEGVIFYGDTNPKDDWFM*LGLR.D
R.TWDPEGVIFYGDTNPKDDWFMLGLR.D
R.KFCRDIQDPTQLAEMIFNLLLEEK.R
R.NELIRQEKLEQLAR.R
R.KNLSER.W
R.KWYNLMIQNK.D
K.SRLDTLAQEVALLK.E
K.RLDVNAAGIWEPKK.G
R.SILFLGK.V
R.ELISDLEHRLQGSVM*ELLQGVDGVIK.R
K.EDFTSLSLVLYSR.K
K.ELSSFIDKGQELCADYSENTFTEYK.K
K.ELSSFIDKGQELCADYSENTFTEYKK.K

K.EVVSLTEACCAEGADPDCYDTR.T
K.TAMDVFVCTYFMPAAQLPELPDVELPTNKDVCDPGNTK.V
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R.VCSQYAAYGEK.K
K.LIRDVWGIEGPIDAAFTR.I
R.DVWGIEGPIDAAFTR.I
R.ERVYFFK.G
R.FEDGVLDPDYPR.N
R.IYISGM*APRPSLAK.K
K.TRFLLR.T
K.HELTDEELQSLFTNFANWDK.C
R.NPFVFAPTLLTVAVHFEEVAK.S
K.ADLSGITGAR.N
K.MEEVEAMLLPETLKR.W
K.WEMPFDPQDTHQSR.F
R.LYGSEAFATDFQDSAAAK.K
K.HQFLLTGDTQGR.Y
K.NGVAQEPVHLDSPAIK.H
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K.VTLTCVAPLSGVDFQLRR.G
R.C*EGPIPDVTFELLR.E
R.C*LAPLEGAR.F
R.CLAPLEGAR.F
R.GVTFLLR.R
R.LHDNQNGWSGDSAPVELILSDETLPAPEFSPEPESGR.A
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K.HQM*DLVATLSQLGLQELFQAPDLR.G
R.LCQDLGPGAFR.L
R.WFLLEQPEIQVAHFPFK.N
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K.QPFVQGLALYTPVVLPR.S
R.AAM*VGM*LANFLGFR.I
K.LVPFATELHER.L
R.LLPHANEVSQK.I
R.SLAPYAQDTQEKLNHQLEGLTFQMK.K
K.FPEVDVLTK.Y
K.HINIDQFVR.K
K.LLSGGNTLHLVSTTK.T
K.Q*VFLYPEKDEPTYILNIKR.G
K.QVFLYPEKDEPTYILNIKR.G
K.SLHMYANR.L
K.SVSDGIAALDLNAVANK.I
K.SVSLPSLDPASAKIEGNLIFDPNNYLPK.E
K.TEVIPPLIENR.Q
K.VLVDHFGYTK.D
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R.GWVTDGFSSLKDYWSTVK.D
R.GEVQAMLGQSTEELR.V
R.LAVYQAGAR.E
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K.FICPLTGLWPINTLK.C
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K.MWSMTLGLHPWIANIDDTQYLAAK.R

K.VFQYIDLHQDEFVQTLK.E
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K.AEEEHLGILGPQLHADVGDKVK.I
K.ALYLQYTDETFR.T
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R.HYYIAAEEIIWNYAPSGIDIFTK.E
R.IYHSHIDAPK.D
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R.QKDVDKEFYLFPTVFDENESLLLEDNIR.M
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R.SALVLQYLR.V
K.EFNPLVIVGLSK.D
R.NPDNDIRPWCFVLNR.D
R.VVGGLVALR.G
K.NSLLGMEGANSIFSGFLLFPDMEA.-
K.VPGLYYFTYHASSR.G
R.Q*THQPPAPNSLIR.F
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K.RNDYLDIYAIGVGK.L
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K.FACYYPR.V
K.LHLETDSLALVALGALDTALYAAGSK.S
K.LVNGQSHISLSK.A
K.M*RPSTDTITVMVENSHGLR.V
K.MRPSTDTITVMVENSHGLR.V
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R.DLLYIGK.D
R.GDSGGPLIVHK.R
R.LEDSVTYHCSR.G
R.LPPTTTCQQQK.E
K.CLHPCVISR.E
K.CTSTGWIPAPR.C
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K.ITFELVYEELLKR.R
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K.TAFISDFAVTADGNAFIGDIKDK.V
R. GHMLENHVER. L
R.GM*ADQDGLKPTIDKPSEDSPPLEMLGPR.R
R.LWAYLTIQELLAK.R
R.NHM*QYEIVIK.V
K.AHVSFKPTVAQQR.I

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K.YGFYTHVFR.L
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K.KDPEGLFLQDNIVAEFSVDETGQMSATAK.G
K.AQWANPFDPSKTEDSSSFLIDK.T
K.GWVDLFVPK.F
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R.SFMLLILER.S
K.EFSHLGKEDFTSLSLVLYSR.K
K.EYANQFM*WEYSTNYGQAPLSLLVSYTK.S
K.HQPQEFPTYVEPTNDEICEAFRK.D
K.SYLSM*VGSCCTSASPTVCFLK.E
K.TAM*DVFVCTYFMPAAQLPELPDVELPTNK.D
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K.EQLSLLDR.F

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R.EIGELYLPK.F
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R.NLAVSQVVHK.A
K.AAISGENAGLVR.A
K.GSLVQASEANLQAAQDFVR.G
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K.VTYDVSR.D
R.EVAFDLEIPK.T
R.LWAYLTIQELLAK.R
K.FYNQVSTPLLR.N
K.HLEVDVWVIEPQGLR.F
K.TAGLVR.S
R.IYLQPGR.L
R.LSNENHGIAQR.I
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K.AQWANPFDPSK.T
K.AVLHIGEK.G
K.FLNDVK.T
K.FSISATYDLGATLLK.M
K.GWVDLFVPK.F
K.NALALFVLPK.E
R.SILFLGK.V
R.DFNQFSSGEK.N
K.GYQELLEK.C
K.GEEELQK.Y
K.FIYEIAR.R

