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- (54) Title:** COMPOSITIONS AND METHODS FOR SCREENING, MONITORING AND TREATING GASTROINTESTINAL DISEASES

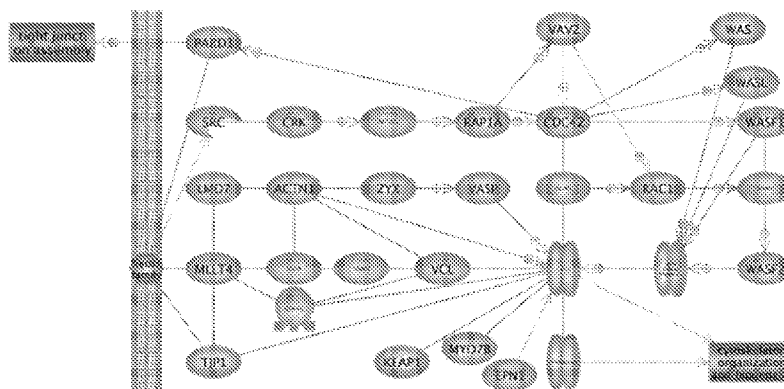


FIG. 1

- (S7) Abstract:** Provided are compositions and methods for screening, monitoring and treating a gastrointestinal (GI) cancer patient. In the methods, the patient's sample is screened for a profile of abnormal pathways and glycosylated protein biomarkers indicative of a GI cancer.

COMPOSITIONS AND METHODS FOR SCREENING, MONITORING AND TREATING GASTROINTESTINAL DISEASES

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims a benefit of priority to US Patent Application 62/321,294, filed April 12, 2016, the entire disclosure of which is incorporated herein by reference.

TECHNICAL FIELD

This invention relates to compositions and methods for screening, diagnosing, monitoring and treating gastrointestinal (GI) diseases, including colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer.

BACKGROUND OF THE INVENTION

Gastrointestinal (GI) diseases are complex chronic human disorders. GI diseases include colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer. GI cancers account for a large percentage of cancer mortalities.

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the third leading cause of cancer death in both men and women in the United States. Diet, environmental, genetic and inflammation factors contribute in the CRC etiology. Colorectal cancer usually develops over a period of 10 to 20 years. A significant progress has been made in the past decade in reducing the CRC incidence and death rates in the United States, largely due to prevention and early detection of colorectal cancer.

About 25,000 new stomach (gastric) cancer cases are reported in the United States annually. Before a stomach cancer develops, pre-cancerous changes often occur in the inner lining, mucosa, of the stomach. These early changes rarely cause symptoms and therefore often go undetected. The overall 5-year survival rate for patients with stomach cancer is 29% as most patients with stomach cancer are diagnosed after the cancer has already spread to other parts of the body. If stomach cancer is diagnosed and treated before it has spread outside the stomach, the 5-year survival rate is 65%. This data supports a high unmet need for developing a molecular test for detecting stomach cancer at early stages while the patient has not developed symptoms and the cancer has not spread outside the stomach.

Liver cancer is the 10th most common cancer and the 5th most common cause of cancer death among men. It is also the 8th most common cause of cancer death among

women. The overall 5-year survival rate for patients with liver cancer is 18%. For 43% of people who are diagnosed at an early stage, the 5-year survival rate is 31%.

Pancreatic cancer (PC) is a lethal malignancy with a very high mortality rate. Pancreatic cancer is a group of heterogeneous diseases and includes cancer of the endocrine (islet cell carcinoma, neuroendocrine carcinoma and carcinoma of carcinoid tumors) and exocrine (pancreatic ductal adenocarcinoma and acinar) pancreas. Among these pathologies, pancreatic ductal adenocarcinoma accounts for approximately 90% of all cases. Notably, a significantly better treatment outcome has been reported in cases where a tumor was detected at an early stage.

Table A lists methods currently available for diagnosing pancreatic cancer.

Table A. Current Pancreatic Cancer Diagnostic Tests

Modality	Issues
CA19-9 test	• Low selectivity and specificity • Detect mostly late stage of cancer • Limited accuracy in identifying patients with small tumors • Not recommended as a screening test
CT Scan	• Suboptimal for early pancreatic neoplasm • High concern for repeat radiation exposure • High cost
MRI/MRCP	• High cost • No published data on accuracy or yield
ERCP	• High cost • Invasive procedure with high risk of pancreatitis • The patient has to be sedated or anaesthetized

As shown in Table A, detection of pancreatic cancer relies heavily on procedures, notably imaging. Advances in the imaging technology have allowed improved detection of small lesions. However, these advances have also led to increases in false-positive findings, necessitating invasive procedures to make a definitive diagnosis. Given the

probability of false-positive findings associated with the CT screening, there is a substantial need for additional test methods to discriminate between benign vs malignant nodules. There are similar challenges in imaging-based screening for other GI malignancies and a high unmet need for highly sensitive and non-invasive diagnostic tests.

More than 2% of adults harbor a pancreatic cyst, a subset of which progresses to invasive lesions with lethal consequences. As the result of the increasing use of imaging technologies in standard medical practice, pancreatic cysts are being identified with an increasing frequency. Management of these cysts is concomitantly becoming a major clinical problem. Cystic lesions occur in more than 20% of patients examined at autopsy, in as many as 19.6% of patients evaluated by MRI, and in as many as 2.6% of patients evaluated by computed tomography. In the vast majority of cases, the cysts are identified as incidental findings in patients undergoing imaging for symptoms unrelated to pancreatic pathology. However, once a cyst is identified, it poses a challenging life-long management problem. Some cyst types are virtually always benign, some are low-grade malignant, and others are precursors to invasive pancreatic ductal adenocarcinomas. The distinction among cyst types is therefore critical for the effective management of patients with pancreatic cysts.

The potential for malignant transformation varies among pancreatic cystic neoplasms (PCN) subtypes. Imaging and a cyst fluid analysis are sometimes used to identify premalignant or malignant cases that should undergo operative resection. Therefore, there is a critical need to develop an efficient and noninvasive liquid biopsy test which can be used to distinguish a patient with a benign, non-premalignant disease from a patient with malignant pancreatic cysts.

A cancer is associated with major changes in biopathways, including upregulation of fucosyltransferases, sialyltransferases, mannosyl (α -1,6-)-glycoprotein β -1,6-N-acetyl-glucosaminyltransferase. Changes in the expression of glycosyltransferases result in altered glycan assembly, which occurs in the endoplasmic reticulum and Golgi. Accordingly, the glycoprotein products of tumor cells carry aberrant carbohydrate structures compared with their normal counterparts. Typical changes include increased levels of fucose and sialic acid, the addition of polylactosamine units and N-acetylglucosamine, and higher-ordered branching of N-linked glycans. O-linked glycans are also affected in cancer, typically carrying incomplete or prematurely truncated structures relative to those found on normal cells. After secretion or proteolytic cleavage, glycosylated molecules and/or their cleavage products can be released into the interstitial space, where they can enter the circulation. (Drake et al. 2010, Clin Chem, 56(2): 223-236)

Tumors produce glycoproteins that carry oligosaccharides with structures that are markedly different from the same protein produced by a normal cell. A single protein can have many glycosylation sites that greatly amplify the signals they generate compared with their protein backbones, thus tumor glycoproteins can serve as cancer biomarkers. The glycosylation machinery appears to be particularly sensitive to malignant transformation; as a result, the saccharide structures that are added to normal cellular proteins change, resulting in neoglycoforms that can be released from the cell through conventional secretory pathways, or as the result of enhanced proteinase activity. (Drake et al. 2010, Clin Chem, 56(2): 223-236)

Carbohydrates and their associated glycoproteins represent a rich, underexplored source of biomarkers. Glycoproteins with complex glycans are membrane bound or secreted. There is a substantial evidence that cancer cells exhibit altered glycans relative to normal cells. The potential of targeting glycoproteins to identify biomarkers was investigated by enriching N-linked glycopeptides from tissues, cells, and plasma and identifying corresponding peptide sequences and proteins by mass spectrometry. A significant overlap was observed between glycoproteins identified in tissues and cells and glycoproteins identified in plasma, leading to the conclusion that extracellular glycoproteins originating from tissues and cells are released into the blood at concentrations that are detectable by mass spectrometry. See US Patent Publication 2007/0099251.

It has been demonstrated that in pancreatic cancer glucose metabolism pathways and glycosylation levels are changing throughout disease progression, specifically on a background of hypoxia. Hypoxia promotes selective pressure on malignant cells that must develop adaptive metabolic responses to reach their energetic and biosynthetic demands. In a mouse model of pancreatic cancer, it was demonstrated that hypoxic areas from pancreatic ductal adenocarcinoma are mainly composed of epithelial cells harboring epithelial-mesenchymal transition features and expressing glycolytic markers, two characteristics associated with tumor aggressiveness. In this model, it has been also shown that hypoxia increases the “glycolytic” switch of pancreatic cancer cells from oxidative phosphorylation to lactate production and demonstrated that increased lactate efflux from hypoxic cancer cells favors the growth of normoxic cancer cells. (Guillaumond et al. 2013, PNAS, 110(10): 3919-3924).

Metabolized glucose and glutamine converge toward a common pathway, termed the hexosamine biosynthetic pathway, which allows O-linked N-acetylglucosamine modifications of proteins. Importantly, it was reported that hypoxia increases transcription of hexosamine biosynthetic pathway genes as well as levels of O-glycosylated proteins and that

O-linked N-acetylglucosaminylation of proteins is a process required for hypoxic pancreatic cancer cell survival. Hypoxia-driven metabolic adaptive processes, such as high glycolytic rate and the hexosamine biosynthetic pathway activation, favor hypoxic and normoxic cancer cell survival and correlate with pancreatic cancer aggressiveness. (Guillaumond et al. 2013, PNAS, Mr 5; 110(10): 3919-3924).

In other studies, it was demonstrated that mucins, specifically, MUC1 and MUC4, are differentially glycosylated as the disease progressed from the early stage to metastatic disease. De novo expression of several mucins correlated with increased metastasis, indicating a potentially more invasive tumor phenotype. (Remmers et al. 2013, Clin Cancer Res. Apr 15: 19(8)).

There remains the need for an accurate and non-invasive test that can be used to detect and monitor a GI cancer.

SUMMARY

Provided is a method for screening, monitoring and/or treating a gastrointestinal (GI) cancer patient, wherein the GI cancer is selected from the group consisting of colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer. A sample from the patient is obtained and glycosylated proteins are isolated from the sample. The isolated glycoproteins are then analyzed for the presence of any of biomarkers from Tables 1A, 2A, 3A, 4A, 5A, 6A, 7A, and any combination thereof. The presence of at least some of the biomarkers in the sample being indicative a GI cancer. The isolated glycosylated proteins can be also grouped into a profile of pathways, and matched with at least one profile selected from the group of profiles of Tables 1, 2, 3, 4, 5, 6, 7, 8, and any combination thereof. At least a partial match with at least one profile from Tables 1, 2, 3, 4, 5, 6, 7, 8 being indicative of a GI cancer.

The sample can be selected from the group consisting of a human tissue biopsy or biosample including pancreas biopsy sample, gastrointestinal sample, blood sample, plasma sample, serum sample, circulating tumor cells sample, tear sample, saliva sample, sperm sample, urine sample, fecal sample and hair sample. Blood or plasma samples are particularly preferred.

The sample can be analyzed using one or more techniques selected from the group consisting of chromatography, gas chromatography, liquid chromatography, mass

spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay. The sample can be analyzed using a combination of a detection techniques of nucleic acids and proteins or peptides.

In the further embodiments of the method, any of biomarkers of Tables 1A, 1, 2A, 2, 3A, 3, 4A, 4, 5A, 5, 6A, 6, 7A and 7 are immobilized on a solid support.

The method can be conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 1A, 1, 2A, 2, 3A, 3, 4A, 4, 5A, 6A, 6, 7A or 7. In further embodiments, the method can be conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 1A, 1, 2A, 2, 3A, 3, 4A, 4, 5A, 6A, 6, 7A or 7.

Further embodiments in provide a panel comprising a profile of biomarkers selected from the group consisting of Tables 1A, 1, 2A, 2, 3A, 3, 4A, 4, 5A, 6A, 6, 7A, 7 or 8, and any combination thereof. Kits comprising the panels are provided as well.

Further embodiments provide a method for detecting or monitoring a disorder of the pancreas, the method comprising obtaining a sample from a patient and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9. The disorder of the pancreas is selected from the group consisting of acute pancreatitis, chronic pancreatitis, hereditary pancreatitis, pancreatic neoplasm, and pancreatic cancer. The testing can be conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9. The testing is conducted by reacting the patient's sample with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9. The testing can be also conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9.

Further embodiments provide a method for treating a disorder of the pancreas, the method comprising obtaining a sample from a mammal in need of the treatment and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows the relationship between 33 proteins in the Adherens Junction Assembly (Nectin) pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 2 shows the relationship between 66 proteins in the Bradykinin Effects in Inflammation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 3 shows the relationship between 38 proteins in the coagulation cascade pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 4 shows the relationship between 25 proteins in the complement activation pathway by lectin. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 5 shows the relationship between 45 proteins in the complement activation in macular degeneration pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 6 shows the relationship between 30 proteins in the complement alternative pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 7 shows the relationship between 29 proteins in the complement cascade activation by pentraxin pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 8 shows the relationship between 28 proteins in the complement classical pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 9 shows the relationship between 37 proteins in the focal junction assembly pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 10 shows the relationship between 36 proteins in the glycolysis pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 11 shows the relationship between 33 proteins in the histidine-rich glycoprotein (HRG) pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 12 shows the relationship between 44 proteins in the lipogenesis regulation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 13 shows the relationship between 26 proteins in the microtubule cytoskeleton pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 14 shows the relationship between proteins in the Neutrophil Activation via Adherence on Endothelial Cells pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 15 shows the relationship between proteins in the Plasmin Effects in Inflammation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 16 shows the relationship between proteins in the Platelet Activation via Adhesion Molecules pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 17 shows the relationship between proteins in the Platelet Activation via GPCR Signaling pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 18 shows the relationship between proteins in the Positive Acute Phase Proteins Synthesis pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 19 shows the relationship between proteins in the Protein Folding pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 20 shows the relationship between proteins in the Scavenger Receptors in Platelet Activation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 21 shows the relationship between proteins in the Scavenger Receptors in Platelet Aggregation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 22 shows the relationship between proteins in the TAM Receptors in Platelet Aggregation pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

Fig. 23 shows the relationship between proteins in the Vascular Endothelial Cell Activation by Blood Coagulation Factors pathway. This figure was generated with ELSEVIER PATHWAY STUDIO^R.

DETAILED DESCRIPTION

This invention provides compositions and methods for detection, screening, monitoring and treatment of gastrointestinal (GI) cancers, including colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer.

Provided is a method by which a patient's protein expression profile is obtained by isolating glycosylated proteins from the patient's liquid biopsy sample. Suitable liquid biopsy samples include blood, plasma, serum or urine. The glycosylated proteins in the profile are grouped into pathways and analyzed for deviations from a profile of a healthy individual. A deviation in a number of the glycosylated proteins in at least one pathway is indicative of the patient's GI cancer. This analysis can be used for developing a treatment plan for a patient with a particular emphasis on using drugs suitable for targeting the affected pathways and/or proteins.

A patient's profile of glycosylated proteins can be also obtained to evaluate results of cancer treatment, including a surgery, chemotherapy, radiation and/or immunotherapy. In this embodiment of the method, a patient's profile of glycosylated proteins after the cancer treatment is compared to the patient's profile of glycosylated proteins before the cancer treatment. A decrease in the number of abnormally glycosylated proteins means that the treatment is beneficial to the patient. No changes or an increase in the number of abnormally glycosylated proteins means that the treatment plan needs to be modified or cancelled.

A patient's profile of glycosylated proteins can be also obtained to monitor the patient for an onset of a GI cancer. Many patients, including patients with a hereditary history of a GI cancer in a family, can benefit from this procedure which monitors the patient's profile of glycosylated proteins and pathways, and detects any changes in the profile over a period of time.

In one embodiment of the present methods, a patient's profile of glycosylated proteins is prepared by obtaining a blood, plasma, or serum sample from the patient. Glycosylated proteins are then isolated from the sample. Mass spectrometry of protein expression profile is performed to identify the glycosylated proteins in the sample. The patient's profile is then compared to a profile of a healthy individual in order to diagnose a GI cancer. This method can be used to diagnose a GI cancer. In alternative, a patient's profile of glycosylated proteins in a blood, plasma, or serum sample is monitored over a period of

time by periodically repeating the analysis in order to detect an early onset of GI cancer or to determine if a particular cancer treatment is beneficial to the patient.

In alternative to the mass spectrometry analysis, a patient's profile of glycosylated proteins and affected pathways can be analyzed with a chip which comprises a set of biomarkers of a GI cancer. In further embodiments, the profiling of glycosylated proteins may comprise identifying affected pathways.

Table 1A discloses glycoproteins differentially expressed in plasma of colorectal cancer (CRC) female patients. These glycoproteins can be used for diagnosing, monitoring and treating a CRC patient by the present methods. In these methods, glycoproteins of Table 1A are used as a set of biomarkers indicative of CRC.