R.HPFLYAPTILLWAAR.Y
R.TFQAITVTK.L
K.LTTLER.G
R.HPQLAVSVILR.V
K.LGEYYLQNAFLVAYTK.K
R.ILPSVPK.D
K.AEHPTWGDEQLFQTTR.L
R.LILIGETIK.I
R.LQPFNEYR.K
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QLYGDTGVLGR_589.8_501.3
VNHVTLSQPK_374.9_459.3
TLLPVSKPEIR_418.3_288.2
SEYGAALAWEK_612.8_845.5
YGIEEHGK_311.5_341.2
DAGLSWGSAR_510.3_390.2
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FQSVFTVTR_542.8_623.4
VPGLYYFTYHASSR_554.3_420.2
AYSDLSR_406.2_577.3
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NAVVQGLEQPHGLVVHPLR_688.4_890.6
TSDQIHFFFAK_447.6_659.4
GTYLYNDCPGPGQDTDCR_697.0_335.2
TSYQVYSK_488.2_787.4
ALNSIIDVYHK_424.9_774.4
VELAPLPSWQPVGK_760.9_342.2
LSETNR_360.2_330.2
HFQNLGK_422.2_527.2
ELPQSIVYK_538.8_417.7
LPATEKPVLLSK_432.6_347.2
SPEAEDPLGVER_649.8_314.1
DEIPHNDIALLK_459.9_510.8
FFQYDTWK_567.8_712.3
LIEIANHVDK_384.6_498.3
AGFAGDDAPR_488.7_701.3
YEFLNGR_449.7_606.3
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SLSQQIENIR_594.3_531.3
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LDFHFSSDR_375.2_464.2
IPSNPSHR_303.2_496.3
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EVFSKPISWEELLQ_852.9_376.2
YENYTSSFFIR_713.8_756.4
SPQAFYR_434.7_556.3
SVDEALR_395.2_488.3
FVFGTTPEDILR_697.9_742.4

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HYGGLTGLNK_530.3_759.4
NQSPVLEPVGR_598.3_866.5
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VFQFLEK_455.8_811.4
VLEPTLK_400.3_458.3
SLDFTELDVAAEK_719.4_316.2
TLAFVR_353.7_492.3
YGIEEHGK_311.5_599.3
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LLAPSDSPEWLSFDVTGVVR_730.1_430.3
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YGIEEHGK_311.5_341.2
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TLAFVR_353.7_492.3
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EVFSKPISWEELLQ_852.9_376.2
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YISPDQLADLYK_713.4_277.2
TLPFSR_360.7_506.3
SPEAEDPLGVER_649.8_314.1
ALEQDLPVNIK_620.4_798.5
YSHYNER_323.5_418.2
VGVISFAQK_474.8_580.3
LQDAGVYR_461.2_680.3
AEIEYLEK_497.8_389.2
TSYQVYSK_488.2_787.4
SWLIPLGAVDDGEHSQNEK_703.0_798.4
ALEQDLPVNIK_620.4_570.4
ILDGGNK_358.7_603.3
AVYEAVLR_460.8_587.4
AEIEYLEK_497.8_552.3
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TGVAVNKPAEFTVDAK_549.6_258.1
AYSDLSR_406.2_375.2
LIEIANHVDK_384.6_683.4
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ILDGGNK_358.7_603.3
VGVISFAQK_474.8_580.3
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TEQAAVAR_423.2_615.4
SGVDLADSNQK_567.3_662.3
VLSSIEQK_452.3_691.4
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TSYQVYSK_488.2_787.4
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TAVTANLDIR_537.3_288.2
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TASDFITK_441.7_781.4
SPQAFYR_434.7_556.3
NHYTESISVAK_624.8_415.2
LTTVDIVTLR_565.8_815.5
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CO6_DLHLSDVFLK_396.2_366.2
VCAM1_TQIDSPLSGK_523.3_816.5
LRP1_NAWQGLEQPHGLVVHPLR_688.4_285.2
CBG_QINSYVK_426.2_496.3
CO6_ENPAVIDFELAPIVDLVR_670.7_811.5
ADA12_FGFGGSTDSGPIR_649.3_745.4
CO6_DLHLSDVFLK_396.2_260.2
ENPP2_TYLHTYESEI_628.3_908.4

A1BG_LLELTGPK_435.8_227.2
FRIH_QNYHQDSEAAINR_515.9_544.3
ENPP2_TEFLSNYLTNVDDITLVPGTLGR_846.8_600.3
CBG_WSAGLTSSQVDLYIPK_883.0_515.3
C1QC_FQSVFTVTR_542.8_623.4
GELS_DPDQTDGLGLSYLSSHIANVER_796.4_456.2
A1BG_ATWSGAVLAGR_544.8_643.4
APOA1_AKPALEDLR_506.8_813.5
ENPP2_TYLHTYESEI_628.3_515.3
PEPD_AVYEAVLR_460.8_750.4
TIMP1_GFQALGDAADIR_617.3_717.4
ADA12_LIEIANHVDK_384.6_498.3
PGRP2_WGAAPYR_410.7_577.3
PSG9_LFIPQITR_494.3_614.4
HABP2_FLNWIK_410.7_560.3
CBG_WSAGLTSSQVDLYIPK_883.0_357.2
PSG2_IHPSYTNYR_384.2_452.2
PSG5_LSIPQITTK_500.8_800.5
HABP2_FLNWIK_410.7_561.3
CO6_SEYGAALAWEK_612.8_788.4
ADA12_LIEIANHVDK_384.6_683.4
EGLN_TQILEWAAER_608.8_632.3
CO6_ENPAVIDFELAPIVDLVR_670.7_601.4
FA7_FSLVSGWGQLLDR_493.3_447.3
ITIH3_ALDLSLK_380.2_575.3
ADA12_FGFGGSTDSGPIR_649.3_946.5
FETUA_AALAAFNAQNNGSNFQLEEISR_789.1_746.4
FBLN1_AITPPHPASQANIIFDITEGNLR_825.8_459.3
TSP1_FVFGTTPEDILR_697.9_843.5
VCAM1_NTVISVNPSTK_580.3_732.4
ENPP2_TEFLSNYLTNVDDITLVPGTLGR_846.8_699.4
FBLN3_ELPQSIVYK_538.8_409.2
ACTB_VAPEEHPVLLTEAPLNPK_652.0_892.5
TSP1_FVFGTTPEDILR_697.9_742.4
PLMN_EAQLPVIENK_570.8_699.4
C1S_IIGGSDADIK_494.8_260.2
IL1A_ANDQYLTAAALHNLDEAVK_686.4_317.2
PGRP2_WGAAPYR_410.7_634.3
PSG5_LSIPQITTK_500.8_687.4
PSG6_SNPVTLNVLYGPDLPR_585. 7_654.4
PRG2_WNFAYWAAHQPWSR_607.3_545.3
CXCL2_CQCLQTLQGIHLK_13p8RT_533.6_567.4
CXCL2_CQCLQTLQGIHLK_13p48RT_533.6_695.4
G6PE_LLDFEFSSGR_585.8_553.3
GELS_TASDFITK_441.7_710.4
B2MG_VEHSDLSFSK_383.5_468.2
CO8B-IPGIFELGISSQSDR_809.9_849.4
PSG8_LQLSETNR_480.8-606.3
LBP_GLQYAAQEGLLALQSELLR_1037.1_929.5
AFAM_LPNNVLQEK_527.8_844.5
MAGE
PSG2_IHPSYTNYR_384.2_338.2
PSG9_LFIPQITR_494.3_727.4
TFR1_YNSQLLSFVR_613.8_734.5
C1R_QRPPDLDTSSNAVDLLFFTDESGDSR_961.5_866.3
PGH1_ILPSVPK_377.2_264.2
FA7_SEPRPGVLLR_375.2_454.3
FA7_TLAFVR_353.7_274.2