Table 1A. Glycoproteins differentially expressed in plasma of CRC female patients

Identified Proteins (739)	Accession Number
14-3-3 protein sigma OS=Homo sapiens GN=SFN PE=1 SV=1	sp P31947 1433S_HUMAN
14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	sp P63104 1433Z_HUMAN
78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2	sp P11021 GRP78_HUMAN
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Actin-related protein 2/3 complex subunit 2 OS=Homo sapiens GN=ARPC2 PE=1 SV=1	sp O15144 ARPC2_HUMAN
Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5	sp Q01518 CAP1_HUMAN
ADP/ATP translocase 2 OS=Homo sapiens GN=SLC25A5 PE=1 SV=7	sp P05141 ADT2_HUMAN sp P61204 ARF3_HUMAN (+1)
ADP-ribosylation factor 3 OS=Homo sapiens GN=ARF3 PE=1 SV=2	sp P01009 A1AT_HUMAN
Alpha-1-antitrypsin OS=Homo sapiens GN=SERPINA1 PE=1 SV=3	sp P04217 A1BG_HUMAN
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	sp P02765 FETUA_HUMAN
Alpha-2-HS-glycoprotein OS=Homo sapiens GN=AHSG PE=1 SV=1	sp P12814 ACTN1_HUMAN
Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2	sp P06733 ENOA_HUMAN
Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2	sp P01019 ANGT_HUMAN
Angiotensinogen OS=Homo sapiens GN=AGT PE=1 SV=1	sp P02647 APOA1_HUMAN
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	sp P02649 APOE_HUMAN
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp O14791 APOL1_HUMAN
Apolipoprotein L1 OS=Homo sapiens GN=APOL1 PE=1 SV=5	sp P08519 APOA_HUMAN
Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	sp P18054 LOX12_HUMAN
Arachidonate 12-lipoxygenase, 12S-type OS=Homo sapiens GN=ALOX12 PE=1 SV=4	sp P06576 ATPB_HUMAN
ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATP5B PE=1 SV=3	sp O75882 ATRN_HUMAN
Attractin OS=Homo sapiens GN=ATRN PE=1 SV=2	sp Q9HBI1 PARVB_HUMAN
Beta-parvin OS=Homo sapiens GN=PARVB PE=1 SV=1	sp P07384 CAN1_HUMAN
Calpain-1 catalytic subunit OS=Homo sapiens GN=CAPN1 PE=1 SV=1	sp P00915 CAH1_HUMAN
Carbonic anhydrase 1 OS=Homo sapiens GN=CA1 PE=1 SV=2	sp P15169 CBPN_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P08311 CATG_HUMAN
Cathepsin G OS=Homo sapiens GN=CTSG PE=1 SV=2	sp Q00610 CLH1_HUMAN
Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5	

Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Coagulation factor IX OS=Homo sapiens GN=F9 PE=1 SV=2	sp P00740 FA9_HUMAN
Coagulation factor V OS=Homo sapiens GN=F5 PE=1 SV=4	sp P12259 FA5_HUMAN
Coagulation factor X OS=Homo sapiens GN=F10 PE=1 SV=2	sp P00742 FA10_HUMAN
Coagulation factor XIII B chain OS=Homo sapiens GN=F13B PE=1 SV=3	sp P05160 F13B_HUMAN
Complement C1q subcomponent subunit C OS=Homo sapiens GN=C1QC PE=1 SV=3	sp P02747 C1QC_HUMAN
Complement C1r subcomponent OS=Homo sapiens GN=C1R PE=1 SV=2	sp P00736 C1R_HUMAN
Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	sp P09871 C1S_HUMAN
Complement C2 OS=Homo sapiens GN=C2 PE=1 SV=2	sp P06681 CO2_HUMAN
Complement component C9 OS=Homo sapiens GN=C9 PE=1 SV=2	sp P02748 CO9_HUMAN
Complement factor B OS=Homo sapiens GN=CFB PE=1 SV=2	sp P00751 CFAB_HUMAN
Complement factor I OS=Homo sapiens GN=CFI PE=1 SV=2	sp P05156 CFAI_HUMAN
Corticosteroid-binding globulin OS=Homo sapiens GN=SERPINA6 PE=1 SV=1	sp P08185 CBG_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Endoplasmin OS=Homo sapiens GN=HSP90B1 PE=1 SV=1	sp P14625 ENPL_HUMAN
Erythrocyte band 7 integral membrane protein OS=Homo sapiens GN=STOM PE=1 SV=3	sp P27105 STOM_HUMAN
Ezrin OS=Homo sapiens GN=EZR PE=1 SV=4	sp P15311 EZRI_HUMAN
Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1	sp Q86UX7 URP2_HUMAN
Fetuin-B OS=Homo sapiens GN=FETUB PE=1 SV=2	sp Q9UGM5 FETUB_HUMAN
Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2	sp P02675 FIBB_HUMAN
Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	sp P02679 FIBG_HUMAN
Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4	sp P02751 FINC_HUMAN
Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4	sp P21333 FLNA_HUMAN
Fructose-bisphosphate aldolase A OS=Homo sapiens GN=ALDOA PE=1 SV=2	sp P04075 ALDOA_HUMAN
Galectin-3-binding protein OS=Homo sapiens GN=LGALS3BP PE=1 SV=1	sp Q08380 LG3BP_HUMAN
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	sp P06396 GELS_HUMAN
Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3	sp P04406 G3P_HUMAN
Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	sp P00738 HPT_HUMAN
Haptoglobin-related protein OS=Homo sapiens GN=HPR PE=2 SV=2	sp P00739 HPTR_HUMAN
Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1	sp P11142 HSP7C_HUMAN
Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4	sp P08238 HS90B_HUMAN
Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1 SV=2	sp P69905 HBA_HUMAN
Heterogeneous nuclear ribonucleoprotein K OS=Homo sapiens GN=HNRNPK PE=1 SV=1	sp P61978 HNRPK_HUMAN
Hexokinase-1 OS=Homo sapiens GN=HK1 PE=1 SV=3	sp P19367 HXX1_HUMAN
Ig delta chain C region OS=Homo sapiens GN=IGHD PE=1 SV=2	sp P01880 IGHD_HUMAN
Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1	sp P01857 IGHG1_HUMAN
Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1	sp P01861 IGHG4_HUMAN
Ig heavy chain V-I region HG3 OS=Homo sapiens PE=3 SV=1	sp P01743 HV102_HUMAN
Ig heavy chain V-I region WOL OS=Homo sapiens PE=1 SV=1	sp P01760 HV105_HUMAN
Ig heavy chain V-II region ARH-77 OS=Homo sapiens PE=4 SV=1	sp P06331 HV209_HUMAN
Ig heavy chain V-II region SESS OS=Homo sapiens PE=2 SV=1	sp P04438 HV208_HUMAN
Ig heavy chain V-III region BUR OS=Homo sapiens PE=1 SV=1	sp P01773 HV312_HUMAN
Ig heavy chain V-III region CAM OS=Homo sapiens PE=1 SV=1	sp P01768 HV307_HUMAN
Ig heavy chain V-III region HIL OS=Homo sapiens PE=1 SV=1	sp P01771 HV310_HUMAN
Ig heavy chain V-III region NIE OS=Homo sapiens PE=1 SV=1	sp P01770 HV309_HUMAN

Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1	sp P01834 IGKC_HUMAN
Ig kappa chain V-I region Lay OS=Homo sapiens PE=1 SV=1	sp P01605 KV113_HUMAN
Ig kappa chain V-I region Mev OS=Homo sapiens PE=1 SV=1	sp P01612 KV120_HUMAN
Ig kappa chain V-II region FR OS=Homo sapiens PE=1 SV=1	sp P01615 KV202_HUMAN
Ig kappa chain V-II region MIL OS=Homo sapiens PE=1 SV=1	sp P01616 KV203_HUMAN
Ig kappa chain V-II region RPMI 6410 OS=Homo sapiens PE=4 SV=1	sp P06310 KV206_HUMAN
Ig kappa chain V-III region CLL OS=Homo sapiens PE=4 SV=2	sp P04207 KV308_HUMAN
Ig kappa chain V-III region IARC/BL41 OS=Homo sapiens PE=4 SV=1	sp P06311 KV311_HUMAN
Ig kappa chain V-III region NG9 (Fragment) OS=Homo sapiens PE=2 SV=1	sp P01621 KV303_HUMAN
Ig lambda chain V region 4A OS=Homo sapiens PE=4 SV=1	sp P04211 LV001_HUMAN
Ig lambda chain V-I region HA OS=Homo sapiens PE=1 SV=1	sp P01700 LV102_HUMAN
Ig lambda chain V-I region NEW OS=Homo sapiens PE=1 SV=1	sp P01701 LV103_HUMAN
	sp P01702 LV104_HUMAN
	(+1)
Ig lambda chain V-I region NIG-64 OS=Homo sapiens PE=1 SV=1	sp P01719 LV501_HUMAN
Ig lambda chain V-V region DEL OS=Homo sapiens PE=1 SV=1	
Insulin-like growth factor-binding protein complex acid labile subunit OS=Homo sapiens GN=IGFALS PE=1 SV=1	sp P35858 ALS_HUMAN
Integrin alpha-IIb OS=Homo sapiens GN=ITGA2B PE=1 SV=3	sp P08514 ITA2B_HUMAN
Integrin beta-3 OS=Homo sapiens GN=ITGB3 PE=1 SV=2	sp P05106 ITB3_HUMAN
Integrin-linked protein kinase OS=Homo sapiens GN=ILK PE=1 SV=2	sp Q13418 ILK_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens GN=ITIH1 PE=1 SV=3	sp P19827 ITIH1_HUMAN
Isocitrate dehydrogenase [NADP], mitochondrial OS=Homo sapiens GN=IDH2 PE=1 SV=2	sp P48735 IDHP_HUMAN
Kallistatin OS=Homo sapiens GN=SERPINA4 PE=1 SV=3	sp P29622 KAIN_HUMAN
Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2	sp P01042 KNG1_HUMAN
Leucine-rich alpha-2-glycoprotein OS=Homo sapiens GN=LRG1 PE=1 SV=2	sp P02750 A2GL_HUMAN
LIM and senescent cell antigen-like-containing domain protein 1 OS=Homo sapiens GN=LIMS1 PE=1 SV=4	sp P48059 LIMS1_HUMAN
Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	sp P18428 LBP_HUMAN
L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2	sp P00338 LDHA_HUMAN
L-lactate dehydrogenase B chain OS=Homo sapiens GN=LDHB PE=1 SV=2	sp P07195 LDHB_HUMAN
Multimerin-1 OS=Homo sapiens GN=MMRN1 PE=1 SV=3	sp Q13201 MMRN1_HUMAN
Myosin light polypeptide 6 OS=Homo sapiens GN=MYL6 PE=1 SV=2	sp P60660 MYL6_HUMAN
Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	sp P35579 MYH9_HUMAN
Peptidyl-prolyl cis-trans isomerase B OS=Homo sapiens GN=PPIB PE=1 SV=2	sp P23284 PPIB_HUMAN
Phosphate carrier protein, mitochondrial OS=Homo sapiens GN=SLC25A3 PE=1 SV=2	sp Q00325 MPCP_HUMAN
Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=2	sp P05155 IC1_HUMAN
Plasma serine protease inhibitor OS=Homo sapiens GN=SERPINA5 PE=1 SV=3	sp P05154 IPSP_HUMAN
Platelet glycoprotein Ib alpha chain OS=Homo sapiens GN=GP1BA PE=1 SV=2	sp P07359 GP1BA_HUMAN
Platelet glycoprotein Ib beta chain OS=Homo sapiens GN=GP1BB PE=1 SV=1	sp P13224 GP1BB_HUMAN
Pleckstrin OS=Homo sapiens GN=PLEK PE=1 SV=3	sp P08567 PLEK_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein disulfide-isomerase A3 OS=Homo sapiens GN=PDIA3 PE=1 SV=4	sp P30101 PDIA3_HUMAN
Proteoglycan 4 OS=Homo sapiens GN=PRG4 PE=1 SV=2	sp Q92954 PRG4_HUMAN
Purine nucleoside phosphorylase OS=Homo sapiens GN=PNP PE=1 SV=2	sp P00491 PNPH_HUMAN
Putative V-set and immunoglobulin domain-containing-like protein IGHV4OR15-8 OS=Homo sapiens GN=IGHV4OR15-8 PE=5 SV=2	sp A6NJ16 IV4F8_HUMAN
Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4	sp P14618 KPYM_HUMAN
Ras-related protein Rab-10 OS=Homo sapiens GN=RAB10 PE=1 SV=1	sp P61026 RAB10_HUMAN

Ras-related protein Rap-1b OS=Homo sapiens GN=RAP1B PE=1 SV=1	sp P61224 RAP1B_HUMAN
Reticulon-4 OS=Homo sapiens GN=RTN4 PE=1 SV=2	sp Q9NQC3 RTN4_HUMAN
Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 OS=Homo sapiens GN=ATP2A3 PE=1 SV=2	sp Q93084 AT2A3_HUMAN
Serum amyloid P-component OS=Homo sapiens GN=APCS PE=1 SV=2	sp P02743 SAMP_HUMAN
Solute carrier family 2, facilitated glucose transporter member 3 OS=Homo sapiens GN=SLC2A3 PE=1 SV=1	sp P11169 GTR3_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	sp P07996 TSP1_HUMAN
Transgelin-2 OS=Homo sapiens GN=TAGLN2 PE=1 SV=3	sp P37802 TAGL2_HUMAN
Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	sp P02766 TTHY_HUMAN
Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1	sp P68363 TBA1B_HUMAN
Tubulin alpha-4A chain OS=Homo sapiens GN=TUBA4A PE=1 SV=1	sp P68366 TBA4A_HUMAN
Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1	sp Q9H4B7 TBB1_HUMAN
Tubulin beta-2A chain OS=Homo sapiens GN=TUBB2A PE=1 SV=1	sp Q13885 TBB2A_HUMAN
Vinculin OS=Homo sapiens GN=VCL PE=1 SV=4	sp P18206 VINC_HUMAN
Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1	sp P02774 VTDB_HUMAN
Vitronectin OS=Homo sapiens GN=VTN PE=1 SV=1	sp P04004 VTNC_HUMAN
Voltage-dependent anion-selective channel protein 3 OS=Homo sapiens GN=VDAC3 PE=1 SV=1	sp Q9Y277 VDAC3_HUMAN
von Willebrand factor OS=Homo sapiens GN=VWF PE=1 SV=4	sp P04275 VWF_HUMAN
WD repeat-containing protein 1 OS=Homo sapiens GN=WDR1 PE=1 SV=4	sp O75083 WDR1_HUMAN

Table 1 provides a profile of abnormalities detected in pathways and glycosylated proteins in plasma of colorectal cancer female patients. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a CRC patient by the present methods. In these methods, the profile of Table 1 is used as a set of biomarkers indicative of CRC.

Table 1. A profile of abnormalities in pathways and glycosylated proteins in a CRC female patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
Complement Activation in Macular Degeneration	CFB, CFI, C2, CIR, C1S, C1QC, C9, CRP, VTN, CLU	1.11151E-8	4.97512E-2
Focal Junction Assembly	ACTN1, FLNA, FN1, TLN1, ILK, VCL, CAPN1, VTN, LIMS1, ITGB3	1.66465E-8	4.87805E-2
Platelet Activation via Adhesion Molecules	GP1BA, FGB, FGG, ARPC2, VCL, VWF, ITGA2B, ITGB3, TLN1, GPIBB	3.16888E-6	3.58423E-2
Glycolysis	HK1, GAPDH, ENO1, PKM, ALDOA	1.60626E-5	3.40136E-2
TAM Receptors in Platelet Aggregation	FGB, FGG, VWF, ITGB3	9.25453E-5	2.87770E-2

Scavenger Receptors in Platelet Activation	GP1BA, APOA1, APOE, ITGA2B, ITGB3, GPIBB	9.76831E-5	3.10881E-2
Complement Cascade Activation by Pentraxins	CFB, APCS, C2, C1S, C9, CRP	1.26998E-4	3.04569E-2
Complement Classical Pathway	C2, C1R, C1S, C1QC, C9	1.29618E-4	3.01205E-2
Coagulation Cascade	FGB, FGG, KNG1, F5, F9, F10	1.83636E-4	2.95567E-2
Scavenger Receptors in Platelet Aggregation	FGB, FGG, TLN1, ITGA2B, ITGB3	1.96450E-4	2.92398E-2

Table 2A discloses glycoproteins differentially expressed in plasma of colorectal cancer (CRC) male patients. These glycoproteins can be used for diagnosing, monitoring and treating a CRC patient by the present methods. In these methods, glycoproteins of Table 2A are used as a set of biomarkers indicative of CRC.

Table 2A. Glycoproteins differentially expressed in plasma of CRC male patients

Identified Proteins (739)	Accession Number
14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	sp P63104 1433Z_HUMAN
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5	sp Q01518 CAP1_HUMAN
ADP/ATP translocase 2 OS=Homo sapiens GN=SLC25A5 PE=1 SV=7	sp P05141 ADT2_HUMAN
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	sp P04217 A1BG_HUMAN
Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2	sp P12814 ACTN1_HUMAN
Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	sp P04114 APOB_HUMAN
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp P02649 APOE_HUMAN
Apolipoprotein L1 OS=Homo sapiens GN=APOL1 PE=1 SV=5	sp O14791 APOL1_HUMAN
ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1	sp P25705 ATPA_HUMAN
ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATP5B PE=1 SV=3	sp P06576 ATPB_HUMAN
Beta-2-glycoprotein 1 OS=Homo sapiens GN=APOH PE=1 SV=3	sp P02749 APOH_HUMAN
C4b-binding protein beta chain OS=Homo sapiens GN=C4BPB PE=1 SV=1	sp P20851 C4BPB_HUMAN
Cholesteryl ester transfer protein OS=Homo sapiens GN=CETP PE=1 SV=2	sp P11597 CETP_HUMAN
Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5	sp Q00610 CLH1_HUMAN
Coagulation factor IX OS=Homo sapiens GN=F9 PE=1 SV=2	sp P00740 FA9_HUMAN
Coagulation factor XI OS=Homo sapiens GN=F11 PE=1 SV=1	sp P03951 FA11_HUMAN
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	sp P00748 FA12_HUMAN
Coagulation factor XIII A chain OS=Homo sapiens GN=F13A1 PE=1 SV=4	sp P00488 F13A_HUMAN
Complement C1q subcomponent subunit A OS=Homo sapiens GN=C1QA PE=1 SV=2	sp P02745 C1QA_HUMAN
Complement C1r subcomponent OS=Homo sapiens GN=C1R PE=1 SV=2	sp P00736 C1R_HUMAN
Complement factor B OS=Homo sapiens GN=CFB PE=1 SV=2	sp P00751 CFAB_HUMAN
Corticosteroid-binding globulin OS=Homo sapiens GN=SERPINA6 PE=1 SV=1	sp P08185 CBG_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	sp P15924 DESP_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Erythrocyte band 7 integral membrane protein OS=Homo sapiens GN=STOM	sp P27105 STOM_HUMAN

PE=1 SV=3

Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1

Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2

Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2

Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3

Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4

Fibulin-1 OS=Homo sapiens GN=FBLN1 PE=1 SV=4

Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4

Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1

Glutathione peroxidase 3 OS=Homo sapiens GN=GPX3 PE=1 SV=2

Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH
PE=1 SV=3Guanine nucleotide-binding protein G(k) subunit alpha OS=Homo sapiens
GN=GNAI3 PE=1 SV=3

Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1

Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4

Hepatocyte growth factor-like protein OS=Homo sapiens GN=MST1 PE=1 SV=2

Histone H4 OS=Homo sapiens GN=HIST1H4A PE=1 SV=2

Hyaluronan-binding protein 2 OS=Homo sapiens GN=HABP2 PE=1 SV=1

Ig alpha-1 chain C region OS=Homo sapiens GN=IGHA1 PE=1 SV=2

Ig alpha-2 chain C region OS=Homo sapiens GN=IGHA2 PE=1 SV=3

Ig delta chain C region OS=Homo sapiens GN=IGHD PE=1 SV=2

Ig heavy chain V-I region 5 (Fragment) OS=Homo sapiens GN=IGKV1-5 PE=4
SV=2

Ig heavy chain V-I region EU OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-I region V35 OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-II region ARH-77 OS=Homo sapiens PE=4 SV=1

Ig heavy chain V-II region NEWM OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-II region SESS OS=Homo sapiens PE=2 SV=1

Ig heavy chain V-II region WAH OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region GA OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region KOL OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region NIE OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region TIL OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region WEA OS=Homo sapiens PE=1 SV=1

Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1

Ig kappa chain V-I region DEE OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-I region Lay OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-I region WEA OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-II region MIL OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-II region TEW OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-III region IARC/BL41 OS=Homo sapiens PE=4 SV=1