PGRP2_DGSPDVTTADIGANTPDATK_973.5_844.4
C1S_IIGGSDADIK_494.8_762.4
PEPD_VPLALFALNR_557.3_620.4
C1S_EDTPNSVWEPAK_686.8_630.3
CHL1_TAVTANLDIR_537.3_802.4
CHL1_VIAVNEVGR_478.8_744.4
SDF1_ILNTPNCALQIVAR_791.9_341.2
PAI1_EVPLSALTNILSAQLISHWK_740.8_996.6
AMBP_AFIQLWAFDAVK_704.9_650.4
G6PE_LLDFEFSSGR_585.8_944.4
THBG_SILFLGK_389.2_577.4
PRDX2_GLFIIDGK_431.8_545.3
ENPP2_WWGGQPLWITATK_772.4_373.2
VGFR3_SGVDLADSNQK_567.3_662.3
C1S_EDTPNSVWEPAK_686.8_315.2
AFAM_DADPDTFFAK_563.8_302.1
CBG_SETEIHQGFQHLHQLFAK_717.4_447.2
C1S_LLEVPEGR_456.8_686.4
PTGDS_GPGEDFR_389.2_623.3
ITIH2_IYLQPGR_423.7_329.2
FA7_TLAFVR_353.7_492.3
FA7_FSLVSGWGQLLDR_493.3_403.2
SAMP_VGEYSLYIGR_578.8_871.5
APOH_EHSSLAFWK_552.8_267.1
PGRP2_AGLLRPDYALLGHR_518.0_595.4
C1QC_FNAVLTNPQGDYDTSTGK_964.5_333.2
PGRP2_AGLLRPDYALLGHR_518.0_369.2
PGRP2_TFTLLDPK_467.8_686.4
CO5_TDAPDLPEENQAR_728.3_843.4
HRB_ELLESYIDGR_597.8_839.4
GELS_DPDQTDGLGLSYLSSHIANVER_796.4_328.1
TRFL_YYGYTGAFR_549.3_450.3
HEMO_QGHNSVFLIK_381.6_260.2
C1S_GDSGGAFAVQDPNDK_739.3_716.3
B1A4H9_AHQLAIDTYQEFR_531. 3_450.3
C1S_SSNNPHSPIVEEFQVPYNK_729.4_261.2
HYOU1_LPATEKPVLLSK_432.6_347.2
FETA_GYQELLEK_490.3_502.3
LRP1_SERPPIFEIR_415.2_288.2
CO6_SEYGAALAWEK_612.8_845.5
CERU_TTIEKPVWLGFLGPIIK_638.0_844.5
IBP1_AQETSGEEISK_589.8_850.4
SHBG_VVLSSGSGPGLDLPLVLGLPLQLK_791.5_768.5
CBG_SETEIHQGFQHLHQLFAK_717.4_318.1
A1AT_LSITGTYDLK_555.8_696.4
PGRP2_DGSPDVTTADIGANTPDATK_973.5_531.3
C1QB_LEQGENVFLQATDK_796.4_675.4
EGLN_GPITSAAELNDPQSILLR_632.4_826.5
IL12B_YENYTSSFFIR_713.8_293.1
B2MG_VEHSDLSFSK_383.5_234.1
PGH1_AEHPTWGDEQLFQTTR_639.3_765.4
INHBE_ALVLELAK_428.8_331.2
HYOU1_LPATEKPVLLSK_432.6_460.3
CXCL2_CQCLQTLQGIHLK_13p48RT_533.6_567.4
PZP_AVGYLITGYQR_620.8_523.3
AFAM_IAPQLSTEELVSLGEK_857.5_333.2
ICAM1_VELAPLPSWQPVGK_760.9_400.3
CHL1_VIAVNEVGR_478.8_284.2

APOB_ITENDIQIALDDAK_779.9_632.3
SAMP_AYSDLSR_406.2_577.3
AMBP_AFIQLWAFDAVK_704.9_836.4
EGLN_GPITSAAELNDPQSILLR_632.4_601.4
LRP1_NAVVQGLEQPHGLVVHPLR_688.4_890.6
SHBG_VVLSSGSGPGLDLPLVLGLPLQLK_791.5_598.4
IBP1_AQETSGEEISK_589.8_979.5
PSG6_SNPVTLNVLYGPDLPR_585.7_817.4
APOC3_DYWSTVK_449.7_347.2
C1R_WILTAAHTLYPK_471.9_621.4
ANGT_ADSQAQLLLSTVVGVFTAPGLHLK_822.5_983.6
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_328.2
A1AT_AVLTIDEK_444.8_605.3
PSGx_ILILPSVTR_506.3_785.5
THRB_ELLESYIDGR_597.8_710.4
SHBG_ALALPPLGLAPLLNLWAKPQGR_770.5_256.2
PZP_QTLSWTVTPK_580.8_545.3
SHBG_ALALPPLGLAPLLNLWAKPQGR_770.5_457.3
PSG4_TLFIFGVTK_513.3_811.5
PLMN_YEFLNGR_449.7_293.1
PEPD_AVYEAVLR_460.8_587.4
PLMN_LSSPAVITDK_515.8_830.5
FINC_SYTITGLQPGTDYK_772.4_352.2
C1R_WILTAAHTLYPK_471.9_407.2
CHL1_TAVTANLDIR_537.3_288.2
TENA_AVDIPGLEAATPYR_736.9_286.1
CRP_YEVQGEVFTKPQLWP_911.0_293.1
APOB_SVSLPSLDPASAK_636.4_885.5
PRDX2_SVDEALR_395.2_488.3
CO8A_YHFEALADTGISSEFYDNANDLLSK_940.8_301.1
C1QC_FQSVFTVTR_542.8_722.4
PSGx_ILILPSVTR_506.3_559.3
VCAM1_TQIDSPLSGK_523.3_703.4
VCAM1_NTVISVNPSTK_580.3_845.5
CSH_ISLLLIESWLEPVR_834.5_500.3
HGFA_EALVPLVADHK_397.9_439.8
CGB1_CRPINATLAVEK_457.9_660.4
APOB_IEGNLIFDPNNYLPK_874.0_414.2
C1QB_LEQGENVFLQATDK_796.4_822.4
APOH_EHSSLAFWK_552.8_838.4
CO5_LQGTLPVEAR_542.3_842.5
SHBG_IALGGLLFPASNLR_481.3_412.3
B2MG_VNHVTLSQPK_374.9_459.3
APOA2_SPELQAEAK_486.8_659.4
FLNA_TGVAVNKPAEFTVDAK_549.6_258.1
PLMN_YEFLNGR_449.7_606.3
HABP2_FLNWIK_410.7_561.3
ADA12_FGFGGSTDSGPIR_649.3_946.5
A1BG_LLELTGPK_435.8_227.2
B2MG_VEHSDLSFSK_383.5_234.1
ADA12_FGFGGSTDSGPIR_649.3_745.4
B2MG_VEHSDLSFSK_383.5_468.2
APOB_IEGNLIFDPNNYLPK_874.0_414.2
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_960.5
A1BG_LLELTGPK_435.8_644.4
ITIH3_ALDLSLK_380.2_185.1
ENPP2_TYLHTYESEI_628.3_908.4
IL12B_YENYTSSFFIR_713.8_293.1