Ig kappa chain V-III region VG (Fragment) OS=Homo sapiens PE=1 SV=1

Ig lambda chain V region 4A OS=Homo sapiens PE=4 SV=1

Ig lambda chain V-I region HA OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-I region NEW OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-I region NEWM OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-I region WAH OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-III region LOI OS=Homo sapiens PE=1 SV=1

sp|Q86UX7|URP2_HUMAN

sp|P02671|FIBA_HUMAN

sp|P02675|FIBB_HUMAN

sp|P02679|FIBG_HUMAN

sp|P02751|FINC_HUMAN

sp|P23142|FBLN1_HUMAN

sp|P21333|FLNA_HUMAN

sp|P06396|GELS_HUMAN

sp|P22352|GPX3_HUMAN

sp|P04406|G3P_HUMAN

sp|P08754|GNAI3_HUMAN

sp|P11142|HSP7C_HUMAN

sp|P08238|HS90B_HUMAN

sp|P26927|HGFL_HUMAN

sp|P62805|H4_HUMAN

sp|Q14520|HABP2_HUMAN

sp|P01876|IGHA1_HUMAN

sp|P01877|IGHA2_HUMAN

sp|P01880|IGHD_HUMAN

sp|P01602|KV110_HUMAN

sp|P01742|HV101_HUMAN

sp|P23083|HV103_HUMAN

sp|P06331|HV209_HUMAN

sp|P01825|HV207_HUMAN

sp|P04438|HV208_HUMAN

sp|P01824|HV206_HUMAN

sp|P01769|HV308_HUMAN

sp|P01772|HV311_HUMAN

sp|P01770|HV309_HUMAN

sp|P01765|HV304_HUMAN

sp|P01763|HV302_HUMAN

sp|P01834|IGKC_HUMAN

sp|P01597|KV105_HUMAN

sp|P01605|KV113_HUMAN

sp|P01610|KV118_HUMAN

sp|P01616|KV203_HUMAN

sp|P01617|KV204_HUMAN

sp|P06311|KV311_HUMAN

sp|P04433|KV309_HUMAN

sp|P04211|LV001_HUMAN

sp|P01700|LV102_HUMAN

sp|P01701|LV103_HUMAN

sp|P01703|LV105_HUMAN

sp|P04208|LV106_HUMAN

sp|P80748|LV302_HUMAN

Ig lambda chain V-III region SH OS=Homo sapiens PE=1 SV=1	sp P01714 LV301_HUMAN
Ig lambda chain V-IV region Hil OS=Homo sapiens PE=1 SV=1	sp P01717 LV403_HUMAN
IgGfC-binding protein OS=Homo sapiens GN=FCGBP PE=1 SV=3	sp Q9Y6R7 FCGBP_HUMAN
Insulin-like growth factor-binding protein complex acid labile subunit OS=Homo sapiens GN=IGFALS PE=1 SV=1	sp P35858 ALS_HUMAN
Integrin alpha-IIb OS=Homo sapiens GN=ITGA2B PE=1 SV=3	sp P08514 ITA2B_HUMAN
Integrin beta-3 OS=Homo sapiens GN=ITGB3 PE=1 SV=2	sp P05106 ITB3_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens GN=ITIH1 PE=1 SV=3	sp P19827 ITIH1_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITIH2 PE=1 SV=2	sp P19823 ITIH2_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4	sp Q14624 ITIH4_HUMAN
Isocitrate dehydrogenase [NADP], mitochondrial OS=Homo sapiens GN=IDH2 PE=1 SV=2	sp P48735 IDHP_HUMAN
Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3	sp P14923 PLAK_HUMAN
Keratinocyte proline-rich protein OS=Homo sapiens GN=KPRP PE=1 SV=1	sp Q5T749 KPRP_HUMAN
Leucine-rich alpha-2-glycoprotein OS=Homo sapiens GN=LRG1 PE=1 SV=2	sp P02750 A2GL_HUMAN
Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	sp P18428 LBP_HUMAN
Multimerin-1 OS=Homo sapiens GN=MMRN1 PE=1 SV=3	sp Q13201 MMRN1_HUMAN
Myeloperoxidase OS=Homo sapiens GN=MPO PE=1 SV=1	sp P05164 PERM_HUMAN
Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	sp P35579 MYH9_HUMAN
Peptidyl-prolyl cis-trans isomerase B OS=Homo sapiens GN=PPIB PE=1 SV=2	sp P23284 PPIB_HUMAN
Phosphate carrier protein, mitochondrial OS=Homo sapiens GN=SLC25A3 PE=1 SV=2	sp Q00325 MPCP_HUMAN
Phosphatidylinositol-glycan-specific phospholipase D OS=Homo sapiens GN=GPLD1 PE=1 SV=3	sp P80108 PHLD_HUMAN
Phospholipid transfer protein OS=Homo sapiens GN=PLTP PE=1 SV=1	sp P55058 PLTP_HUMAN
Pleckstrin OS=Homo sapiens GN=PLEK PE=1 SV=3	sp P08567 PLEK_HUMAN
Pregnancy zone protein OS=Homo sapiens GN=PZP PE=1 SV=4	sp P20742 PZP_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein disulfide-isomerase A3 OS=Homo sapiens GN=PDIA3 PE=1 SV=4	sp P30101 PDIA3_HUMAN
Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1	sp P05109 S10A8_HUMAN
Protein Z-dependent protease inhibitor OS=Homo sapiens GN=SERPINA10 PE=1 SV=1	sp Q9UK55 ZPI_HUMAN
Proteoglycan 4 OS=Homo sapiens GN=PRG4 PE=1 SV=2	sp Q92954 PRG4_HUMAN
Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4	sp P14618 KPYM_HUMAN
Ras-related protein Rab-10 OS=Homo sapiens GN=RAB10 PE=1 SV=1	sp P61026 RAB10_HUMAN
Ras-related protein Rap-1b OS=Homo sapiens GN=RAP1B PE=1 SV=1	sp P61224 RAP1B_HUMAN
Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 OS=Homo sapiens GN=ATP2A3 PE=1 SV=2	sp Q93084 AT2A3_HUMAN
Serum paraoxonase/arylesterase 1 OS=Homo sapiens GN=PON1 PE=1 SV=3	sp P27169 PON1_HUMAN
Sex hormone-binding globulin OS=Homo sapiens GN=SHBG PE=1 SV=2	sp P04278 SHBG_HUMAN
Small proline-rich protein 2D OS=Homo sapiens GN=SPRR2D PE=2 SV=2	sp P22532 SPR2D_HUMAN
Solute carrier family 2, facilitated glucose transporter member 3 OS=Homo sapiens GN=SLC2A3 PE=1 SV=1	sp P11169 GTR3_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	sp P07996 TSP1_HUMAN
Thyroxine-binding globulin OS=Homo sapiens GN=SERPINA7 PE=1 SV=2	sp P05543 THBG_HUMAN
Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	sp P02766 TTHY_HUMAN
Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1	sp P68363 TBA1B_HUMAN
Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2	sp P07437 TBB5_HUMAN
Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1	sp Q9H4B7 TBB1_HUMAN

Tubulin beta-2A chain OS=Homo sapiens GN=TUBB2A PE=1 SV=1
 Vinculin OS=Homo sapiens GN=VCL PE=1 SV=4
 Voltage-dependent anion-selective channel protein 3 OS=Homo sapiens
 GN=VDAC3 PE=1 SV=1
 von Willebrand factor OS=Homo sapiens GN=VWF PE=1 SV=4
 WD repeat-containing protein 1 OS=Homo sapiens GN=WDR1 PE=1 SV=4

sp|Q13885|TBB2A_HUMAN
 sp|P18206|VINC_HUMAN
 sp|Q9Y277|VDAC3_HUMAN
 sp|P04275|VWF_HUMAN
 sp|O75083|WDR1_HUMAN

Table 2 provides a profile of abnormalities in pathways and glycosylated proteins in a colorectal cancer male patient. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a CRC patient by the present methods. In these methods, the profile of Table 2 is used as a set of biomarkers indicative of CRC.

Table 2. A profile of abnormalities in pathways and glycosylated proteins in a CRC male patient.

Pathway	Glycosylated Protein	p-value	Jaccard similarity
<u>Scavenger Receptors in Platelet Aggregation</u>	APOB, FGA, FGB, FGG, TLN1, ITGA2B, ITGB3	1.08924E-7	4.66667E-2
<u>Coagulation Cascade</u>	FGA, FGB, FGG, F9, F11, F12, F13A1, SERPINA10	1.41766E-7	4.39560E-2
<u>TAM Receptors in Platelet Aggregation</u>	FGA, FGB, FGG, VWF, ITGB3	7.49345E-7	4.20168E-2
<u>Platelet Activation via Adhesion Molecules</u>	FGA, FGB, FGG, VCL, VWF, ITGA2B, ITGB3, TLN1	1.56396E-5	3.05344E-2
<u>Focal Junction Assembly</u>	ACTN1, FLNA, FN1, TLN1, VCL, ITGB3	4.36457E-5	3.15789E-2
<u>Histidine-Rich Glycoprotein (HRG)</u>	FGA, FGB, FGG, C1QA, THBS1, F12	2.85537E-4	2.60870E-2
<u>Platelet Activation via GPCR Signaling</u>	FGA, FGB, FGG, ITGB3, TLN1, GNAI3	4.94723E-4	2.44898E-2
<u>Plasmin Effects in Inflammation</u>	FGA, FGB, FGG, FN1, C1QA, C1R, F12	1.66747E-3	1.97183E-2
<u>Protein Folding</u>	TUBB2A, TUBB, TUBA1B, TUBB1, HSPA8	1.75381E-3	2.22222E-2

<u>Scavenger Receptors in Platelet Activation</u>	APOB, APOE, ITGA2B, ITGB3	2.10901E-3	2.27273E-2
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Table 3A discloses glycoproteins differentially expressed in plasma of gastric cancer female patients. These glycoproteins can be used for diagnosing, monitoring and treating a gastric cancer patient by the present methods. In these methods, glycoproteins of Table 3A are used as a set of biomarkers indicative of gastric cancer.

Table 3A Glycoproteins differentially expressed in plasma of gastric cancer female patients

14-3-3 protein sigma OS=Homo sapiens GN=SFN PE=1 SV=1	sp P31947 1433S_HUMAN
14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	sp P63104 1433Z_HUMAN
78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2	sp P11021 GRP78_HUMAN
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Actin-related protein 2/3 complex subunit 1B OS=Homo sapiens GN=ARPC1B PE=1 SV=3	sp O15143 ARPC1B_HUMAN
Actin-related protein 2/3 complex subunit 4 OS=Homo sapiens GN=ARPC4 PE=1 SV=3	sp P59998 ARPC4_HUMAN
Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5	sp Q01518 CAP1_HUMAN
ADP/ATP translocase 2 OS=Homo sapiens GN=SLC25A5 PE=1 SV=7	sp P05141 ADT2_HUMAN
ADP-ribosylation factor 3 OS=Homo sapiens GN=ARF3 PE=1 SV=2	sp P61204 ARF3_HUMAN (+1)
Alpha-2-antiplasmin OS=Homo sapiens GN=SERPINF2 PE=1 SV=3	sp P08697 A2AP_HUMAN
Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	sp P01023 A2MG_HUMAN
Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2	sp P12814 ACTN1_HUMAN
Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2	sp P06733 ENOA_HUMAN
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	sp P02647 APOA1_HUMAN
Apolipoprotein L1 OS=Homo sapiens GN=APOL1 PE=1 SV=5	sp O14791 APOL1_HUMAN
Apolipoprotein M OS=Homo sapiens GN=APOM PE=1 SV=2	sp O95445 APOM_HUMAN
Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	sp P08519 APOA_HUMAN
ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1	sp P25705 ATPA_HUMAN
Beta-1,4-galactosyltransferase 1 OS=Homo sapiens GN=B4GALT1 PE=1 SV=5	sp P15291 B4GT1_HUMAN
Beta-2-glycoprotein 1 OS=Homo sapiens GN=APOH PE=1 SV=3	sp P02749 APOH_HUMAN
Beta-parvin OS=Homo sapiens GN=PARVB PE=1 SV=1	sp Q9HBI1 PARVB_HUMAN
Carbonic anhydrase 1 OS=Homo sapiens GN=CA1 PE=1 SV=2	sp P00915 CAH1_HUMAN
Carboxypeptidase B2 OS=Homo sapiens GN=CPB2 PE=1 SV=2	sp Q96IY4 CBPB2_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P15169 CBPN_HUMAN
Carboxypeptidase N subunit 2 OS=Homo sapiens GN=CPN2 PE=1 SV=3	sp P22792 CPN2_HUMAN
Cartilage acidic protein 1 OS=Homo sapiens GN=CRTAC1 PE=1 SV=2	sp Q9NQ79 CRAC1_HUMAN
Cholinesterase OS=Homo sapiens GN=BCHE PE=1 SV=1	sp P06276 CHLE_HUMAN
Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5	sp Q00610 CLH1_HUMAN
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Coagulation factor IX OS=Homo sapiens GN=F9 PE=1 SV=2	sp P00740 FA9_HUMAN
Coagulation factor V OS=Homo sapiens GN=F5 PE=1 SV=4	sp P12259 FA5_HUMAN
Coagulation factor X OS=Homo sapiens GN=F10 PE=1 SV=2	sp P00742 FA10_HUMAN

Coagulation factor XI OS=Homo sapiens GN=F11 PE=1 SV=1	sp P03951 FA11_HUMAN
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	sp P00748 FA12_HUMAN
Coagulation factor XIII A chain OS=Homo sapiens GN=F13A1 PE=1 SV=4	sp P00488 F13A_HUMAN
Complement C1q subcomponent subunit A OS=Homo sapiens GN=C1QA PE=1 SV=2	sp P02745 C1QA_HUMAN
Complement C1r subcomponent OS=Homo sapiens GN=C1R PE=1 SV=2	sp P00736 C1R_HUMAN
Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2	sp P01024 CO3_HUMAN
Complement component C8 beta chain OS=Homo sapiens GN=C8B PE=1 SV=3	sp P07358 CO8B_HUMAN
Complement factor H-related protein 1 OS=Homo sapiens GN=CFHR1 PE=1 SV=2	sp Q03591 FHR1_HUMAN
Complement factor H-related protein 5 OS=Homo sapiens GN=CFHR5 PE=1 SV=1	sp Q9BXR6 FHR5_HUMAN
Complement factor I OS=Homo sapiens GN=CFI PE=1 SV=2	sp P05156 CFAI_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit OS=Homo sapiens GN=DDOST PE=1 SV=4	sp P39656 OST48_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Endoplasmic reticulum protein OS=Homo sapiens GN=HSP90B1 PE=1 SV=1	sp P14625 ENPL_HUMAN
Erythrocyte band 7 integral membrane protein OS=Homo sapiens GN=STOM PE=1 SV=3	sp P27105 STOM_HUMAN
Ezrin OS=Homo sapiens GN=EZR PE=1 SV=4	sp P15311 EZRI_HUMAN
F-actin-capping protein subunit beta OS=Homo sapiens GN=CAPZB PE=1 SV=4	sp P47756 CAPZB_HUMAN
Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1	sp Q86UX7 URP2_HUMAN
Fetuin-B OS=Homo sapiens GN=FETUB PE=1 SV=2	sp Q9UGM5 FETUB_HUMAN
Fibulin-1 OS=Homo sapiens GN=FBLN1 PE=1 SV=4	sp P23142 FBLN1_HUMAN
Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4	sp P21333 FLNA_HUMAN
Fructose-bisphosphate aldolase A OS=Homo sapiens GN=ALDOA PE=1 SV=2	sp P04075 ALDOA_HUMAN
Galectin-3-binding protein OS=Homo sapiens GN=LGALS3BP PE=1 SV=1	sp Q08380 LG3BP_HUMAN
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	sp P06396 GELS_HUMAN
Glutathione peroxidase 3 OS=Homo sapiens GN=GPX3 PE=1 SV=2	sp P22352 GPX3_HUMAN
Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3	sp P04406 G3P_HUMAN
Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	sp P00738 HPT_HUMAN
Haptoglobin-related protein OS=Homo sapiens GN=HPR PE=2 SV=2	sp P00739 HPTR_HUMAN
Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1	sp P11142 HSP7C_HUMAN
Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4	sp P08238 HS90B_HUMAN
Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1 SV=2	sp P69905 HBA_HUMAN
Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1 SV=2	sp P68871 HBB_HUMAN
Heparin cofactor 2 OS=Homo sapiens GN=SERPIND1 PE=1 SV=3	sp P05546 HEP2_HUMAN
Hepatocyte growth factor-like protein OS=Homo sapiens GN=MST1 PE=1 SV=2	sp P26927 HGFL_HUMAN
Histidine-rich glycoprotein OS=Homo sapiens GN=HRG PE=1 SV=1	sp P04196 HRG_HUMAN
Identified Proteins (739)	Accession Number
Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1	sp P01861 IGHG4_HUMAN
Ig heavy chain V-I region EU OS=Homo sapiens PE=1 SV=1	sp P01742 HV101_HUMAN
Ig heavy chain V-I region HG3 OS=Homo sapiens PE=3 SV=1	sp P01743 HV102_HUMAN
Ig heavy chain V-I region WOL OS=Homo sapiens PE=1 SV=1	sp P01760 HV105_HUMAN
Ig heavy chain V-II region ARH-77 OS=Homo sapiens PE=4 SV=1	sp P06331 HV209_HUMAN
Ig heavy chain V-II region WAH OS=Homo sapiens PE=1 SV=1	sp P01824 HV206_HUMAN
Ig heavy chain V-III region 23 OS=Homo sapiens GN=IGHV3-23 PE=1 SV=2	sp P01764 HV303_HUMAN
Ig heavy chain V-III region BRO OS=Homo sapiens PE=1 SV=1	sp P01766 HV305_HUMAN
Ig heavy chain V-III region BUT OS=Homo sapiens PE=1 SV=1	sp P01767 HV306_HUMAN

Ig heavy chain V-III region GAL OS=Homo sapiens PE=1 SV=1	sp P01781 HV320_HUMAN
Ig heavy chain V-III region NIE OS=Homo sapiens PE=1 SV=1	sp P01770 HV309_HUMAN
Ig heavy chain V-III region WEA OS=Homo sapiens PE=1 SV=1	sp P01763 HV302_HUMAN
Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1	sp P01834 IGKC_HUMAN
Ig kappa chain V-I region CAR OS=Homo sapiens PE=1 SV=1	sp P01596 KV104_HUMAN
Ig kappa chain V-I region Mev OS=Homo sapiens PE=1 SV=1	sp P01612 KV120_HUMAN
Ig kappa chain V-II region FR OS=Homo sapiens PE=1 SV=1	sp P01615 KV202_HUMAN
Ig kappa chain V-II region RPMI 6410 OS=Homo sapiens PE=4 SV=1	sp P06310 KV206_HUMAN
Ig kappa chain V-IV region STH (Fragment) OS=Homo sapiens PE=1 SV=1	sp P83593 KV405_HUMAN
Ig lambda chain V region 4A OS=Homo sapiens PE=4 SV=1	sp P04211 LV001_HUMAN
Ig lambda chain V-I region HA OS=Homo sapiens PE=1 SV=1	sp P01700 LV102_HUMAN
Ig lambda chain V-I region NEWM OS=Homo sapiens PE=1 SV=1	sp P01703 LV105_HUMAN
Ig lambda chain V-I region NIG-64 OS=Homo sapiens PE=1 SV=1	sp P01702 LV104_HUMAN (+1)
Ig lambda chain V-II region TRO OS=Homo sapiens PE=1 SV=1	sp P01707 LV204_HUMAN
IgGfc-binding protein OS=Homo sapiens GN=FCGBP PE=1 SV=3	sp Q9Y6R7 FCGBP_HUMAN
Integrin alpha-IIb OS=Homo sapiens GN=ITGA2B PE=1 SV=3	sp P08514 ITA2B_HUMAN
Integrin beta-3 OS=Homo sapiens GN=ITGB3 PE=1 SV=2	sp P05106 ITB3_HUMAN
Integrin-linked protein kinase OS=Homo sapiens GN=ILK PE=1 SV=2	sp Q13418 ILK_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens GN=ITIH1 PE=1 SV=3	sp P19827 ITIH1_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H3 OS=Homo sapiens GN=ITIH3 PE=1 SV=2	sp Q06033 ITIH3_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4	sp Q14624 ITIH4_HUMAN
Isocitrate dehydrogenase [NADP], mitochondrial OS=Homo sapiens GN=IDH2 PE=1 SV=2	sp P48735 IDHP_HUMAN
Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3	sp P14923 PLAK_HUMAN
Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	sp P35527 K1C9_HUMAN
Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	sp P04264 K2C1_HUMAN
Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2	sp P35908 K22E_HUMAN
Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2	sp P01042 KNG1_HUMAN
LIM and senescent cell antigen-like-containing domain protein 1 OS=Homo sapiens GN=LIMS1 PE=1 SV=4	sp P48059 LIMS1_HUMAN
L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2	sp P00338 LDHA_HUMAN
Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1	sp P61626 LYSC_HUMAN
Multimerin-1 OS=Homo sapiens GN=MMRN1 PE=1 SV=3	sp Q13201 MMRN1_HUMAN
Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	sp P35579 MYH9_HUMAN
N-acetylmuramoyl-L-alanine amidase OS=Homo sapiens GN=PGLYRP2 PE=1 SV=1	sp Q96PD5 PGRP2_HUMAN
Peptidyl-prolyl cis-trans isomerase B OS=Homo sapiens GN=PPIB PE=1 SV=2	sp P23284 PPIB_HUMAN
Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5	sp P32119 PRDX2_HUMAN
Peroxiredoxin-6 OS=Homo sapiens GN=PRDX6 PE=1 SV=3	sp P30041 PRDX6_HUMAN
Phosphate carrier protein, mitochondrial OS=Homo sapiens GN=SLC25A3 PE=1 SV=2	sp Q00325 MPCP_HUMAN
Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	sp P36955 PEDF_HUMAN
Plasma serine protease inhibitor OS=Homo sapiens GN=SERPINA5 PE=1 SV=3	sp P05154 IPSP_HUMAN
Plastin-2 OS=Homo sapiens GN=LCP1 PE=1 SV=6	sp P13796 PLSL_HUMAN
Platelet glycoprotein Ib alpha chain OS=Homo sapiens GN=GP1BA PE=1 SV=2	sp P07359 GP1BA_HUMAN
Platelet glycoprotein Ib beta chain OS=Homo sapiens GN=GP1BB PE=1 SV=1	sp P13224 GP1BB_HUMAN
Pleckstrin OS=Homo sapiens GN=PLEK PE=1 SV=3	sp P08567 PLEK_HUMAN
Pregnancy zone protein OS=Homo sapiens GN=PZP PE=1 SV=4	sp P20742 PZP_HUMAN
Prenylcysteine oxidase 1 OS=Homo sapiens GN=PCYOX1 PE=1 SV=3	sp Q9UHG3 PCYOX_HUMAN

Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein broad-minded OS=Homo sapiens GN=TBC1D32 PE=2 SV=4	sp Q96NH3 BROMI_HUMAN
Protein disulfide-isomerase A3 OS=Homo sapiens GN=PDIA3 PE=1 SV=4	sp P30101 PDIA3_HUMAN
Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1	sp P05109 S10A8_HUMAN
Protein S100-A9 OS=Homo sapiens GN=S100A9 PE=1 SV=1	sp P06702 S10A9_HUMAN
Proto-oncogene tyrosine-protein kinase Src OS=Homo sapiens GN=SRC PE=1 SV=3	sp P12931 SRC_HUMAN
Putative V-set and immunoglobulin domain-containing-like protein IGHV4OR15-8 OS=Homo sapiens GN=IGHV4OR15-8 PE=5 SV=2	sp A6NJ16 IV4F8_HUMAN
Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4	sp P14618 KPYM_HUMAN
Ras-related protein Rab-10 OS=Homo sapiens GN=RAB10 PE=1 SV=1	sp P61026 RAB10_HUMAN
Ras-related protein Rap-1b OS=Homo sapiens GN=RAP1B PE=1 SV=1	sp P61224 RAP1B_HUMAN
Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	sp P02753 RET4_HUMAN
Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 OS=Homo sapiens GN=ATP2A3 PE=1 SV=2	sp Q93084 AT2A3_HUMAN
Serum amyloid P-component OS=Homo sapiens GN=APCS PE=1 SV=2	sp P02743 SAMP_HUMAN
Small proline-rich protein 2D OS=Homo sapiens GN=SPRR2D PE=2 SV=2	sp P22532 SPR2D_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Telomere length regulation protein TEL2 homolog OS=Homo sapiens GN=TELO2 PE=1 SV=2	sp Q9Y4R8 TELO2_HUMAN
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	sp P07996 TSP1_HUMAN
Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	sp P02766 TTHY_HUMAN
Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1	sp P68363 TBA1B_HUMAN
Tubulin alpha-4A chain OS=Homo sapiens GN=TUBA4A PE=1 SV=1	sp P68366 TBA4A_HUMAN
Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2	sp P07437 TBB5_HUMAN
Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1	sp Q9H4B7 TBB1_HUMAN
Tubulin beta-2A chain OS=Homo sapiens GN=TUBB2A PE=1 SV=1	sp Q13885 TBB2A_HUMAN
Ubiquitin-60S ribosomal protein L40 OS=Homo sapiens GN=UBA52 PE=1 SV=2	sp P62987 RL40_HUMAN
Vinculin OS=Homo sapiens GN=VCL PE=1 SV=4	sp P18206 VINC_HUMAN
Voltage-dependent anion-selective channel protein 3 OS=Homo sapiens GN=VDAC3 PE=1 SV=1	sp Q9Y277 VDAC3_HUMAN
von Willebrand factor OS=Homo sapiens GN=VWF PE=1 SV=4	sp P04275 VWF_HUMAN
WD repeat-containing protein 1 OS=Homo sapiens GN=WDR1 PE=1 SV=4	sp O75083 WDR1_HUMAN

Table 3 provides a profile of abnormalities in pathways and glycosylated proteins in a gastric cancer female patient. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a gastric cancer patient by the present methods. In these methods, the profile of Table 3 is used as a set of biomarkers indicative of gastric cancer.

Table 3. A profile of abnormalities in pathways and glycosylated proteins in a gastric cancer female patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
Complement Activation in Macular Degeneration	CFI, C1QA, C3, C1R, C8B, CRP, CLU, CFHR1	3.77674E-6	3.63636E-2

<u>Focal Junction Assembly</u>	SRC, ACTN1, FLNA, TLN1, ILK, VCL, LIMS1, ITGB3	5.15265E-6	3.57143E-2
<u>Platelet Activation via Adhesion Molecules</u>	GP1BA, SRC, ARPC4, ARPC1B, VCL, VWF, ITGA2B, ITGB3, TLN1, GP1BB	6.77864E-6	3.37838E-2
<u>Coagulation Cascade</u>	KNG1, F5, F9, F11, F10, F12, F13A1	3.29309E-5	3.19635E-2
<u>Adherens Junction Assembly (Nectin)</u>	SRC, ARPC4, ARPC1B, ACTN1, VCL	1.91850E-4	2.73224E-2
<u>Protein Folding</u>	TUBB2A, TUBA4A, TUBB, TUBA1B, TUBB1, HSPA8, HSP90B1	3.15167E-4	2.70270E-2
<u>Glycolysis</u>	GAPDH, ENO1, PKM, ALDOA	4.01213E-4	2.42424E-2
<u>Neutrophil Activation via Adherence on Endothelial Cells</u>	ARPC4, ARPC1B, ACTN1, TLN1, VCL, ITGB3	5.85006E-4	2.57511E-2
<u>Scavenger Receptors in Platelet Activation</u>	GP1BA, APOA1, ITGA2B, ITGB3, GP1BB	1.29150E-3	2.36967E-2
<u>Microtubule Cytoskeleton</u>	TUBB2A, TUBA4A, TUBB, TUBA1B, TUBB1	1.29150E-3	2.36967E-2

Table 4A discloses glycoproteins differentially expressed in plasma of gastric cancer male patients. These glycoproteins can be used for diagnosing, monitoring and treating a gastric cancer patient by the present methods. In these methods, glycoproteins of Table 4A are used as a set of biomarkers indicative of gastric cancer.

Table 4A. Glycoproteins differentially expressed in plasma of gastric male patients

Identified Proteins (739)	Accession Number
14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	sp P63104 1433Z_HUMAN
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAP1 PE=1 SV=5	sp Q01518 CAP1_HUMAN
ADP/ATP translocase 2 OS=Homo sapiens GN=SLC25A5 PE=1 SV=7	sp P05141 ADT2_HUMAN
Afamin OS=Homo sapiens GN=AFM PE=1 SV=1	sp P43652 AFAM_HUMAN
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	sp P04217 A1BG_HUMAN
Alpha-2-antiplasmin OS=Homo sapiens GN=SERPINF2 PE=1 SV=3	sp P08697 A2AP_HUMAN
Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	sp P01023 A2MG_HUMAN
Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2	sp P12814 ACTN1_HUMAN
Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2	sp P06733 ENOA_HUMAN
Angiotensinogen OS=Homo sapiens GN=AGT PE=1 SV=1	sp P01019 ANGT_HUMAN
Antithrombin-III OS=Homo sapiens GN=SERPINC1 PE=1 SV=1	sp P01008 ANT3_HUMAN
Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	sp P04114 APOB_HUMAN
Apolipoprotein D OS=Homo sapiens GN=APOD PE=1 SV=1	sp P05090 APOD_HUMAN

Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp P02649 APOE_HUMAN
Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	sp P08519 APOA_HUMAN
ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1	sp P25705 ATPA_HUMAN
ATP synthase subunit beta, mitochondrial OS=Homo sapiens GN=ATP5B PE=1 SV=3	sp P06576 ATPB_HUMAN
C4b-binding protein beta chain OS=Homo sapiens GN=C4BPB PE=1 SV=1	sp P20851 C4BPB_HUMAN
Calpain-1 catalytic subunit OS=Homo sapiens GN=CAPN1 PE=1 SV=1	sp P07384 CAN1_HUMAN
Carbonic anhydrase 1 OS=Homo sapiens GN=CA1 PE=1 SV=2	sp P00915 CAH1_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P15169 CBPN_HUMAN
Carboxypeptidase N subunit 2 OS=Homo sapiens GN=CPN2 PE=1 SV=3	sp P22792 CPN2_HUMAN
Ceruloplasmin OS=Homo sapiens GN=CP PE=1 SV=1	sp P00450 CERU_HUMAN
Clathrin heavy chain 1 OS=Homo sapiens GN=CLTC PE=1 SV=5	sp Q00610 CLH1_HUMAN
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Coagulation factor V OS=Homo sapiens GN=F5 PE=1 SV=4	sp P12259 FA5_HUMAN
Coagulation factor X OS=Homo sapiens GN=F10 PE=1 SV=2	sp P00742 FA10_HUMAN
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	sp P00748 FA12_HUMAN
Coagulation factor XIII A chain OS=Homo sapiens GN=F13A1 PE=1 SV=4	sp P00488 F13A_HUMAN
Coagulation factor XIII B chain OS=Homo sapiens GN=F13B PE=1 SV=3	sp P05160 F13B_HUMAN
Complement C1q subcomponent subunit A OS=Homo sapiens GN=C1QA PE=1 SV=2	sp P02745 C1QA_HUMAN
Complement C1q subcomponent subunit B OS=Homo sapiens GN=C1QB PE=1 SV=3	sp P02746 C1QB_HUMAN
Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	sp P09871 C1S_HUMAN
Complement C2 OS=Homo sapiens GN=C2 PE=1 SV=2	sp P06681 CO2_HUMAN
Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2	sp P01024 CO3_HUMAN
Complement C4-A OS=Homo sapiens GN=C4A PE=1 SV=2	sp P0C0L4 CO4A_HUMAN
Complement C4-B OS=Homo sapiens GN=C4B PE=1 SV=2	sp P0C0L5 CO4B_HUMAN
Complement C5 OS=Homo sapiens GN=C5 PE=1 SV=4	sp P01031 CO5_HUMAN
Complement component C6 OS=Homo sapiens GN=C6 PE=1 SV=3	sp P13671 CO6_HUMAN
Complement component C7 OS=Homo sapiens GN=C7 PE=1 SV=2	sp P10643 CO7_HUMAN
Complement component C8 alpha chain OS=Homo sapiens GN=C8A PE=1 SV=2	sp P07357 CO8A_HUMAN
Complement component C8 beta chain OS=Homo sapiens GN=C8B PE=1 SV=3	sp P07358 CO8B_HUMAN
Complement factor H OS=Homo sapiens GN=CFH PE=1 SV=4	sp P08603 CFAH_HUMAN
Complement factor H-related protein 1 OS=Homo sapiens GN=CFHR1 PE=1 SV=2	sp Q03591 FHR1_HUMAN
Complement factor I OS=Homo sapiens GN=CFI PE=1 SV=2	sp P05156 CFAI_HUMAN
Corticosteroid-binding globulin OS=Homo sapiens GN=SERPINA6 PE=1 SV=1	sp P08185 CBG_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	sp P15924 DESP_HUMAN
Endoplasmin OS=Homo sapiens GN=HSP90B1 PE=1 SV=1	sp P14625 ENPL_HUMAN
Erythrocyte band 7 integral membrane protein OS=Homo sapiens GN=STOM PE=1 SV=3	sp P27105 STOM_HUMAN
Ezrin OS=Homo sapiens GN=EZR PE=1 SV=4	sp P15311 EZRI_HUMAN
Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1	sp Q86UX7 URP2_HUMAN
Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4	sp P21333 FLNA_HUMAN
Fructose-bisphosphate aldolase A OS=Homo sapiens GN=ALDOA PE=1 SV=2	sp P04075 ALDOA_HUMAN
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	sp P06396 GELS_HUMAN
Glutathione peroxidase 3 OS=Homo sapiens GN=GPX3 PE=1 SV=2	sp P22352 GPX3_HUMAN
Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens	sp P04406 G3P_HUMAN

GN=GAPDH PE=1 SV=3

Heat shock cognate 71 kDa protein OS=Homo sapiens GN=HSPA8 PE=1 SV=1

Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4

Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1 SV=2

Hemopexin OS=Homo sapiens GN=HPX PE=1 SV=2

Hexokinase-1 OS=Homo sapiens GN=HK1 PE=1 SV=3

Histone H4 OS=Homo sapiens GN=HIST1H4A PE=1 SV=2

Hyaluronan-binding protein 2 OS=Homo sapiens GN=HABP2 PE=1 SV=1

Ig heavy chain V-I region EU OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-I region HG3 OS=Homo sapiens PE=3 SV=1

Ig heavy chain V-I region V35 OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-I region WOL OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region 23 OS=Homo sapiens GN=IGHV3-23 PE=1 SV=2

Ig heavy chain V-III region BUT OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region CAM OS=Homo sapiens PE=1 SV=1

Ig heavy chain V-III region GAL OS=Homo sapiens PE=1 SV=1

Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1

Ig kappa chain V-I region DEE OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-I region Mev OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-I region WEA OS=Homo sapiens PE=1 SV=1

Ig kappa chain V-II region RPMI 6410 OS=Homo sapiens PE=4 SV=1

Ig kappa chain V-III region HAH OS=Homo sapiens PE=2 SV=1

Ig kappa chain V-III region VG (Fragment) OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-I region VOR OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-III region LOI OS=Homo sapiens PE=1 SV=1

Ig lambda chain V-IV region Hil OS=Homo sapiens PE=1 SV=1

IgGfc-binding protein OS=Homo sapiens GN=FCGBP PE=1 SV=3

Insulin-like growth factor-binding protein complex acid labile subunit OS=Homo sapiens GN=IGFALS PE=1 SV=1