ENPP2_WWGGQPLWITATK_772.4_373.2
ENPP2_TYLHTYESEI_628.3_515.3
PSG9_LFIPQITR_494.3_614.4
MAGE
ENPP2_WWGGQPLWITATK_772.4_929.5
CERU_TTIEKPVWLGFLGPIIK_638.0_640.4
ITIH3_ALDLSLK_380.2_575.3
PSG2_IHPSYTNYR_384.2_452.2
ITIH1_LWAYLTIQELLAK_781.5_371.2
INHBE_ALVLELAK_428.8_331.2
HGFA_LHKPGVYTR_357.5_692.4
TRFL_YYGYTGAFR_549.3_450.3
THBG_AVLHIGEK_28 9.5_34 8.7
GELS_TASDFITK_441.7_710.4
PSG9_LFIPQITR_494.3_727.4
VGFR3_SGVDLADSNQK_567.3_662.3
INHA_TTSDGGYSFK_531.7_860.4
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_328.2
HYOU1_LPATEKPVLLSK_432.6_347.2
CO8G_VQEAHLTEDQIFYFPK_655.7_701.4
BMI
HGFA_LHKPGVYTR_357.5_479.3
PSG2_IHPSYTNYR_384.2_338.2
GELS_AQPVQVAEGSEPDGFWEALGGK_758.0_623.4
PSG6_SNPVTLNVLYGPDLPR_585.7_654.4
HABP2_FLNWIK_410.7_560.3
PGH1_ILPSVPK_377.2_527.3
HYOU1_LPATEKPVLLSK_432.6_460.3
CO6_ALNHLPLEYNSALYSR_621.0_696.4
INHBE_ALVLELAK_428.8_672.4
PLMN_LSSPAVITDK_515.8_743.4
PSG9_DVLLLVHNLPQNLPGYFWYK_810.4_215.1
BGH3_LTLLAPLNSVFK_658.4_875.5
AFAM_LPNNVLQEK_527.8_730.4
ITIH2_LSNENHGIAQR_413.5_519.8
GELS_TASDFITK_441.7_781.4
FETUA_AHYDLR_387.7_566.3
CERU_TTIEKPVWLGFLGPIIK_638.0_844.5
PSGx_ILILPSVTR_506.3_785.5
APOB_SVSLPSLDPASAK_636.4_885.5
FLNA_TGVAVNKPAEFTVDAK_549.6_258.1
PLMN_YEFLNGR_449.7_606.3
PSGx_ILILPSVTR_506.3_559.3

Claims

1. An isolated biomarker consisting of the sequence IALGGLLFPASNLR.

2. A method of determining probability for preterm birth or term birth in a pregnant female, the method comprising:

   detecting a measurable feature of each of one or more biomarkers in a biological sample obtained from said pregnant female, and
   analyzing said measurable feature to determine the probability for preterm birth or term birth in said pregnant female,
   wherein the one or more biomarkers comprise a biomarker consisting of the sequence IALGGLLFPASNLR;
   wherein said measurable feature is defined as the presence, absence, or concentration of the biomarker, or a fragment thereof; an altered structure, such as the presence or amount of a post-translational modification; or

the presence of an altered conformation in comparison to the conformation of the biomarker in normal control subj ects; and
wherein the fragment comprises at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 consecutive amino acid residues.

3. A method of predicting gestational age at birth (GAB) or time to birth in a pregnant female, the method comprising:

detecting a measurable feature of each of one or more biomarkers in a biological sample obtained from said pregnant female, and
analyzing said measurable feature to predict GAB or time to birth in said pregnant female,
wherein the one or more biomarkers comprise a biomarker consisting of the sequence IALGGLLFPASNLR;
wherein said measurable feature is defined as the presence, absence, or concentration of the biomarker, or a fragment thereof; an altered structure, such as the presence or amount of a post-translational modification; or the presence of an altered conformation in comparison to the conformation of the biomarker in normal control subj ects; and
wherein the fragment comprises at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 consecutive amino acid residues.

4. The method according to claim 2 further comprising:

(a) quantifying an amount of the one or more biomarkers;
(b) multiplying said amount by a predetermined coefficient, and
(c) determining the probability for preterm birth in the pregnant female comprising adding said individual products to obtain a total risk score that corresponds to said probability.

5. The method according to claims 2 or 4, wherein said analyzing of said measurable feature initially comprises prediction of gestational age at birth (GAB) prior to said determining the probability for preterm birth;
optionally wherein said prediction of the GAB is used to determine the probability for preterm birth.

6. The method according to claim 3 further comprising:

(a) quantifying an amount of the one or more biomarkers;
(b) multiplying and/or thresholding said amount by a predetermined coefficient;
(c) determining the predicted GAB in the pregnant female, the determination comprising adding said individual products to obtain a total risk score that corresponds to said predicted GAB; and optionally
(d) subtracting the estimated gestational age (GA) at the time the biological sample was obtained from the predicted GAB to predict time to birth in said pregnant female.