Integrin alpha-IIb OS=Homo sapiens GN=ITGA2B PE=1 SV=3

Integrin beta-3 OS=Homo sapiens GN=ITGB3 PE=1 SV=2

Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens GN=ITIH1 PE=1 SV=3

Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITIH2 PE=1 SV=2

Inter-alpha-trypsin inhibitor heavy chain H3 OS=Homo sapiens GN=ITIH3 PE=1 SV=2

Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4

Isocitrate dehydrogenase [NADP], mitochondrial OS=Homo sapiens GN=IDH2 PE=1 SV=2

Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3

Kallistatin OS=Homo sapiens GN=SERPINA4 PE=1 SV=3

Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6

Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2

Keratin, type II cytoskeletal 78 OS=Homo sapiens GN=KRT78 PE=2 SV=2

Keratinocyte proline-rich protein OS=Homo sapiens GN=KPRP PE=1 SV=1

Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2

Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3

sp|P11142|HSP7C_HUMAN

sp|P08238|HS90B_HUMAN

sp|P68871|HBB_HUMAN

sp|P02790|HEMO_HUMAN

sp|P19367|HKK1_HUMAN

sp|P62805|H4_HUMAN

sp|Q14520|HABP2_HUMAN

sp|P01742|HV101_HUMAN

sp|P01743|HV102_HUMAN

sp|P23083|HV103_HUMAN

sp|P01760|HV105_HUMAN

sp|P01764|HV303_HUMAN

sp|P01767|HV306_HUMAN

sp|P01768|HV307_HUMAN

sp|P01781|HV320_HUMAN

sp|P01834|IGKC_HUMAN

sp|P01597|KV105_HUMAN

sp|P01612|KV120_HUMAN

sp|P01610|KV118_HUMAN

sp|P06310|KV206_HUMAN

sp|P18135|KV312_HUMAN

sp|P04433|KV309_HUMAN

sp|P01699|LV101_HUMAN

sp|P80748|LV302_HUMAN

sp|P01717|LV403_HUMAN

sp|Q9Y6R7|FCGBP_HUMAN

sp|P35858|ALS_HUMAN

sp|P08514|ITA2B_HUMAN

sp|P05106|ITB3_HUMAN

sp|P19827|ITIH1_HUMAN

sp|P19823|ITIH2_HUMAN

sp|Q06033|ITIH3_HUMAN

sp|Q14624|ITIH4_HUMAN

sp|P48735|IDHP_HUMAN

sp|P14923|PLAK_HUMAN

sp|P29622|KAIN_HUMAN

sp|P04264|K2C1_HUMAN

sp|P35908|K22E_HUMAN

sp|Q8N1N4|K2C78_HUMAN

sp|Q5T749|KPRP_HUMAN

sp|P01042|KNG1_HUMAN

sp|P18428|LBP_HUMAN

L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2	sp P00338 LDHA_HUMAN
Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1	sp P61626 LYSC_HUMAN
Multimerin-1 OS=Homo sapiens GN=MMRN1 PE=1 SV=3	sp Q13201 MMRN1_HUMAN
Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	sp P35579 MYH9_HUMAN
N-acetylmuramoyl-L-alanine amidase OS=Homo sapiens GN=PGLYRP2 PE=1 SV=1	sp Q96PD5 PGRP2_HUMAN
Peptidyl-prolyl cis-trans isomerase B OS=Homo sapiens GN=PPIB PE=1 SV=2	sp P23284 PPIB_HUMAN
Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5	sp P32119 PRDX2_HUMAN
Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	sp P36955 PEDF_HUMAN
Plasma kallikrein OS=Homo sapiens GN=KLKB1 PE=1 SV=1	sp P03952 KLKB1_HUMAN
Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=2	sp P05155 IC1_HUMAN
Plasma serine protease inhibitor OS=Homo sapiens GN=SERPINA5 PE=1 SV=3	sp P05154 IPSP_HUMAN
Platelet glycoprotein Ib alpha chain OS=Homo sapiens GN=GP1BA PE=1 SV=2	sp P07359 GP1BA_HUMAN
Platelet glycoprotein Ib beta chain OS=Homo sapiens GN=GP1BB PE=1 SV=1	sp P13224 GP1BB_HUMAN
Pleckstrin OS=Homo sapiens GN=PLEK PE=1 SV=3	sp P08567 PLEK_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein AMBP OS=Homo sapiens GN=AMBP PE=1 SV=1	sp P02760 AMBP_HUMAN
Protein broad-minded OS=Homo sapiens GN=TBC1D32 PE=2 SV=4	sp Q96NH3 BROMI_HUMAN
Protein disulfide-isomerase A3 OS=Homo sapiens GN=PDIA3 PE=1 SV=4	sp P30101 PDIA3_HUMAN
Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1	sp P05109 S10A8_HUMAN
Prothrombin OS=Homo sapiens GN=F2 PE=1 SV=2	sp P00734 THRB_HUMAN
Purine nucleoside phosphorylase OS=Homo sapiens GN=PNP PE=1 SV=2	sp P00491 PNPH_HUMAN
Pyruvate kinase PKM OS=Homo sapiens GN=PKM PE=1 SV=4	sp P14618 KPYM_HUMAN
Ras-related protein Rab-10 OS=Homo sapiens GN=RAB10 PE=1 SV=1	sp P61026 RAB10_HUMAN
Ras-related protein Rap-1b OS=Homo sapiens GN=RAP1B PE=1 SV=1	sp P61224 RAP1B_HUMAN
Reticulon-4 OS=Homo sapiens GN=RTN4 PE=1 SV=2	sp Q9NQC3 RTN4_HUMAN
Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	sp P02753 RET4_HUMAN
Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 OS=Homo sapiens GN=ATP2A3 PE=1 SV=2	sp Q93084 AT2A3_HUMAN
Serum paraoxonase/arylesterase 1 OS=Homo sapiens GN=PON1 PE=1 SV=3	sp P27169 PON1_HUMAN
Skin-specific protein 32 OS=Homo sapiens GN=XP32 PE=1 SV=1	sp Q5T750 XP32_HUMAN
Small proline-rich protein 2D OS=Homo sapiens GN=SPRR2D PE=2 SV=2	sp P22532 SPR2D_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Telomere length regulation protein TEL2 homolog OS=Homo sapiens GN=TELO2 PE=1 SV=2	sp Q9Y4R8 TELO2_HUMAN
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	sp P07996 TSP1_HUMAN
Thyroxine-binding globulin OS=Homo sapiens GN=SERPINA7 PE=1 SV=2	sp P05543 THBG_HUMAN
Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1	sp P68363 TBA1B_HUMAN
Tubulin beta chain OS=Homo sapiens GN=TUBB PE=1 SV=2	sp P07437 TBB5_HUMAN
Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1	sp Q9H4B7 TBB1_HUMAN
Tubulin beta-2A chain OS=Homo sapiens GN=TUBB2A PE=1 SV=1	sp Q13885 TBB2A_HUMAN
Vinculin OS=Homo sapiens GN=VCL PE=1 SV=4	sp P18206 VINC_HUMAN
Voltage-dependent anion-selective channel protein 3 OS=Homo sapiens GN=VDAC3 PE=1 SV=1	sp Q9Y277 VDAC3_HUMAN
von Willebrand factor OS=Homo sapiens GN=VWF PE=1 SV=4	sp P04275 VWF_HUMAN
WD repeat-containing protein 1 OS=Homo sapiens GN=WDR1 PE=1 SV=4	sp O75083 WDR1_HUMAN
Zinc-alpha-2-glycoprotein OS=Homo sapiens GN=AZGP1 PE=1 SV=2	sp P25311 ZA2G_HUMAN

Table 4 provides a profile of abnormalities in pathways and glycosylated proteins in a gastric cancer male patient. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a gastric cancer patient by the present methods.

Table 4. A profile of abnormalities in pathways and glycosylated proteins in a gastric cancer male patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
<u>Complement Activation in Macular Degeneration</u>	CFI, C1QA, C3, C4B, C1QB, C2, C1S, C5, C8A, C6, C8B, C7, CRP, CLU, CFHR1, CFH	5.30067E-16	7.58294E-2
<u>Complement Classical Pathway</u>	C1QA, C3, C4B, C1QB, C2, C1S, C5, C8A, C6, C8B, C7	3.59745E-12	6.25000E-2
<u>Complement Cascade Activation by Pentraxins</u>	C1QA, C3, C4B, C2, C1S, C5, C8A, C6, C8B, C7, CRP, CFH	3.59689E-11	5.79710E-2
<u>Complement Activation by Lectin</u>	C3, C4B, C2, C5, C8A, C6, C8B, C7	1.19784E-8	4.70588E-2
<u>Complement Alternative Pathway</u>	CFI, C3, C5, C8A, C6, C8B, C7, CFH	2.84784E-7	4.16667E-2
<u>Coagulation Cascade</u>	KLKB1, KNG1, SERPINC1, F2, F5, F10, F12, F13A1	3.21514E-6	3.68664E-2
<u>Glycolysis</u>	HK1, GAPDH, ENO1, PKM, ALDOA	2.40683E-5	3.06748E-2
<u>Scavenger Receptors in Platelet Activation</u>	GP1BA, APOB, APOE, ITGA2B, ITGB3, GP1BB	1.54933E-4	2.87081E-2
<u>Plasmin Effects in Inflammation</u>	A2M, KLKB1, SERPING1, C1QA, KNG1, C1QB, C1S, ENO1, SERPINF2, F12	2.53755E-4	2.58398E-2
<u>Focal Junction Assembly</u>	ACTN1, FLNA, TLN1, VCL, CAPN1, ITGB3	4.05858E-4	2.66667E-2

Table 5A discloses glycoproteins differentially expressed in plasma of pancreatic adenocarcinoma female patients. These glycoproteins can be used for diagnosing, monitoring and treating a pancreatic adenocarcinoma patient by the present methods. In these methods, glycoproteins of Table 5A are used as a set of biomarkers indicative of pancreatic adenocarcinoma cancer.

Table 5A. Glycoproteins differentially expressed in plasma of pancreatic adenocarcinoma cancer (PADC) female patients

Identified Proteins	Accession Number
Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1	sp P60709 ACTB_HUMAN
Alpha-1-acid glycoprotein 1 OS=Homo sapiens GN=ORM1 PE=1 SV=1	sp P02763 A1AG1_HUMAN
Alpha-1-antichymotrypsin OS=Homo sapiens GN=SERPINA3 PE=1 SV=2	sp P01011 AACT_HUMAN
Alpha-1-antitrypsin OS=Homo sapiens GN=SERPINA1 PE=1 SV=3	sp P01009 A1AT_HUMAN
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	sp P04217 A1BG_HUMAN
Alpha-2-antiplasmin OS=Homo sapiens GN=SERPINF2 PE=1 SV=3	sp P08697 A2AP_HUMAN
Angiotensinogen OS=Homo sapiens GN=AGT PE=1 SV=1	sp P01019 ANGT_HUMAN
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	sp P02647 APOA1_HUMAN
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp P02649 APOE_HUMAN
Beta-2-glycoprotein 1 OS=Homo sapiens GN=APOH PE=1 SV=3	sp P02749 APOH_HUMAN
C4b-binding protein alpha chain OS=Homo sapiens GN=C4BPA PE=1 SV=2	sp P04003 C4BPA_HUMAN
Carboxypeptidase B2 OS=Homo sapiens GN=CPB2 PE=1 SV=2	sp Q96IY4 CBPB2_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P15169 CBPN_HUMAN
Carboxypeptidase N subunit 2 OS=Homo sapiens GN=CPN2 PE=1 SV=3	sp P22792 CPN2_HUMAN
CD5 antigen-like OS=Homo sapiens GN=CD5L PE=1 SV=1	sp O43866 CD5L_HUMAN
Ceruloplasmin OS=Homo sapiens GN=CP PE=1 SV=1	sp P00450 CERU_HUMAN
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	sp P09871 C1S_HUMAN
Complement C5 OS=Homo sapiens GN=C5 PE=1 SV=4	sp P01031 CO5_HUMAN
Complement component C7 OS=Homo sapiens GN=C7 PE=1 SV=2	sp P10643 CO7_HUMAN
Complement component C9 OS=Homo sapiens GN=C9 PE=1 SV=2	sp P02748 CO9_HUMAN
Complement factor I OS=Homo sapiens GN=CFI PE=1 SV=2	sp P05156 CFAI_HUMAN
Corticosteroid-binding globulin OS=Homo sapiens GN=SERPINA6 PE=1 SV=1	sp P08185 CBG_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	sp P15924 DESP_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	sp P02671 FIBA_HUMAN
Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4	sp P02751 FINC_HUMAN
Fibulin-1 OS=Homo sapiens GN=FBLN1 PE=1 SV=4	sp P23142 FBLN1_HUMAN
Ficolin-3 OS=Homo sapiens GN=FCN3 PE=1 SV=2	sp O75636 FCN3_HUMAN
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	sp P06396 GELS_HUMAN
Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	sp P00738 HPT_HUMAN
Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1 SV=2	sp P69905 HBA_HUMAN
Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1 SV=2	sp P68871 HBB_HUMAN
Heparin cofactor 2 OS=Homo sapiens GN=SERPIND1 PE=1 SV=3	sp P05546 HEP2_HUMAN
Histidine-rich glycoprotein OS=Homo sapiens GN=HRG PE=1 SV=1	sp P04196 HRG_HUMAN
Hornerin OS=Homo sapiens GN=HRNR PE=1 SV=2	sp Q86YZ3 HORN_HUMAN

Ig alpha-2 chain C region OS=Homo sapiens GN=IGHA2 PE=1 SV=3	sp P01877 IGHA2_HUMAN
Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1	sp P01861 IGHG4_HUMAN
Ig heavy chain V-II region WAH OS=Homo sapiens PE=1 SV=1	sp P01824 HV206_HUMAN
Ig kappa chain V-I region DEE OS=Homo sapiens PE=1 SV=1	sp P01597 KV105_HUMAN
Ig kappa chain V-I region WEA OS=Homo sapiens PE=1 SV=1	sp P01610 KV118_HUMAN
Ig kappa chain V-II region FR OS=Homo sapiens PE=1 SV=1	sp P01615 KV202_HUMAN
Ig kappa chain V-II region TEW OS=Homo sapiens PE=1 SV=1	sp P01617 KV204_HUMAN
Ig kappa chain V-IV region Len OS=Homo sapiens PE=1 SV=2	sp P01625 KV402_HUMAN
Ig lambda chain V-I region NEW OS=Homo sapiens PE=1 SV=1	sp P01701 LV103_HUMAN
Ig lambda chain V-III region LOI OS=Homo sapiens PE=1 SV=1	sp P80748 LV302_HUMAN
Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3	sp P01871 IGHM_HUMAN
Immunoglobulin J chain OS=Homo sapiens GN=IGJ PE=1 SV=4	sp P01591 IGJ_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITIH2 PE=1 SV=2	sp P19823 ITIH2_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H3 OS=Homo sapiens GN=ITIH3 PE=1 SV=2	sp Q06033 ITIH3_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4	sp Q14624 ITIH4_HUMAN
Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3	sp P14923 PLAK_HUMAN
Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	sp P35527 K1C9_HUMAN
Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	sp P04264 K2C1_HUMAN
Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2	sp P01042 KNG1_HUMAN
Leucine-rich alpha-2-glycoprotein OS=Homo sapiens GN=LRG1 PE=1 SV=2	sp P02750 A2GL_HUMAN
Peptidyl-prolyl cis-trans isomerase FKBP1A OS=Homo sapiens GN=FKBP1A PE=1 SV=2	sp P62942 FKB1A_HUMAN
Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5	sp P32119 PRDX2_HUMAN
Phosphatidylinositol-glycan-specific phospholipase D OS=Homo sapiens GN=GPLD1 PE=1 SV=3	sp P80108 PHLD_HUMAN
Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	sp P36955 PEDF_HUMAN
Plasma kallikrein OS=Homo sapiens GN=KLKB1 PE=1 SV=1	sp P03952 KLKB1_HUMAN
Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=2	sp P05155 IC1_HUMAN
Plasma serine protease inhibitor OS=Homo sapiens GN=SERPINA5 PE=1 SV=3	sp P05154 IPSP_HUMAN
Pregnancy zone protein OS=Homo sapiens GN=PZP PE=1 SV=4	sp P20742 PZP_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein AMBP OS=Homo sapiens GN=AMBP PE=1 SV=1	sp P02760 AMBP_HUMAN
Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1	sp P05109 S10A8_HUMAN
Prothrombin OS=Homo sapiens GN=F2 PE=1 SV=2	sp P00734 THRB_HUMAN
Serotransferrin OS=Homo sapiens GN=TF PE=1 SV=3	sp P02787 TRFE_HUMAN
Thyroxine-binding globulin OS=Homo sapiens GN=SERPINA7 PE=1 SV=2	sp P05543 THBG_HUMAN
Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	sp P02766 TTHY_HUMAN
Vitamin K-dependent protein S OS=Homo sapiens GN=PROS1 PE=1 SV=1	sp P07225 PROS_HUMAN
Zinc-alpha-2-glycoprotein OS=Homo sapiens GN=AZGP1 PE=1 SV=2	sp P25311 ZA2G_HUMAN

Table 5 provides a profile of abnormalities in pathways and abnormally glycosylated proteins in a pancreatic adenocarcinoma female patient. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a pancreatic adenocarcinoma patient by the present methods.

Table 5. A profile of abnormalities in pathways and glycosylated proteins in a pancreatic adenocarcinoma female patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
<u>Complement Activation in Macular Degeneration</u>	CFI, C1S, C5, C9, C7, CRP, CLU	2.82682E-7	4.48718E-2
<u>Complement Cascade Activation by Pentraxins</u>	C4BPA, C1S, C5, C9, C7, CRP	3.20201E-6	4.02685E-2
<u>Complement Classical Pathway</u>	IGHM, C1S, C5, C9, C7	5.81054E-6	4.23729E-2
<u>Plasmin Effects in Inflammation</u>	FGA, FN1, KLKB1, SERPING1, KNG1, TF, C1S, SERPINF2	3.08961E-5	2.46154E-2
<u>Coagulation Cascade</u>	FGA, KLKB1, KNG1, PROS1, F2	7.58898E-5	3.20513E-2
<u>Positive Acute Phase Proteins Synthesis</u>	APOA1, APOE, SERPINA3, CP, CRP, SERPINA1, FGA, FN1, ORM1, HP	8.37736E-5	1.81818E-2
<u>Complement Alternative Pathway</u>	CFI, C5, C9, C7	2.98648E-4	3.03030E-2
<u>Complement Activation by Lectin</u>	C5, C9, C7	1.35026E-3	2.70270E-2
<u>Bradykinin Effects in Inflammation</u>	KLKB1, KNG1, CPN1, AGT	1.54179E-3	2.36686E-2
<u>Histidine-Rich Glycoprotein (HRG)</u>	FGA, HRG, SERPIND1, SERPINA5	4.26986E-3	1.97044E-2

Table 6A discloses glycoproteins differentially expressed in plasma of pancreatic adenocarcinoma male patients. These glycoproteins can be used for diagnosing, monitoring and treating a pancreatic adenocarcinoma patient by the present methods. In these methods, glycoproteins of Table 6A are used as a set of biomarkers indicative of pancreatic adenocarcinoma cancer.