7. The method according to any of claims 2 to 6, wherein the method further comprises calculating the probability for preterm birth or term birth, or GAB, or time to birth in said pregnant female based on quantifying an amount of each of the one or more biomarkers.

8. The method according to any of claims 2 to 7, wherein said analyzing comprises a use of a predictive model; optionally wherein said analyzing comprises comparing the measurable feature with a reference feature.

9. The method according to claim 8, wherein said analyzing comprises using one or more of: a linear discriminant analysis model, a support vector machine classification algorithm, a recursive feature elimination model, a prediction analysis of microarray model, a logistic regression model, a multiple regression model, a survival model, a CART algorithm, a flex tree algorithm, a LART algorithm, a random forest algorithm, a MART algorithm, a machine learning algorithm, a penalized regression method, and a combination thereof.

10. The method according to any of claims 2 to 9, wherein the biological sample is selected from the group consisting of whole blood, plasma, and serum.

11. The method according to any of claims 4 to 10, wherein said quantifying comprises mass spectrometry (MS) or liquid chromatography-mass spectrometry (LC-MS).

12. The method according to claim 11, wherein said MS comprises multiple reaction monitoring (MRM) or selected reaction monitoring (SRM); optionally wherein said MRM or SRM comprises scheduled MRM or SRM

13. The method according to any of claims 4 to 10, wherein said quantifying comprises an assay that utilizes a capture agent.

14. The method according to claim 13, wherein:

said capture agent is selected from the group consisting of an antibody, antibody fragment, nucleic acid-based protein binding reagent, and small molecule or variant thereof; and/or
said assay is selected from the group consisting of enzyme immunoassay (EIA), enzyme-linked immunosorbent assay (ELISA), and radioimmunoassay (RIA); and/or
said quantifying further comprises mass spectrometry (MS) or co-immunoprecipitation-mass spectrometry (co-IP MS).

15. The method according to any of claims 2 to 14, further comprising detecting one or more risk indicia;
optionally wherein the one or more risk indicia are selected from the group consisting of age, prior pregnancy, history of previous low birth weight or preterm delivery, multiple second trimester spontaneous abortion, prior first trimester induced abortion, familial and intergenerational factors, history of infertility, nulliparity, placental abnormalities, cervical and uterine anomalies, gestational bleeding, intrauterine growth restriction, in utero diethylstilbestrol exposure, multiple gestations, infant sex, short stature, low prepregnancy weight/low body mass index, diabetes, hypertension, hypothyroidism, asthma, education level, tobacco use, and urogenital infections.

Patentansprüche

1. Isolierter Biomarker, bestehend aus der Sequenz IALGGLLFPASNLR.

2. Verfahren zum Bestimmen der Wahrscheinlichkeit einer Frühgeburt oder einer Reifgeburt bei einer schwangeren Frau, wobei das Verfahren umfasst:

Nachweisen eines messbaren Merkmals jedes von einem oder mehreren Biomarkern in einer biologischen Probe, die von der schwangeren Frau gewonnen wurde, und
Analysieren des messbaren Merkmals, um die Wahrscheinlichkeit einer Frühgeburt oder einer Reifgeburt bei der schwangeren Frau zu bestimmen, wobei der eine oder die mehreren Biomarker einen Biomarker umfassen, der aus der Sequenz IALGGLLFPASNLR besteht;
wobei das messbare Merkmal definiert ist als das Vorhandensein, das Fehlen oder die Konzentration des Biomarkers oder eines Fragments davon; eine veränderte Struktur, wie beispielsweise das Vorhandensein oder die Menge einer posttranslationalen Modifikation; oder das Vorhandensein einer veränderten Konformation im Vergleich zur Konformation des Biomarkers bei normalen Kontrollpersonen; und
wobei das Fragment mindestens 5, mindestens 6, mindestens 7, mindestens 8, mindestens 9, mindestens 10, mindestens 11, mindestens 12 oder mindestens 13 aufeinanderfolgende Aminosäurereste umfasst.

3. Verfahren zur Vorhersage des Gestationsalters bei der Geburt (GAB) oder der Zeit bis zur Geburt bei einer schwangeren Frau, wobei das Verfahren umfasst:

Nachweisen eines messbaren Merkmals jedes von einem oder mehreren Biomarkern in einer biologischen Probe, die von der schwangeren Frau gewonnen wurde, und
Analysieren des messbaren Merkmals, um das GAB oder die Zeit bis zur Geburt bei der schwangeren Frau vorherzusagen,
wobei der eine oder die mehreren Biomarker einen Biomarker umfassen, der aus der Sequenz IALGGLLFPASNLR besteht;
wobei das messbare Merkmal definiert ist als das Vorhandensein, das Fehlen oder die Konzentration des Biomarkers oder eines Fragments davon;
eine veränderte Struktur, wie beispielsweise das Vorhandensein oder die Menge einer posttranslationalen Modifikation; oder das Vorhandensein einer veränderten Konformation im Vergleich zur Konformation des Biomarkers bei normalen Kontrollpersonen; und
wobei das Fragment mindestens 5, mindestens 6, mindestens 7, mindestens 8, mindestens 9, mindestens 10, mindestens 11, mindestens 12 oder mindestens 13 aufeinanderfolgende Aminosäurereste umfasst.

4. Verfahren nach Anspruch 2, weiter umfassend:

(a) Quantifizieren einer Menge des einen oder der mehreren Biomarker;
(b) Multiplizieren der Menge mit einem vorbestimmten Koeffizienten, und
(c) Bestimmen der Wahrscheinlichkeit für eine Frühgeburt bei der schwangeren Frau, umfassend das Hinzufügen der einzelnen Produkte, um einen Gesamtrisikowert zu gewinnen, der der Wahrscheinlichkeit entspricht.

5. Verfahren nach den Ansprüchen 2 oder 4, wobei die Analyse des messbaren Merkmals zunächst die Vorhersage des Gestationsalters bei der Geburt (GAB) vor dem Bestimmen der Wahrscheinlichkeit für eine Frühgeburt umfasst; optional wobei die Vorhersage des GAB verwendet wird, um die Wahrscheinlichkeit für eine Frühgeburt zu bestimmen.

6. Verfahren nach Anspruch 3, weiter umfassend:

(a) Quantifizieren einer Menge des einen oder der mehreren Biomarker;
(b) Multiplizieren und/oder Schwellenwertbildung des Betrags mit einem vorbestimmten Koeffizienten;
(c) Bestimmen des vorhergesagten GAB bei der schwangeren Frau, wobei die Bestimmung das Hinzufügen der einzelnen Produkte umfasst, um einen Gesamtrisikowert zu gewinnen, der dem vorhergesagten GAB entspricht; und optional
(d) Subtrahieren des geschätzten Gestationsalters (GA) zum Zeitpunkt der Gewinnung der biologischen Probe von dem vorhergesagten GAB, um die Zeit bis zur Geburt bei der schwangeren Frau vorherzusagen.

7. Verfahren nach einem der Ansprüche 2 bis 6, wobei das Verfahren ferner das Berechnen der Wahrscheinlichkeit für eine Frühgeburt oder eine Reifgeburt oder ein GAB oder eine Zeit bis zur Geburt bei der schwangeren Frau, basierend auf dem Quantifizieren einer Menge von jedem der einen oder mehreren Biomarker, umfasst.

8. Verfahren nach einem der Ansprüche 2 bis 7, wobei das Analysieren die Verwendung eines Prognosemodells umfasst; optional wobei das Analysieren ein Vergleichen des messbaren Merkmals mit einem Referenzmerkmal umfasst.

9. Verfahren nach Anspruch 8, wobei das Analysieren die Verwendung umfasst von einem oder mehreren von: einem linearen Diskriminanzanalysemodell, einem Unterstützungsvektor-Maschinenklassifikationsalgorithmus, einem rekursiven Merkmalseliminierungsmodell, einer Vorhersageanalyse des Microarray-Modells, einem logistischen Regressionsmodell, einem multiplen Regressionsmodell, einem Überlebensmodell, einem CART-Algorithmus, einem Flex-Tree-Algorithmus, einem LART-Algorithmus, einem Random-Forest-Algorithmus, einem MART-Algorithmus, einem maschinellen Lernalgorithmus, einem bestraften Regressionsverfahren und einer Kombination davon.

10. Verfahren nach einem der Ansprüche 2 bis 9, wobei die biologische Probe ausgewählt ist aus der Gruppe bestehend aus Vollblut, Plasma und Serum.

11. Verfahren nach einem der Ansprüche 4 bis 10, wobei die Quantifizierung eine Massenspektrometrie (MS) oder eine Flüssigchromatographie-Massenspektrometrie (LC-MS) umfasst.

12. Verfahren nach Anspruch 11, wobei die MS eine Mehrfachreaktionsüberwachung (MRM) oder eine ausgewählte Reaktionsüberwachung (SRM) umfasst; optional, wobei die MRM oder SRM eine geplante MRM oder SRM umfasst.

13. Verfahren nach einem der Ansprüche 4 bis 10, wobei die Quantifizierung einen Assay umfasst, der ein Erfassungsmittel verwendet.

14. Verfahren nach Anspruch 13, wobei:

das Einfangmittel ausgewählt ist aus der Gruppe bestehend aus einem Antikörper, einem Antikörperfragment, einem nukleinsäurebasierten Proteinbindungsreagenz, und einem kleinen Molekül oder einer Variante davon; und/oder
der Assay ausgewählt ist aus der Gruppe bestehend aus einem Enzymimmunoassay (EIA), einem enzymgebundenem Immunosorbentassay (ELISA) und einem Radioimmunoassay (RIA); und/oder
die Quantifizierung ferner eine Massenspektrometrie (MS) oder eine Ko-Immunoprezipitations-Massenspektrometrie (Co-IP MS) umfasst.

15. Verfahren nach einem der Ansprüche 2 bis 14, ferner umfassend das Nachweisen eines oder mehrerer Risikokennzeichen;
optional wobei das eine oder die mehreren Risikokennzeichen ausgewählt sind aus der Gruppe bestehend aus Alter, vorheriger Schwangerschaft, Anamnese eines früheren niedrigen Geburtsgewichts oder einer Frühgeburt, mehrfachen Spontanaborten im zweiten Trimester, früherem im ersten Trimester induziertem Abort, familiären und intergenerationellen Faktoren, Anamnese der Unfruchtbarkeit, Nulliparität, Anomalien der Plazenta, Gebärmutterhals- und Gebärmutteranomalien, Schwangerschaftsblutungen, intrauteriner Wachstumsretardierung, Belastung mit Diethylstilbestrol in utero, Mehrlingsschwangerschaften, Geschlecht des Kindes, Kleinwuchs, niedrigem Schwangerschaftsgewicht / niedrigem Körpermassenindex, Diabetes, Bluthochdruck, Hypothyreose, Asthma, Bildungsniveau, Tabakkonsum und Urogenitalinfektionen.

Revendications

1. Biomarqueur isolé constituer de la séquence IALGGLLFPASNLR.

2. Procédé de détermination d'une probabilité d'une naissance prématurée ou d'une naissance à terme chez une femme enceinte, le procédé comprenant:

détecter une caractéristique mesurable de chacun d'un ou plusieurs biomarqueurs dans un échantillon biologique obtenu à partir de ladite femme enceinte, et
analyser ladite caractéristique mesurable pour déterminer la probabilité d'une naissance prématurée ou d'une naissance à terme chez ladite femme enceinte,
dans lequel l'un ou plusieurs biomarqueurs comprennent un biomarqueur consistant en la séquence IALGGLLFPASNLR;
dans lequel ladite caractéristique mesurable est définie comme la présence, l'absence, ou la concentration du biomarqueur, ou d'un fragment de celui-ci; une structure altérée, telle que la présence ou la quantité d'une modification post-translationnelle; ou la présence d'une conformation altérée en comparaison à la conformation du biomarqueur chez des sujets témoins normaux; et
dans lequel le fragment comprend au moins 5, au moins 6, au moins 7, au moins 8, au moins 9, au moins 10, au moins 11, au moins 12, ou au moins 13 résidus d'acides aminés consécutifs.

3. Procédé de prédiction d'un âge gestationnel à la naissance (GAB) ou d'un temps jusqu'à la naissance chez une femme enceinte, le procédé comprenant:

détecter une caractéristique mesurable de chacun d'un ou plusieurs biomarqueurs dans un échantillon biologique obtenu à partir de ladite femme enceinte, et
analyser ladite caractéristique mesurable pour prédire un GAB ou un temps jusqu'à la naissance chez ladite femme enceinte,
dans lequel l'un ou plusieurs biomarqueurs comprennent un biomarqueur consistant en la séquence IALGGLLFPASNLR;
dans lequel ladite caractéristique mesurable est définie comme la présence, l'absence, ou la concentration du biomarqueur, ou d'un fragment de celui-ci; une structure altérée, telle que la présence ou la quantité d'une modification post-translationnelle;
ou la présence d'une conformation altérée en comparaison à la conformation du biomarqueur chez des sujets témoins normaux; et
dans lequel le fragment comprend au moins 5, au moins 6, au moins 7, au moins 8, au moins 9, au moins 10, au moins 11, au moins 12, ou au moins 13 résidus d'acides aminés consécutifs.