Table 6A. Glycoproteins differentially expressed in plasma of pancreatic adenocarcinoma cancer (PADC) male patients

Identified Proteins

Accession Number

Afamin OS=Homo sapiens GN=AFM PE=1 SV=1	sp P43652 AFAM_HUMAN
Alpha-1-acid glycoprotein 1 OS=Homo sapiens GN=ORM1 PE=1 SV=1	sp P02763 A1AG1_HUMAN
Alpha-1-antitrypsin OS=Homo sapiens GN=SERPINA1 PE=1 SV=3	sp P01009 A1AT_HUMAN
Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	sp P01023 A2MG_HUMAN
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	sp P02647 APOA1_HUMAN
Apolipoprotein A-II OS=Homo sapiens GN=APOA2 PE=1 SV=1	sp P02652 APOA2_HUMAN
Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	sp P04114 APOB_HUMAN
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp P02649 APOE_HUMAN
C4b-binding protein alpha chain OS=Homo sapiens GN=C4BPA PE=1 SV=2	sp P04003 C4BPA_HUMAN
Carboxypeptidase B2 OS=Homo sapiens GN=CPB2 PE=1 SV=2	sp Q96IY4 CBPB2_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P15169 CBPN_HUMAN
Carboxypeptidase N subunit 2 OS=Homo sapiens GN=CPN2 PE=1 SV=3	sp P22792 CPN2_HUMAN
Ceruloplasmin OS=Homo sapiens GN=CP PE=1 SV=1	sp P00450 CERU_HUMAN
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	sp P09871 C1S_HUMAN
Complement C5 OS=Homo sapiens GN=C5 PE=1 SV=4	sp P01031 CO5_HUMAN
Complement factor B OS=Homo sapiens GN=CFB PE=1 SV=2	sp P00751 CFAB_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3	sp P15924 DESP_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	sp P02671 FIBA_HUMAN
Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2	sp P02675 FIBB_HUMAN
Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	sp P02679 FIBG_HUMAN
Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4	sp P02751 FINC_HUMAN
Galectin-3-binding protein OS=Homo sapiens GN=LGALS3BP PE=1 SV=1	sp Q08380 LG3BP_HUMAN
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	sp P06396 GELS_HUMAN
Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	sp P00738 HPT_HUMAN
Hornerin OS=Homo sapiens GN=HRNR PE=1 SV=2	sp Q86YZ3 HORN_HUMAN
Identified Proteins (228)	Accession Number
Ig alpha-2 chain C region OS=Homo sapiens GN=IGHA2 PE=1 SV=3	sp P01877 IGHA2_HUMAN
Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1	sp P01861 IGHG4_HUMAN
Ig heavy chain V-III region BUR OS=Homo sapiens PE=1 SV=1	sp P01773 HV312_HUMAN
Ig kappa chain V-I region WEA OS=Homo sapiens PE=1 SV=1	sp P01610 KV118_HUMAN
Ig kappa chain V-II region FR OS=Homo sapiens PE=1 SV=1	sp P01615 KV202_HUMAN
Ig lambda chain V-I region NEW OS=Homo sapiens PE=1 SV=1	sp P01701 LV103_HUMAN
Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3	sp P01871 IGHM_HUMAN
IgGfC-binding protein OS=Homo sapiens GN=FCGBP PE=1 SV=3	sp Q9Y6R7 FCGBP_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITI2 PE=1 SV=2	sp P19823 ITI2_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H3 OS=Homo sapiens GN=ITI3 PE=1 SV=2	sp Q06033 ITI3_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens	sp Q14624 ITI4_HUMAN

GN=ITIH4 PE=1 SV=4	
Kallistatin OS=Homo sapiens GN=SERPINA4 PE=1 SV=3	sp P29622 KAIN_HUMAN
Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	sp P35527 K1C9_HUMAN
Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	sp P04264 K2C1_HUMAN
Keratinocyte proline-rich protein OS=Homo sapiens GN=KPRP PE=1 SV=1	sp Q5T749 KPRP_HUMAN
Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2	sp P01042 KNG1_HUMAN
Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	sp P18428 LBP_HUMAN
Peptidyl-prolyl cis-trans isomerase FKBP1A OS=Homo sapiens GN=FKBP1A PE=1 SV=2	sp P62942 FKB1A_HUMAN
Phosphatidylinositol-glycan-specific phospholipase D OS=Homo sapiens GN=GPLD1 PE=1 SV=3	sp P80108 PHLD_HUMAN
Polymeric immunoglobulin receptor OS=Homo sapiens GN=PIGR PE=1 SV=4	sp P01833 PIGR_HUMAN
Pregnancy zone protein OS=Homo sapiens GN=PZP PE=1 SV=4	sp P20742 PZP_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Protein AMBP OS=Homo sapiens GN=AMBP PE=1 SV=1	sp P02760 AMBP_HUMAN
Serotransferrin OS=Homo sapiens GN=TF PE=1 SV=3	sp P02787 TRFE_HUMAN
Serum amyloid A-4 protein OS=Homo sapiens GN=SAA4 PE=1 SV=2	sp P35542 SAA4_HUMAN
Sex hormone-binding globulin OS=Homo sapiens GN=SHBG PE=1 SV=2	sp P04278 SHBG_HUMAN
Thyroxine-binding globulin OS=Homo sapiens GN=SERPINA7 PE=1 SV=2	sp P05543 THBG_HUMAN
Vitamin K-dependent protein S OS=Homo sapiens GN=PROS1 PE=1 SV=1	sp P07225 PROS_HUMAN
Zinc-alpha-2-glycoprotein OS=Homo sapiens GN=AZGP1 PE=1 SV=2	sp P25311 ZA2G_HUMAN

Table 6 provides a profile of abnormalities in pathways and glycosylated proteins in a pancreatic adenocarcinoma male patient. This profile, including any of protein biomarkers and pathways, can be used for diagnosing, monitoring and treating a pancreatic adenocarcinoma patient by the present methods.

Table 6. A profile of abnormalities in pathways and glycosylated proteins in a pancreatic adenocarcinoma male patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
<u>Positive Acute Phase Proteins Synthesis</u>	APOA1, APOA2, APOE, A2M, CP, CRP, SERPINA1, LBP, FGA, FGB, FGG, FN1, ORM1, HP	9.40620E-10	2.63653E-2
<u>TAM Receptors in Platelet Aggregation</u>	FGA, FGB, FGG, PROS1	2.84129E-6	5.26316E-2
<u>Plasmin Effects in Inflammation</u>	FGA, FGB, FGG, FN1, A2M, KNG1, TF, C1S	4.87208E-6	2.58065E-2

<u>Complement Cascade Activation by Pentraxins</u>	CFB, C4BPA, C1S, C5, CRP	1.70620E-5	3.70370E-2
<u>Coagulation Cascade</u>	FGA, FGB, FGG, KNG1, PROS1	2.36122E-5	3.54610E-2
<u>Complement Activation in Macular Degeneration</u>	CFB, C1S, C5, CRP, CLU	2.61822E-5	3.49650E-2
<u>Scavenger Receptors in Platelet Aggregation</u>	APOB, FGA, FGB, FGG	7.22674E-5	3.66972E-2
<u>Scavenger Receptors in Platelet Activation</u>	APOB, APOA1, APOA2, APOE	2.56073E-4	3.03030E-2
<u>Vascular Endothelial Cell Activation by Blood Coagulation Factors</u>	FGA, FGB, FGG, PROS1, KNG1	4.45784E-4	2.26244E-2
<u>Lipogenesis Regulation in Adipocytes</u>	APOB, APOA1, APOA2, APOE	4.65075E-4	2.73973E-2

Table 7A discloses glycoproteins differentially expressed in plasma of liver cancer patients. These glycoproteins can be used for diagnosing, monitoring and treating a liver cancer patient by the present methods. In these methods, glycoproteins of Table 5A are used as a set of biomarkers indicative of liver cancer.

Table 7A. Glycoproteins differentially expressed in plasma of liver cancer patients

Identified Proteins (739)	Accession Number
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	sp P04217 A1BG_HUMAN
Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	sp P04114 APOB_HUMAN
Apolipoprotein D OS=Homo sapiens GN=APOD PE=1 SV=1	sp P05090 APOD_HUMAN
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	sp P02649 APOE_HUMAN
Apolipoprotein L1 OS=Homo sapiens GN=APOL1 PE=1 SV=5	sp O14791 APOL1_HUMAN
Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	sp P08519 APOA_HUMAN
ATP-binding cassette sub-family B member 9 OS=Homo sapiens GN=ABCB9 PE=1 SV=1	sp Q9NP78 ABCB9_HUMAN
Attractin OS=Homo sapiens GN=ATRN PE=1 SV=2	sp O75882 ATRN_HUMAN
C4b-binding protein alpha chain OS=Homo sapiens GN=C4BPA PE=1 SV=2	sp P04003 C4BPA_HUMAN
C4b-binding protein beta chain OS=Homo sapiens GN=C4BPB PE=1 SV=1	sp P20851 C4BPB_HUMAN
Carbonic anhydrase 1 OS=Homo sapiens GN=CA1 PE=1 SV=2	sp P00915 CAH1_HUMAN
Carboxypeptidase N catalytic chain OS=Homo sapiens GN=CPN1 PE=1 SV=1	sp P15169 CBPN_HUMAN
Cholesteryl ester transfer protein OS=Homo sapiens GN=CETP PE=1 SV=2	sp P11597 CETP_HUMAN
Coagulation factor V OS=Homo sapiens GN=F5 PE=1 SV=4	sp P12259 FA5_HUMAN
Coagulation factor X OS=Homo sapiens GN=F10 PE=1 SV=2	sp P00742 FA10_HUMAN
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	sp P00748 FA12_HUMAN
Coagulation factor XIII A chain OS=Homo sapiens GN=F13A1 PE=1 SV=4	sp P00488 F13A_HUMAN
Complement C1q subcomponent subunit B OS=Homo sapiens GN=C1QB PE=1 SV=3	sp P02746 C1QB_HUMAN

Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	sp P09871 C1S_HUMAN
Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2	sp P01024 CO3_HUMAN
Complement C4-A OS=Homo sapiens GN=C4A PE=1 SV=2	sp P0C0L4 CO4A_HUMAN
Complement C4-B OS=Homo sapiens GN=C4B PE=1 SV=2	sp P0C0L5 CO4B_HUMAN
Complement C5 OS=Homo sapiens GN=C5 PE=1 SV=4	sp P01031 CO5_HUMAN
Complement component C8 beta chain OS=Homo sapiens GN=C8B PE=1 SV=3	sp P07358 CO8B_HUMAN
Complement component C9 OS=Homo sapiens GN=C9 PE=1 SV=2	sp P02748 CO9_HUMAN
Complement factor B OS=Homo sapiens GN=CFB PE=1 SV=2	sp P00751 CFAB_HUMAN
Complement factor H OS=Homo sapiens GN=CFH PE=1 SV=4	sp P08603 CFAH_HUMAN
Complement factor H-related protein 1 OS=Homo sapiens GN=CFHR1 PE=1 SV=2	sp Q03591 FHR1_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1	sp Q86UX7 URP2_HUMAN
Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	sp P02671 FIBA_HUMAN
Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2	sp P02675 FIBB_HUMAN
Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	sp P02679 FIBG_HUMAN
Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4	sp P02751 FINC_HUMAN
Glutathione peroxidase 3 OS=Homo sapiens GN=GPX3 PE=1 SV=2	sp P22352 GPX3_HUMAN
Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3	sp P04406 G3P_HUMAN
Hepatocyte growth factor-like protein OS=Homo sapiens GN=MST1 PE=1 SV=2	sp P26927 HGFL_HUMAN
Hornerin OS=Homo sapiens GN=HRNR PE=1 SV=2	sp Q86YZ3 HORN_HUMAN
Hyaluronan-binding protein 2 OS=Homo sapiens GN=HABP2 PE=1 SV=1	sp Q14520 HABP2_HUMAN
Ig alpha-2 chain C region OS=Homo sapiens GN=IGHA2 PE=1 SV=3	sp P01877 IGHA2_HUMAN
Ig delta chain C region OS=Homo sapiens GN=IGHD PE=1 SV=2	sp P01880 IGHD_HUMAN
Ig heavy chain V-I region V35 OS=Homo sapiens PE=1 SV=1	sp P23083 HV103_HUMAN
Ig heavy chain V-I region WOL OS=Homo sapiens PE=1 SV=1	sp P01760 HV105_HUMAN
Ig heavy chain V-II region MCE OS=Homo sapiens PE=1 SV=1	sp P01817 HV204_HUMAN
Ig heavy chain V-III region BUR OS=Homo sapiens PE=1 SV=1	sp P01773 HV312_HUMAN
Ig heavy chain V-III region CAM OS=Homo sapiens PE=1 SV=1	sp P01768 HV307_HUMAN
Ig heavy chain V-III region KOL OS=Homo sapiens PE=1 SV=1	sp P01772 HV311_HUMAN
Ig heavy chain V-III region NIE OS=Homo sapiens PE=1 SV=1	sp P01770 HV309_HUMAN
Ig heavy chain V-III region TIL OS=Homo sapiens PE=1 SV=1	sp P01765 HV304_HUMAN
Ig kappa chain V-I region Kue OS=Homo sapiens PE=1 SV=1	sp P01604 KV112_HUMAN
Ig kappa chain V-I region Lay OS=Homo sapiens PE=1 SV=1	sp P01605 KV113_HUMAN
Ig kappa chain V-I region Mev OS=Homo sapiens PE=1 SV=1	sp P01612 KV120_HUMAN
Ig kappa chain V-I region Scw OS=Homo sapiens PE=1 SV=1	sp P01609 KV117_HUMAN
Ig kappa chain V-I region WEA OS=Homo sapiens PE=1 SV=1	sp P01610 KV118_HUMAN
Ig kappa chain V-II region FR OS=Homo sapiens PE=1 SV=1	sp P01615 KV202_HUMAN
Ig kappa chain V-II region MIL OS=Homo sapiens PE=1 SV=1	sp P01616 KV203_HUMAN
Ig kappa chain V-II region TEW OS=Homo sapiens PE=1 SV=1	sp P01617 KV204_HUMAN
Ig kappa chain V-III region CLL OS=Homo sapiens PE=4 SV=2	sp P04207 KV308_HUMAN
Ig kappa chain V-III region IARC/BL41 OS=Homo sapiens PE=4 SV=1	sp P06311 KV311_HUMAN
Ig kappa chain V-III region SIE OS=Homo sapiens PE=1 SV=1	sp P01620 KV302_HUMAN
Ig kappa chain V-III region VG (Fragment) OS=Homo sapiens PE=1 SV=1	sp P04433 KV309_HUMAN
Ig lambda chain V-I region NEWM OS=Homo sapiens PE=1 SV=1	sp P01703 LV105_HUMAN
Ig lambda chain V-I region NIG-64 OS=Homo sapiens PE=1 SV=1	sp P01702 LV104_HUMAN
Ig lambda chain V-I region VOR OS=Homo sapiens PE=1 SV=1	sp P01699 LV101_HUMAN

Ig lambda chain V-II region TRO OS=Homo sapiens PE=1 SV=1	sp P01707 LV204_HUMAN
Ig lambda chain V-V region DEL OS=Homo sapiens PE=1 SV=1	sp P01719 LV501_HUMAN
Ig lambda chain V-VI region SUT OS=Homo sapiens PE=1 SV=1	sp P06317 LV603_HUMAN
Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3	sp P01871 IGHM_HUMAN
Ig mu heavy chain disease protein OS=Homo sapiens PE=1 SV=1	sp P04220 MUCB_HUMAN
Insulin-like growth factor-binding protein complex acid labile subunit OS=Homo sapiens GN=IGFALS PE=1 SV=1	sp P35858 ALS_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H1 OS=Homo sapiens GN=ITIH1 PE=1 SV=3	sp P19827 ITIH1_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITIH2 PE=1 SV=2	sp P19823 ITIH2_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H3 OS=Homo sapiens GN=ITIH3 PE=1 SV=2	sp Q06033 ITIH3_HUMAN
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4	sp Q14624 ITIH4_HUMAN
Junction plakoglobin OS=Homo sapiens GN=JUP PE=1 SV=3	sp P14923 PLAK_HUMAN
Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	sp P35527 K1C9_HUMAN
Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	sp P04264 K2C1_HUMAN
Keratinocyte proline-rich protein OS=Homo sapiens GN=KPRP PE=1 SV=1	sp Q5T749 KPRP_HUMAN
Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	sp P18428 LBP_HUMAN
Loricrin OS=Homo sapiens GN=LOR PE=1 SV=2	sp P23490 LORI_HUMAN
Myosin-9 OS=Homo sapiens GN=MYH9 PE=1 SV=4	sp P35579 MYH9_HUMAN
Phosphatidylinositol-glycan-specific phospholipase D OS=Homo sapiens GN=GPLD1 PE=1 SV=3	sp P80108 PHLD_HUMAN
Polymeric immunoglobulin receptor OS=Homo sapiens GN=PIGR PE=1 SV=4	sp P01833 PIGR_HUMAN
Prenylcysteine oxidase 1 OS=Homo sapiens GN=PCYOX1 PE=1 SV=3	sp Q9UHG3 PCYOX_HUMAN
Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	sp P07737 PROF1_HUMAN
Properdin OS=Homo sapiens GN=CFP PE=1 SV=2	sp P27918 PROP_HUMAN
Protein AMBP OS=Homo sapiens GN=AMBP PE=1 SV=1	sp P02760 AMBP_HUMAN
Protein broad-minded OS=Homo sapiens GN=TBC1D32 PE=2 SV=4	sp Q96NH3 BROMI_HUMAN
Putative V-set and immunoglobulin domain-containing-like protein IGHV4OR15-8 OS=Homo sapiens GN=IGHV4OR15-8 PE=5 SV=2	sp A6NJ16 IV4F8_HUMAN
Ras-related protein Rap-1b OS=Homo sapiens GN=RAP1B PE=1 SV=1	sp P61224 RAP1B_HUMAN
Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	sp P02753 RET4_HUMAN
Selenoprotein P OS=Homo sapiens GN=SEPP1 PE=1 SV=3	sp P49908 SEPP1_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Telomere length regulation protein TEL2 homolog OS=Homo sapiens GN=TELO2 PE=1 SV=2	sp Q9Y4R8 TELO2_HUMAN
Tetranectin OS=Homo sapiens GN=CLEC3B PE=1 SV=3	sp P05452 TETN_HUMAN
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	sp P07996 TSP1_HUMAN
Thyroxine-binding globulin OS=Homo sapiens GN=SERPINA7 PE=1 SV=2	sp P05543 THBG_HUMAN
Transforming growth factor-beta-induced protein ig-h3 OS=Homo sapiens GN=TGFBI PE=1 SV=1	sp Q15582 BGH3_HUMAN
Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1	sp P68363 TBA1B_HUMAN
Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1	sp P02774 VTDB_HUMAN
Vitamin K-dependent protein C OS=Homo sapiens GN=PROC PE=1 SV=1	sp P04070 PROC_HUMAN
Vitronectin OS=Homo sapiens GN=VTN PE=1 SV=1	sp P04004 VTNC_HUMAN
Zinc-alpha-2-glycoprotein OS=Homo sapiens GN=AZGP1 PE=1 SV=2	sp P25311 ZA2G_HUMAN

Table 7 provides a profile of abnormalities in pathways and glycosylated proteins in a liver cancer male patient. This profile, including any of protein biomarkers and

pathways, can be used for diagnosing, monitoring and treating a liver cancer patient by the present methods.

Table 7. A profile of abnormalities in pathways and glycosylated proteins in a liver cancer male patient.

Pathway	Glycosylated Proteins	p-value	Jaccard similarity
<u>Complement Activation in Macular Degeneration</u>	CFB, C3, C4B, C1QB, CFP, C1S, C5, C9, C8B, VTN, CFHR1, CFH	8.32733E-15	7.45342E-2
<u>Complement Classical Pathway</u>	IGHM, C3, C4B, C1QB, C1S, C5, C9, C8B	1.18506E-10	6.40000E-2
<u>Complement Cascade Activation by Pentraxins</u>	CFB, C3, C4B, C4BPA, C1S, C5, C9, C8B, CFH	1.71295E-10	5.76923E-2
<u>Coagulation Cascade</u>	FGA, FGB, FGG, PROC, F5, F10, F12, F13A1	8.71371E-9	4.90798E-2
<u>Complement Alternative Pathway</u>	CFB, C3, CFP, C5, C9, C8B, CFH	2.29775E-8	5.03597E-2
<u>Complement Activation by Lectin</u>	C3, C4B, C5, C9, C8B	2.09678E-6	4.20168E-2
<u>Scavenger Receptors in Platelet Aggregation</u>	APOB, FGA, FGB, FGG, TLN1	7.96085E-6	3.75940E-2
<u>Histidine-Rich Glycoprotein (HRG)</u>	FGA, FGB, FGG, C1QB, THBS1, F12	4.12511E-5	2.84360E-2
<u>Plasmin Effects in Inflammation</u>	FGA, FGB, FGG, FN1, C1QB, C1S, F12	2.02105E-4	2.08333E-2
<u>TAM Receptors in Platelet Aggregation</u>	FGA, FGB, FGG	2.58384E-4	2.94118E-2

As can be appreciated from the data in Tables 1A-7A and Tables 1-7, some of the protein markers associate specifically with a particular type of GI cancer, while other protein markers are common for several different GI cancers. As can be also appreciated from Tables 1A-7A and Tables 1-7, various pathways are affected in each of the cancers.