4. Procédé selon la revendication 2 comprenant en outre:

a) quantifier une quantité de l'un ou plusieurs biomarqueurs;
b) multiplier ladite quantité par un coefficient prédéterminé, et
c) déterminer la probabilité d'une naissance prématurée chez la femme enceinte comprenant ajouter lesdits produits individuels pour obtenir un score de risque total qui correspond à ladite probabilité.

5. Procédé selon les revendications 2 ou 4, dans lequel ladite analyse de ladite caractéristique mesurable comprend initialement une prédiction d'un âge gestationnel à la naissance (GAB) avant ladite détermination de la probabilité

d'une naissance prématurée;
optionnellement dans lequel ladite prédiction du GAB est utilisée pour déterminer la probabilité d'une naissance prématurée.

6. Procédé selon la revendication 3 comprenant en outre:

a) quantifier une quantité de l'un ou plusieurs biomarqueurs;
b) multiplier et/ou seuiller ladite quantité par un coefficient prédéterminé;
c) déterminer le GAB prédit chez la femme enceinte, la détermination comprenant ajouter lesdits produits individuels pour obtenir un score de risque total qui correspond audit GAB prédit; et optionnellement
d) soustraire l'âge gestationnel (GA) estimé au moment où l'échantillon biologique a été obtenu à partir du GAB prédit pour prédire un temps jusqu'à la naissance chez ladite femme enceinte.

7. Procédé selon l'une quelconque des revendications 2 à 6, dans lequel le procédé comprend en outre calculer la probabilité d'une naissance prématurée ou d'une naissance à terme, ou d'un GAB, ou d'un temps jusqu'à la naissance chez ladite femme enceinte sur la base de la quantification d'une quantité de chacun de l'un ou plusieurs biomarqueurs.

8. Procédé selon l'une quelconque des revendications 2 à 7, dans lequel ladite analyse comprend une utilisation d'un modèle prédictif; optionnellement dans lequel ladite analyse comprend comparer la caractéristique mesurable avec une caractéristique de référence.

9. Procédé selon la revendication 8, dans lequel ladite analyse comprend utiliser un ou plusieurs de : un modèle d'analyse discriminante linéaire, un algorithme de classification de machines à vecteurs de support, un modèle d'élimination de caractéristiques récursives, un modèle d'analyse de prédiction de biopuce, un modèle de régression logistique, un modèle de régression multiple, un modèle de survie, un algorithme CART, un algorithme à arbres flexibles, un algorithme LART, un algorithme à forêts aléatoires, un algorithme MART, un algorithme d'apprentissage automatique, un procédé de régression avec pénalité, et une combinaison de ceux-ci.

10. Procédé selon l'une quelconque des revendications 2 à 9, dans lequel l'échantillon biologique est sélectionné parmi le groupe consistant en du sang total, du plasma et du sérum.

11. Procédé selon l'une quelconque des revendications 4 à 10, dans lequel ladite quantification comprend une spectrométrie de masse (MS) ou une chromatographie en phase liquide-spectrométrie de masse (LC-MS).

12. Procédé selon la revendication 11, dans lequel ladite MS comprend un suivi de réactions multiples (MRM) ou un suivi de réactions de réactions choisies (SRM);
optionnellement dans lequel ladite MRM ou SRM comprend une MRM ou SRM planifiée.

13. Procédé selon l'une quelconque des revendications 4 à 10, dans lequel ladite quantification comprend un dosage qui utilise un agent de capture.

14. Procédé selon la revendication 13, dans lequel:

ledit agent de capture est sélectionné parmi le groupe consistant en un anticorps, un fragment d'anticorps, un réactif de liaison à une protéine d'acide nucléique, et une petite molécule ou une variante de ceux-ci; et/ou
ledit dosage est sélectionné parmi le groupe consistant en un immunodosage enzymatique (EIA), un dosage immuno-enzymatique sur support solide (ELISA), et un dosage radio-immunologique (RIA); et/ou
ladite quantification comprend en outre une spectrométrie de masse (MS) ou une co-immunoprécipitation-spectrométrie de masse (co-IP MS).

15. Procédé selon l'une quelconque des revendications 2 à 14, comprenant en outre détecter un ou plusieurs indices de risque;
optionnellement dans lequel l'un ou plusieurs indices de risque sont sélectionnés parmi le groupe consistant en l'âge, une grossesse antérieure, un historique d'un poids insuffisant à la naissance ou d'un accouchement prématuré précédents, des avortements spontanés du deuxième trimestre multiples, un avortement provoqué du premier trimestre antérieur, des facteurs familiaux et intergénérationnels, un historique d'infertilité, de nulliparité, des anormalités placentales, des anomalies cervicales et utérines, des saignements gestationnels, un retard de croissance

intra-utérin, une exposition in utero au diéthylstilbestrol, des gestations multiples, le sexe du nourrisson, une petite taille, un poids de pré-grossesse faible/un indice de masse corporelle faible, du diabète, de l'hypertension, de l'hypothyroïdie, de l'asthme, le niveau d'éducation, l'usage du tabac, et des infections urogénitales.

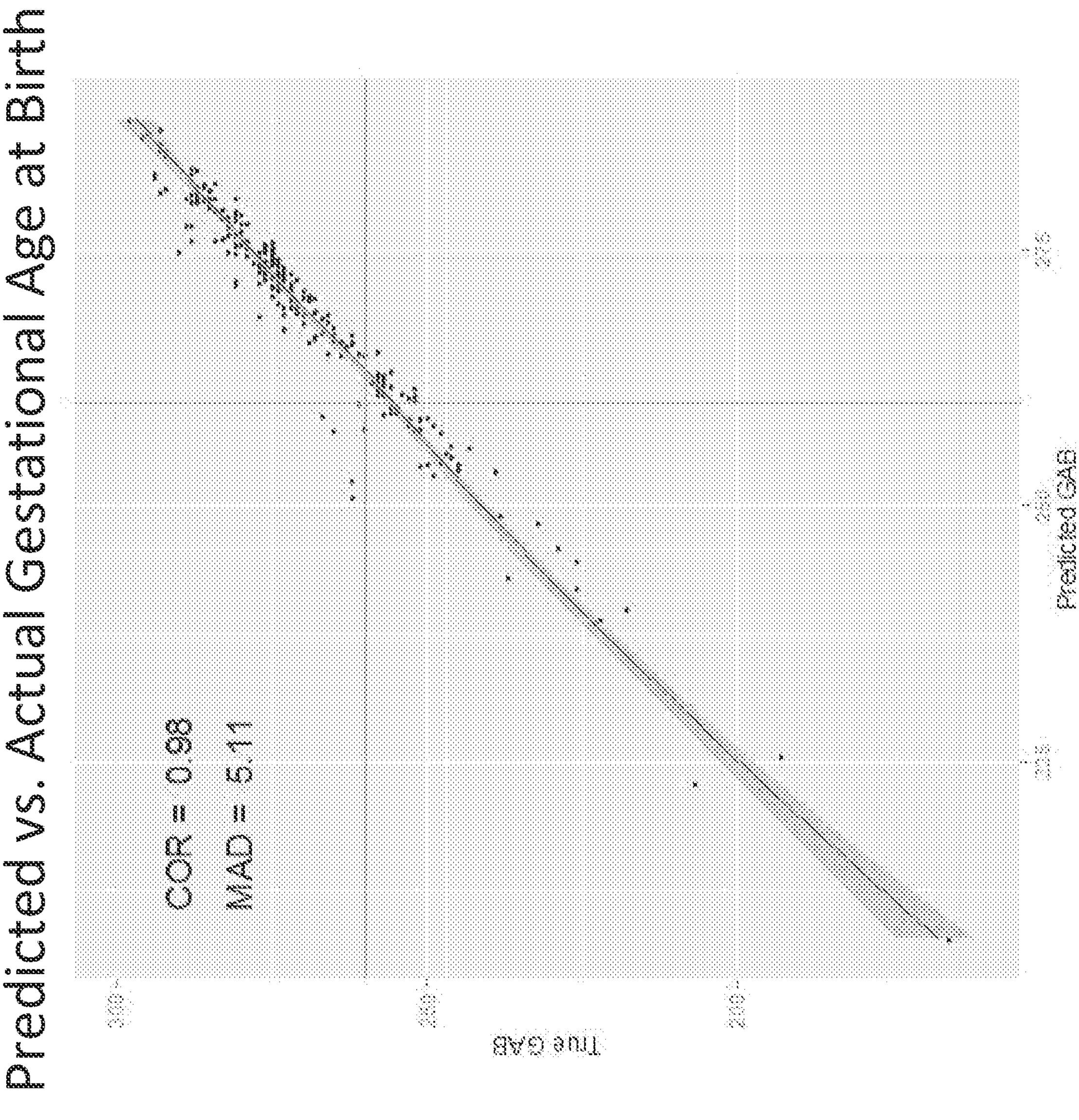
Predicted vs. Actual Gestational Age at Birth
COR = 0.98
MAD = 5.11
True GAB
Predicted GAB

FIGURE 1

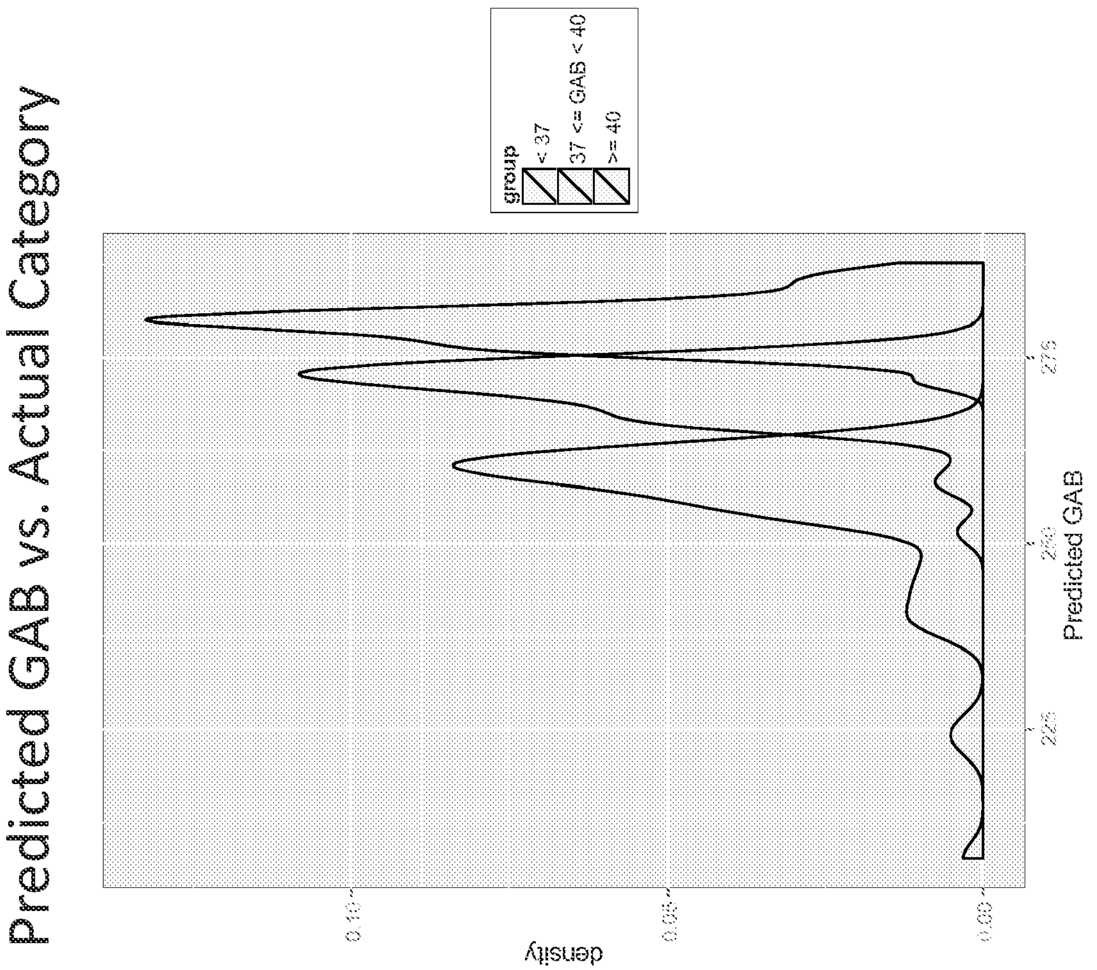
Predicted GAB vs. Actual Category
group
< 37
37 <= GAB < 40
>= 40
density
0.10
0.05
0.00
225
250
275
Predicted GAB

FIGURE 2

REFERENCES CITED IN THE DESCRIPTION

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