The term “biological pathway or pathway” is understood broadly and refers to a set of proteins (and other molecules) that act as a network to initiate, alter or terminate a biological process. Examples of biological pathways include metabolic pathways, gene-regulation pathways, and signal transduction pathways. Dozens and even hundreds of different proteins may comprise a pathway. An activation or inhibition of one protein in a pathway may trigger a chain reaction of activities in the pathway. While two different cancer patients may have a mutation in different proteins, the same pathway may be affected in both

patients and lead to the same symptoms. Thus, identifying pathways affected in a cancer patient is a technical advantage of the present methods because it allows to more accurately assess the differences which cause symptoms.

According to some embodiments of the present methods, the first step is to identify proteins abnormally present in a blood or plasma sample of a patient in comparison to a healthy control, as shown in Tables 1A, 2A, 3A, 4A, 5A, 6A, and 7A. The second step is to identify pathways which are enriched (show statistically significantly overlap) with the proteins from the protein profile lists, as shown in Tables 1, 2, 3, 4, 5, 6 and 7.

Using the Fisher's exact test, nonrandom associations between two categorical variables (a pathway and a protein profile list) are determined. Each of the protein profile lists is compared to a pathway database by applying Fisher's exact test consecutively to all pathways in the database to compare the given protein profile and each of the pathways in the database. One pathway database of pathway maps that can be used for this analysis is PATHWAY STUDIO^R available from Elsevier, Inc. (Nikitin et al. 2003, Bioinformatics, <https://www.elsevier.com/solutions/pathway-studio-biological-research>).

This approach was used to identify pathways for glycosylated protein biomarkers in Tables 1-7. PATHWAY STUDIO^R software was also used to generate Figures 1-23, each of which defines a relationship between proteins in a pathway affected in at least one of GI cancers. Any of the proteins shown in Figs. 1-23 can be included as an additional biomarker for diagnosing, monitoring and/or treating a GI cancer together with protein biomarkers from Tables 1-7.

Table 8 provides a list of pathways which can be used as a biomarker in screening, monitoring and/or treating a GI cancer. In Table 8, a pathway that can be used as a biomarker in colorectal cancer, gastric cancer, liver cancer or pancreatic cancer is identified with an XX.

As can be seen from Table 8, some pathways, such as for example, the adherens junction assembly pathway (Fig. 1) is a specific biomarker for a gastric cancer female patient, while other pathways such as the coagulation cascade pathway (Fig. 3) is a biomarker for all GI cancers, including colorectal cancer, gastric cancer, liver cancer and pancreatic cancer. Table 8 matches each of the pathways with a figure from Figs. 1-23.

Table 8. Summary of pathways of glycobiomarkers of GI cancers

#	Pathway Name	Fig#	CRC (Colorectal cancer)		Gastric cancer		Liver cancer	Pancreatic Adenocarcinoma (PADC)	
			F	M	F	M	M	F	M
1	Adherens Junction Assembly (Nectin)	1			XX				
2	Bradykinin Effects in Inflammation	2						XX	
3	Coagulation Cascade	3	XX	XX	XX	XX	XX	XX	XX
4	Complement Activation by Lectin	4				XX	XX	XX	
5	Complement Activation in Macular Degeneration	5	XX		XX	XX	XX	XX	XX
6	Complement Alternative Pathway	6				XX	XX	XX	
7	Complement Cascade Activation by Pentraxins	7	XX			XX	XX	XX	XX
8	Complement Classical Pathway	8	XX			XX	XX	XX	
9	Focal Junction Assembly	9	XX	XX	XX	XX			
10	Glycolysis	10	XX		XX	XX			
11	Histidine-Rich Glycoprotein (HRG)	11		XX			XX	XX	
12	Lipogenesis Regulation in Adipocytes	12							XX
13	Microtubule Cytoskeleton	13			XX				
14	Neutrophil Activation via Adherence on Endothelial Cells	14			XX				
15	Plasmin Effects in Inflammation	15		XX		XX	XX	XX	
16	Platelet Activation via Adhesion Molecules	16	XX	XX	XX				
17	Platelet Activation via GPCR Signaling	17		XX					
18	Positive Acute Phase Proteins Synthesis	18						XX	XX

19	Protein Folding	19		XX	XX				
20	Scavenger Receptors in Platelet Activation	20	XX	XX	XX	XX			XX
21	Scavenger Receptors in Platelet Aggregation	21	XX	XX			XX		XX
22	TAM Receptors in Platelet Aggregation	22	XX	XX			XX		XX
23	Vascular Endothelial Cell Activation by Blood Coagulation Factors	23							XX

M – Male; F – Female

XX – denotes that the pathway is affected.

Each of the pathways listed in Table 8 (as defined in more detail in Figs. 1-23 by proteins which play a role in the pathway) can be used as a biomarker in a number of various tests. Various proteins from each of the pathway, including those listed in tables 1- 7 and other proteins as shown in Figs. 1-23, can be included as representative biomarkers in screening, monitoring and treating GI cancer patients.

Further embodiments provide diagnostic methods based on any of the biomarkers in Tables 1, 2, 3, 4, 5, 6, 7 and/or 8, as may be further modified based on Figs. 1-23. Various methods are contemplated and may include an immunoassay, biochip assay, nanoassay in which at least one panel with at least one or more biomarkers from Tables 1-8 is used, as may be further modified with any of additional protein biomarkers shown in Figs. 1-23.

At least in some of these methods, a sample is obtained from a patient. This sample may be a human tissue biopsy or biosample including pancreas biopsy sample, gastrointestinal sample, blood sample, plasma sample, serum sample, circulating tumor cells sample, tear sample, saliva sample, sperm sample, urine sample, fecal sample and hair sample or any other human biospecimen. The sample is then screened to obtain a protein profile and to determine whether the protein profile in the sample matches at least partially a profile from any of Tables 1, 2, 3, 4, 5, 6, or 7. The abnormal proteins in the patient's profile are also analyzed to determine which of the pathways are affected, including the pathways shown in Tables 1-8.

Suitable screening methods may include chromatography, gas chromatography, liquid chromatography, mass spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay. Suitable methods further include a combination of a detection techniques of nucleic acids and proteins or peptides.

In some methods, at least one biomarker and/or glycobiomarker of Tables 1-8 is immobilized on a solid support. In some methods, the testing is conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 1-8.

In further embodiments, the testing is conducted by reacting the patient's sample with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 1-8. In some embodiments, the testing is conducted by reacting the patient's sample with a synthetic compound or probe which reacts with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 1-8.

Further embodiments include a method for diagnosing, monitoring and reating a GI cancer, the method comprising obtaining a blood or plasma sample from a patient in need of the treatment, analyzing glycoproteins in the sample, creating a profile of pathways and glycoproteins for the patient, and comparing the profile to the profiles of glycobiomarkers and pathways of Tables 1-8.

In some embodiments, a screening can be conducted with a patient's sample without protein extraction. In further embodiments, proteins are isolated from the patient's sample, such as a blood or plasma sample, and a test is conducted with the isolated proteins. In some embodiments, all proteins in the sample are analyzed. In other embodiments, the analysis is conducted only for proteins which are glycosylated. In further embodiments, only GlcNAc glycosylated proteins are analyzed.

The advantages of these screening methods include: these tests are non-invasive and they can be conducted in a very short period of time. In some embodiments, the same test can be repeated several times within a period of time to monitor progression of a GI cancer and/or evaluate the efficiency of a treatment plan.

Further embodiments provide Multiplex Molecular Diagnostic Protein assays, a combination of protein assay and assay based on detection of DNA or RNA, and kits, including an immunoassay, biochip assay, nanoassay and molecular assay. In some

embodiments, an assay detects protein biomarker and/or glycobiomarkers or peptides derived from the biomarker and/or glycobiomarkers from any of Tables 1-8 and Figs. 1-24.

In further embodiments, a patient's sample is reacted with a set of antibodies, each of which is selectively specific for at least one biomarker and/or glycobiomarker from Tables 1, 2, 3, 4, 5, 6, 7 or 8. The complex between an antibody and a glycobiomarker or a biomarker is then may be detected with a second antibody conjugated to a detection molecule.

Further embodiments include methods for detecting and monitoring a GI cancer. In these methods, a patient's sample is tested for expression of at least some biomarker and/or glycobiomarkers listed in Table 2, 3, 4, 5, 6, 7 or 8.

Further embodiments include methods in which patient's response to therapy, such as for example surgery, radiation, immunotherapy or chemotherapy, is monitored with testing a patient's sample for expression of at least some biomarker and/or glycobiomarkers listed in Tables 1, 2, 3, 4, 5, 6, 7 and 8. Other applications include detecting a recurrent or residual GI cancer by testing a patient's sample for expression of at least some biomarker and/or glycobiomarkers listed in Tables 1, 2, 3, 4, 5, 6 and/or 7.

Other applications include screening of genetically predisposed individuals for a GI cancer by testing the individual's sample for expression of at least some biomarkers and/or glycobiomarkers listed in Tables 1, 2, 3, 4, 5, 6 and/or 7. Such genetically predisposed individuals include, but not limited, to BRCA mutation carriers; PALB2 mutation carriers; p16 mutation carriers; Lynch syndrome patients; Peutz-Jeghers syndrome patients; and individuals with a family history of a GI cancer.

In some methods, a biochip comprising a set of at least one or more biomarker and/or glycobiomarkers listed in Tables 1, 2, 3, 4, 5, 6 and/or 7 can be used as a robust and sensitive tool to monitor a GI cancer progression and response to therapy. These biochips can be also used as a biomarker or molecular modality for drug development or drug optimization.

In some embodiments, a patient can be screened and evaluated based on a test conducted with the patient's sample and a panel of biomarker and/or glycobiomarkers and pathways which include at least one or more biomarkers listed in Tables 1, 2, 3, 4, 5, 6, 7 and/or 8.

This invention also provides compositions and methods for selective detection of pancreatic diseases and/or disorders of the pancreas, including pancreatic cancer, pancreatitis, acute pancreatitis, chronic pancreatitis, hereditary pancreatitis, autoimmune

pancreatitis, and pancreatic neoplasm. It also provides compositions and methods for monitoring progression of a pancreatic disease and/or disorder of the pancreas, including, but not limited to, pancreatic cancer, pancreatitis, and autoimmune pancreatitis

The invention provides a panel of pancreatic disease biomarkers. These biomarkers may include glycosylated biomarkers. In some embodiments, a panel of biomarkers include at least one or more glycosylated biomarkers listed in Tables 5A, 5, 6A, and 6. In other embodiments, a panel of biomarkers include all biomarkers listed in Tables 5A, 5, 6A, and 6. Further embodiments include a panel which comprises at least one or more biomarkers as listed in Table 9. In further embodiments, a panel includes a combination of at least one or more biomarkers from Table 9 and at least one or more biomarkers from any of the tables 5A, 5, 6A, and 6.

In some embodiments, a panel of biomarkers includes at least one or more proteins listed in Table 9. In other embodiments, a panel of biomarkers includes all proteins listed in Table 9. Further embodiments include a panel which comprises at least one or more glycosylated biomarkers as listed in any of the Tables 5A, 5, 6A, and 6.. In further embodiments, a panel includes a combination of at least one or more biomarkers from Tables 5A, 5, 6A, 6 and 9.

Table 9. Proteins differentially expressed in human plasma of pancreatic adenocarcinoma patients

14-3-3 protein gamma OS=Homo sapiens GN=YWHAG PE=1 SV=2	sp P61981 1433G_HUMAN
14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1	sp P63104 1433Z_HUMAN
78 kDa glucose-regulated protein OS=Homo sapiens GN=HSPA5 PE=1 SV=2	sp P11021 GRP78_HUMAN
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	sp P63261 ACTG_HUMAN
Alpha-1-acid glycoprotein 2 OS=Homo sapiens GN=ORM2 PE=1 SV=2	sp P19652 A1AG2_HUMAN
Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	sp P01023 A2MG_HUMAN
Alpha-actinin-1 OS=Homo sapiens GN=ACTN1 PE=1 SV=2	sp P12814 ACTN1_HUMAN
Alpha-enolase OS=Homo sapiens GN=ENO1 PE=1 SV=2	sp P06733 ENOA_HUMAN
Alpha-N-acetylglucosaminidase OS=Homo sapiens GN=NAGLU PE=1 SV=2	sp P54802 ANAG_HUMAN
Aminopeptidase N OS=Homo sapiens GN=ANPEP PE=1 SV=4	sp P15144 AMPN_HUMAN
Angiogenin OS=Homo sapiens GN=ANG PE=1 SV=1	sp P03950 ANGI_HUMAN
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	sp P02647 APOA1_HUMAN
Apolipoprotein A-II OS=Homo sapiens GN=APOA2 PE=1 SV=1	sp P02652 APOA2_HUMAN
Apolipoprotein C-III OS=Homo sapiens GN=APOC3 PE=1 SV=1	sp P02656 APOC3_HUMAN

Apolipoprotein C-IV OS=Homo sapiens GN=APOC4 PE=1 SV=1	sp P55056 APOC4_HUMAN
Apolipoprotein F OS=Homo sapiens GN=APOF PE=1 SV=2	sp Q13790 APOF_HUMAN
Beta-2-microglobulin OS=Homo sapiens GN=B2M PE=1 SV=1	sp P61769 B2MG_HUMAN
Beta-enolase OS=Homo sapiens GN=ENO3 PE=1 SV=5	sp P13929 ENOB_HUMAN
Cadherin-5 OS=Homo sapiens GN=CDH5 PE=1 SV=5	sp P33151 CADH5_HUMAN
Calmodulin OS=Homo sapiens GN=CALM1 PE=1 SV=2	sp P62158 CALM_HUMAN
Calreticulin OS=Homo sapiens GN=CALR PE=1 SV=1	sp P27797 CALR_HUMAN
Carbonic anhydrase 1 OS=Homo sapiens GN=CA1 PE=1 SV=2	sp P00915 CAH1_HUMAN
Carbonic anhydrase 2 OS=Homo sapiens GN=CA2 PE=1 SV=2	sp P00918 CAH2_HUMAN
Cartilage oligomeric matrix protein OS=Homo sapiens GN=COMP PE=1 SV=2	sp P49747 COMP_HUMAN
Catalase OS=Homo sapiens GN=CAT PE=1 SV=3	sp P04040 CATA_HUMAN
Cathepsin D OS=Homo sapiens GN=CTSD PE=1 SV=1	sp P07339 CATD_HUMAN
CD5 antigen-like OS=Homo sapiens GN=CD5L PE=1 SV=1	sp O43866 CD5L_HUMAN
Cell surface glycoprotein MUC18 OS=Homo sapiens GN=MCAM PE=1 SV=2	sp P43121 MUC18_HUMAN
Chloride intracellular channel protein 1 OS=Homo sapiens GN=CLIC1 PE=1 SV=4	sp O00299 CLIC1_HUMAN
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	sp P10909 CLUS_HUMAN
Coagulation factor X OS=Homo sapiens GN=F10 PE=1 SV=2	sp P00742 FA10_HUMAN
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	sp P00748 FA12_HUMAN
Cofilin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3	sp P23528 COF1_HUMAN
Collectin-10 OS=Homo sapiens GN=COLEC10 PE=2 SV=2	sp Q9Y6Z7 COL10_HUMAN
Complement C4-B OS=Homo sapiens GN=C4B PE=1 SV=1	sp P0C0L5 CO4B_HUMAN
Coronin-1A OS=Homo sapiens GN=CORO1A PE=1 SV=4	sp P31146 COR1A_HUMAN
Corticosteroid-binding globulin OS=Homo sapiens GN=SERPINA6 PE=1 SV=1	sp P08185 CBG_HUMAN
C-reactive protein OS=Homo sapiens GN=CRP PE=1 SV=1	sp P02741 CRP_HUMAN
Creatine kinase M-type OS=Homo sapiens GN=CKM PE=1 SV=2	sp P06732 KCRM_HUMAN
Cystatin-C OS=Homo sapiens GN=CST3 PE=1 SV=1	sp P01034 CYTC_HUMAN
Cysteine-rich secretory protein 3 OS=Homo sapiens GN=CRISP3 PE=1 SV=1	sp P54108 CRIS3_HUMAN
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	sp Q12805 FBLN3_HUMAN
Fermitin family homolog 3 OS=Homo sapiens GN=FERMT3 PE=1 SV=1	sp Q86UX7 URP2_HUMAN
Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	sp P02671 FIBA_HUMAN
Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2	sp P02675 FIBB_HUMAN
Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	sp P02679 FIBG_HUMAN
Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4	sp P21333 FLNA_HUMAN
Flavin reductase (NADPH) OS=Homo sapiens GN=BLVRB PE=1 SV=3	sp P30043 BLVRB_HUMAN
Fructose-bisphosphate aldolase A OS=Homo sapiens GN=ALDOA PE=1 SV=2	sp P04075 ALDOA_HUMAN
Galectin-3-binding protein OS=Homo sapiens GN=LGALS3BP PE=1 SV=1	sp Q08380 LG3BP_HUMAN
Gamma-glutamyl hydrolase OS=Homo sapiens GN=GGH PE=1	sp Q92820 GGH_HUMAN

SV=2

Glutathione S-transferase omega-1 OS=Homo sapiens

GN=GSTO1 PE=1 SV=2

sp|P78417|GSTO1_HUMAN

Glyceraldehyde-3-phosphate dehydrogenase OS=Homo

sapiens GN=GAPDH PE=1 SV=3

sp|P04406|G3P_HUMAN

Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1

sp|P00738|HPT_HUMAN

Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1

SV=2

sp|P69905|HBA_HUMAN

Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1

SV=2

sp|P68871|HBB_HUMAN

Hepatocyte growth factor-like protein OS=Homo sapiens

GN=MST1 PE=1 SV=2

sp|P26927|HGFL_HUMAN

Ig gamma-3 chain C region OS=Homo sapiens GN=IGHG3

PE=1 SV=2

sp|P01860|IGHG3_HUMAN

Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1

SV=1

sp|P01834|IGKC_HUMAN

Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3

sp|P01871|IGHM_HUMAN

Immunoglobulin lambda-like polypeptide 5 OS=Homo sapiens

GN=IGLL5 PE=2 SV=2

sp|B9A064|IGLL5_HUMAN
(+4)

Insulin-like growth factor II OS=Homo sapiens GN=IGF2 PE=1

SV=1

sp|P01344|IGF2_HUMAN

Insulin-like growth factor-binding protein 3 OS=Homo sapiens

GN=IGFBP3 PE=1 SV=2

sp|P17936|IBP3_HUMAN

Intercellular adhesion molecule 1 OS=Homo sapiens

GN=ICAM1 PE=1 SV=2

sp|P05362|ICAM1_HUMAN

Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1

PE=1 SV=6

sp|P04264|K2C1_HUMAN

Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens

GN=KRT2 PE=1 SV=2

sp|P35908|K22E_HUMAN

L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA

PE=1 SV=2

sp|P00338|LDHA_HUMAN

L-lactate dehydrogenase B chain OS=Homo sapiens GN=LDHB

PE=1 SV=2

sp|P07195|LDHB_HUMAN

Lysosome-associated membrane glycoprotein 1 OS=Homo

sapiens GN=LAMP1 PE=1 SV=3

sp|P11279|LAMP1_HUMAN

Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1

sp|P61626|LYSC_HUMAN

Mannan-binding lectin serine protease 2 OS=Homo sapiens

GN=MASP2 PE=1 SV=4

sp|O00187|MASP2_HUMAN

Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA

OS=Homo sapiens GN=MAN1A1 PE=1 SV=3

sp|P33908|MA1A1_HUMAN

Multiple epidermal growth factor-like domains protein 8

OS=Homo sapiens GN=MEGF8 PE=1 SV=2

sp|Q7Z7M0|MEGF8_HUMAN

Neural cell adhesion molecule 1 OS=Homo sapiens

GN=NCAM1 PE=1 SV=3

sp|P13591|NCAM1_HUMAN

Neural cell adhesion molecule L1-like protein OS=Homo

sapiens GN=CHL1 PE=1 SV=4

sp|O00533|CHL1_HUMAN

Neutrophil defensin 1 OS=Homo sapiens GN=DEFA1 PE=1

SV=1

sp|P59665|DEF1_HUMAN
(+1)

Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5

sp|P32119|PRDX2_HUMAN

Phosphatidylinositol-glycan-specific phospholipase D

OS=Homo sapiens GN=GPLD1 PE=1 SV=3

sp|P80108|PHLD_HUMAN

Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	sp P36955 PEDF_HUMAN
Plasma alpha-L-fucosidase OS=Homo sapiens GN=FUCA2 PE=1 SV=2	sp Q9BTY2 FUCO2_HUMAN
Plasma kallikrein OS=Homo sapiens GN=KLKB1 PE=1 SV=1	sp P03952 KLKB1_HUMAN
Platelet glycoprotein Ib alpha chain OS=Homo sapiens GN=GP1BA PE=1 SV=1	sp P07359 GP1BA_HUMAN
Pleckstrin OS=Homo sapiens GN=PLEK PE=1 SV=3	sp P08567 PLEK_HUMAN
Pregnancy zone protein OS=Homo sapiens GN=PZP PE=1 SV=4	sp P20742 PZP_HUMAN
Procollagen C-endopeptidase enhancer 1 OS=Homo sapiens GN=PCOLCE PE=1 SV=2	sp Q15113 PCOC1_HUMAN
Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1	sp P05109 S10A8_HUMAN
Pyruvate kinase isozymes M1/M2 OS=Homo sapiens GN=PKM PE=1 SV=4	sp P14618 KPYM_HUMAN
Ras suppressor protein 1 OS=Homo sapiens GN=RSU1 PE=1 SV=3	sp Q15404 RSU1_HUMAN
Receptor-type tyrosine-protein phosphatase eta OS=Homo sapiens GN=PTPRJ PE=1 SV=3	sp Q12913 PTPRJ_HUMAN
Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	sp P02753 RET4_HUMAN
Scavenger receptor cysteine-rich type 1 protein M130 OS=Homo sapiens GN=CD163 PE=1 SV=2	sp Q86VB7 C163A_HUMAN
Secreted phosphoprotein 24 OS=Homo sapiens GN=SPP2 PE=1 SV=1	sp Q13103 SPP24_HUMAN
Serotransferrin OS=Homo sapiens GN=TF PE=1 SV=3	sp P02787 TRFE_HUMAN
Sex hormone-binding globulin OS=Homo sapiens GN=SHBG PE=1 SV=2	sp P04278 SHBG_HUMAN
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	sp Q9Y490 TLN1_HUMAN
Transgelin-2 OS=Homo sapiens GN=TAGLN2 PE=1 SV=3	sp P37802 TAGL2_HUMAN
Triosephosphate isomerase OS=Homo sapiens GN=TP11 PE=1 SV=3	sp P60174 TPIS_HUMAN
Tropomyosin alpha-4 chain OS=Homo sapiens GN=TPM4 PE=1 SV=3	sp P67936 TPM4_HUMAN
Vasodilator-stimulated phosphoprotein OS=Homo sapiens GN=VASP PE=1 SV=3	sp P50552 VASP_HUMAN
Vinculin OS=Homo sapiens GN=VCL PE=1 SV=4	sp P18206 VINC_HUMAN
Vitamin K-dependent protein S OS=Homo sapiens GN=PROS1 PE=1 SV=1	sp P07225 PROS_HUMAN

Other embodiments provide kits which comprise at least one panel as described above in connection with Tables 5A, 5, 6A, 6 and 9. Such kits may further comprise a biochip.

Various methods are contemplated and may include an immunoassay, biochip assay, nanoassay in which at least one panel with at least one or more biomarkers from Tables 5A, 5, 6A and 6 or at least one or more biomarkers from Table 9 are used. At least in

some of these methods, a sample is obtained from a patient. This sample may be a human tissue biopsy or biosample including pancreas biopsy sample, gastrointestinal sample, blood sample, plasma sample, serum sample, circulating tumor cells sample, tear sample, saliva sample, sperm sample, urine sample, fecal sample and hair sample or any other human biospecimen.

The sample is then screened for presence of at least one or more glycosylated markers listed in Tables 5A, 5, 6A, 6 and/or for presence of at least one or more protein markers listed in Table 9.

Suitable screening methods may include chromatography, gas chromatography, liquid chromatography, mass spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay. Suitable methods further include a combination of a detection techniques of nucleic acids and proteins or peptides. In some methods, at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9 is immobilized on a solid support. In some methods, the testing is conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9. In further embodiments, the testing is conducted by reacting the patient's sample with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9. In some embodiments, the testing is conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9.

Further embodiments include a method for treating a disorder of the pancreas, the method comprising obtaining a sample from a mammal in need of the treatment and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9.

A method is provided for determining a state or probability of a pancreatic disorder, the method comprising: (a) determining the level of one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9, and (b) the level of CA 19-9.

A method is provided for determining a state or probability of a pancreatic disorder, the method comprising: (a) determining the level of one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9 and (b) the level of amylase.

A method is provided for determining a state or probability of a pancreatic disorder, the method comprising: (a) determining the level of one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9, and (b) the level of glycosylated protein.

A method is provided for determining a state or probability of a pancreatic disorder, the method comprising: (a) determining the level of one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9, and (b) the level of RNA or DNA.

A method is provided for determining a state or probability of a pancreatic disorder, the method comprising: (a) determining the level of one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9, and (b) the level of virus or viral infection of the patient.

In some embodiments, a screening can be conducted with a patient's sample without protein extraction. In further embodiments, proteins are extracted from the patient's sample and a test is conducted with the extracted proteins. In some embodiments, all proteins in the sample are analyzed. In other embodiments, the analysis is conducted only for proteins which are abnormally glycosylated.

The advantages of these screening methods include: these tests are non-invasive and they can be conducted in a very short period of time. In some embodiments, the same test can be repeated several times within a period of time to monitor progression of a pancreatic disease and/or assess the efficiency of a treatment plan.

Further embodiments provide Multiplex Molecular Diagnostic Protein assays, a combination of protein assay and assay based on detection of DNA or RNA, and kits, including an immunoassay, biochip assay, nanoassay and molecular assay. In some embodiments an assay detects protein biomarker and/or glycobiomarkers or peptides derived from the biomarker and/or glycobiomarkers from Tables 5A, 5, 6A, and 6. In other embodiments, an assay detects biomarkers or peptides derived from biomarkers from Table 9. In other embodiments, an assay detects biomarkers or peptides derived from biomarkers from Table 9. In other embodiments, an assay detects biomarkers or peptides derived from biomarkers from Table 9.

In further embodiments, a patient's sample is reacted with a set of antibodies, each of which is selectively specific for at least one biomarker and/or glycobiomarker from Tables 5A, 5, 6A, 6 and 9. The complex between an antibody and a glycobiomarker or a biomarker is then may be detected with a second antibody conjugated to a detection molecule.

Further embodiments include methods for detecting and monitoring a pancreatic disease, including pancreatic cancer, pancreatitis, and autoimmune pancreatitis. In these methods, a patient's sample is tested for expression of at least some biomarker and/or glycobiomarkers listed in Tables 5A, 5, 6A, 6 and 9. Further embodiments include methods in which patient's response to therapy is monitored with testing a patient's sample for expression of at least some biomarker and/or glycobiomarkers listed in Tables 5A, 5, 6A, 6 and 9. Other applications include detecting a recurrent or residual pancreatic disease by testing a patient's sample for expression of at least some biomarker and/or glycobiomarkers listed in Tables 5A, 5, 6A, 6 and 9.

Other applications include screening of genetically predisposed individuals for a pancreatic disease by testing the individual's sample for expression of at least some biomarkers and/or glycobiomarkers listed in Tables 5A, 5, 6A, 6 and 9. Such genetically predisposed individuals include, but not limited, to BRCA mutation carriers; PALB2 mutation carriers; p16 mutation carriers; Lynch syndrome patients; Peutz–Jeghers syndrome patients; and individuals with a family history of pancreatic cancer cases.

In some methods, a biochip comprising a set of at least one or more biomarker and/or glycobiomarkers listed in Tables 5A, 5, 6A, 6 and 9 can be used as a robust and sensitive tool to monitor disease progression and response to therapy. These biochips can be also used as a biomarker or molecular modality for drug development or drug optimization.

Other applications include tests conducted for detection and measurement of biomarker and/or glycobiomarkers which include at least one or more biomarkers listed in Tables 5A, 5, 6A, 6 and 9. Such tests may include verification and support of clinical and operative decision-making process and management of pancreatic cyst neoplasms.

Further embodiments provide methods for treating a disorder of the pancreas, the method comprising obtaining a sample from a mammal in need of the treatment and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9.

The invention will be now further explained by the following non-limiting examples.

Example 1.

Human plasma was obtained from cancer patients. Human plasma samples from healthy control individuals were used as controls. All patients and control individuals have provided informed consent, and collection of human samples was approved by the local

Review Board. Glycosylated forms of proteins were isolated from human plasma as it has been described before (Khidekel N, Ficarro SB, Peters EC, Hsieh-Wilson LC. "Exploring the O-GlcNAc proteome: direct identification of O-GlcNAc-modified proteins from the brain". PNAS 2004 Sep 7;101(36):13132-7. Yi W, Clark PM, Mason DE, Keenan MC, Hill C, Goddard WA 3rd, Peters EC, Driggers EM, Hsieh-Wilson LC. "Phosphofructokinase 1 glycosylation regulates cell growth and metabolism". Science. 2012 Aug 24;337(6097):975-80.) Then isolated glycosylated forms of proteins from human plasma were used for the proteomics analysis.

Mass Spectrometry of protein expression profiling was performed according to the established protocol. Briefly, each isolated sample was processed by SDS-PAGE, using a 10% Bis-Tris NuPAGE gel (Invitrogen) with the MES buffer system. The entire mobility region was excised and processed by in-gel digestion using a robot (ProGest, DigiLab) with the following protocol: washed with 25mM ammonium bicarbonate followed by acetonitrile; reduced with 10mM dithiothreitol at 60°C followed by alkylation with 50mM iodoacetamide at RT. digested with trypsin (Promega) at 37°C for 4h, quenched with formic acid and the supernatant was analyzed directly without further processing. Mass Spectrometry of each digested sample was analyzed by nano LC-MS/MS with a ThermoFisher EASY-nLC 1000 HPLC system interfaced to a ThermoFisher Q Exactive mass spectrometer.

A sample was then loaded on a trapping column and eluted over a 75µm x 150mm analytical column (Thermo Fisher P/N 164568) at 300nL/min using a 4hr reverse phase gradient; both columns were packed with Acclaim PepMap 100Å, 3 µm resin (Thermo Scientific). The mass spectrometer was operated in the data-dependent mode, with MS and MS/MS performed in the Orbitrap at 70,000 and 17,500 FWHM resolution respectively. The fifteen most abundant ions were selected for MS/MS. The data processing was analyzed using a Mascot. Mascot DAT files were parsed into the Scaffold software for validation, filtering and to create a nonredundant list per sample. The data was filtered using at 1% protein and peptide FDR and requiring at least two unique peptides per protein.

The list of proteins was then additionally analyzed with the ELSVIER PATHWAY STUDIO software.

Example 2.

Human plasma was obtained from cancer patients. Human plasma samples from healthy control individuals were used as controls. All patients and control individuals

have provided informed consent, and collection of human samples was approved by the local Review Board. 10µL of each plasma sample was processed using the Multiple Affinity Removal System (MARS specific for the 14 most abundant human plasma proteins (Agilent (P/N5188-6560))). The sample was processed using the vendor protocol. Depleted samples were buffer exchanged against HPLC grade water and quantified by Qubit fluorometry at a 1:10 dilution and % depletion was assessed. 20µg of each sample was digested with trypsin using the following protocol: reduced with 10mM dithiothreitol at 60°C for 30 minutes in 25mM Ammonium bicarbonate; alkylated with iodoacetamide for at 60°C for 45 minutes in 25mM Ammonium bicarbonate; digested overnight with sequencing grade trypsin at 37°C, enzyme: substrate ratio 1:20; quenched with formic acid. Digested samples were desalted using a Waters HLB µElution plate per the vendor protocol. Desalted samples were suspended in 100µL of 0.1% TFA for analysis.

Mass Spectrometry of protein expression profiling was performed according to the established protocol. Briefly, each isolated sample was processed by SDS-PAGE, using a 10% Bis-Tris NuPAGE gel (Invitrogen) with the MES buffer system. The entire mobility region was excised and processed by in-gel digestion using a robot (ProGest, DigiLab) with the following protocol: washed with 25mM ammonium bicarbonate followed by acetonitrile; reduced with 10mM dithiothreitol at 60°C followed by alkylation with 50mM iodoacetamide at RT. digested with trypsin (Promega) at 37°C for 4h, quenched with formic acid and the supernatant was analyzed directly without further processing. Mass Spectrometry of each digested sample was analyzed by nano LC-MS/MS with a ThermoFisher EASY-nLC 1000 HPLC system interfaced to a ThermoFisher Q Exactive mass spectrometer.

A sample was then loaded on a trapping column and eluted over a 75µm x 150mm analytical column (Thermo Fisher P/N 164568) at 300nL/min using a 4hr reverse phase gradient; both columns were packed with Acclaim PepMap 100Å, 3 3 µm resin (Thermo Scientific). The mass spectrometer was operated in the data-dependent mode, with MS and MS/MS performed in the Orbitrap at 70,000 and 17,500 FWHM resolution respectively. The fifteen most abundant ions were selected for MS/MS. The data processing was analyzed using a Mascot. Mascot DAT files were parsed into the Scaffold software for validation, filtering and to create a nonredundant list per sample. The data was filtered using at 1% protein and peptide FDR and requiring at least two unique peptides per protein.

A List of Abbreviations for Figs. 1-23 and Tables 1, 2, 3, 4, 5, 6, 7 and 8Adherens Junction Assembly (Nectin)

Name	Description
ACTN1	actinin alpha 1
CDC42	cell division cycle 42
CRK	v-crk avian sarcoma virus CT10 oncogene homolog
CTNNA1	catenin alpha 1
RAPGEF1	Rap guanine nucleotide exchange factor 1
LMO7	LIM domain 7
MLLT4	myeloid/lymphoid or mixed-lineage leukemia; translocated to, 4
MYO7B	myosin VIIB
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
RAP1A	RAP1A, member of RAS oncogene family
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
TJP1	tight junction protein 1
VASP	vasodilator-stimulated phosphoprotein
VCL	vinculin
VAV2	vav guanine nucleotide exchange factor 2
WAS	Wiskott-Aldrich syndrome
ZYX	zyxin
IQGAP1	IQ motif containing GTPase activating protein 1
WASF1	WAS protein family member 1
WASL	Wiskott-Aldrich syndrome like
KEAP1	kelch like ECH associated protein 1
WASF2	WAS protein family member 2
BAIAP2	BAI1 associated protein 2
SORBS1	sorbin and SH3 domain containing 1
EPN1	epsin 1
PARD3	par-3 family cell polarity regulator

SSX2IP	synovial sarcoma, X breakpoint 2 interacting protein
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Bradykinin Effects in Inflammation

Name	Description
AGT	angiotensinogen
AGTR1	angiotensin II receptor type 1
AKT1	v-akt murine thymoma viral oncogene homolog 1
BDKRB2	bradykinin receptor B2
BDKRB1	bradykinin receptor B1
CPN1	carboxypeptidase N subunit 1
CPM	carboxypeptidase M
MAPK14	mitogen-activated protein kinase 14
ACE	angiotensin I converting enzyme
F11	coagulation factor XI
F12	coagulation factor XII
GNA11	G protein subunit alpha 11
GNAQ	G protein subunit alpha q
IL1B	interleukin 1 beta
IL1RAP	interleukin 1 receptor accessory protein
IL1A	interleukin 1 alpha
IL1R1	interleukin 1 receptor type 1
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
KLK1	kallikrein 1
KLKB1	kallikrein B1
KNG1	kininogen 1
MAP3K1	mitogen-activated protein kinase kinase kinase 1
MMP1	matrix metalloproteinase 1

NFKBIA	NFKB inhibitor alpha
NOS3	nitric oxide synthase 3
NOS2	nitric oxide synthase 2
PDPK1	3-phosphoinositide dependent protein kinase 1
PLAT	plasminogen activator, tissue type
PLAU	plasminogen activator, urokinase
PLAUR	plasminogen activator, urokinase receptor
PLG	plasminogen
PLCB3	phospholipase C beta 3
PRKCQ	protein kinase C theta
MAP2K3	mitogen-activated protein kinase kinase 3
MAP2K6	mitogen-activated protein kinase kinase 6
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
XPNPEP2	X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound
PTGES	prostaglandin E synthase
PLCB1	phospholipase C beta 1

Coagulation Cascade

Name	Description
SERPINC1	serpin family C member 1
F2	coagulation factor II, thrombin
F5	coagulation factor V

F9	coagulation factor IX
F11	coagulation factor XI
F10	coagulation factor X
F3	coagulation factor III, tissue factor
F12	coagulation factor XII
F13A1	coagulation factor XIII A chain
F8	coagulation factor VIII
F7	coagulation factor VII
KLKB1	kallikrein B1
KNG1	kininogen 1
PLAT	plasminogen activator, tissue type
PLG	plasminogen
PROC	protein C, inactivator of coagulation factors Va and VIIIa
PROS1	protein S (alpha)
TFPI	tissue factor pathway inhibitor
THBD	thrombomodulin
PROZ	protein Z, vitamin K dependent plasma glycoprotein
FGL2	fibrinogen like 2
SERPINA10	serpin family A member 10
VKORC1	vitamin K epoxide reductase complex subunit 1

Complement Activation by Lectin

Name	Description
C3	complement component 3
C4B	complement component 4B (Chido blood group)
C2	complement component 2

C3AR1	complement component 3a receptor 1
C5	complement component 5
C5AR1	complement component 5a receptor 1
C8A	complement component 8 alpha subunit
C6	complement component 6
C9	complement component 9
C7	complement component 7
MBL2	mannose binding lectin 2
MASP1	mannan binding lectin serine peptidase 1
MASP2	mannan binding lectin serine peptidase 2
C5AR2	complement component 5a receptor 2

Complement Activation in Macular Degeneration

Name	Description
CFB	complement factor B
C3	complement component 3
C4B	complement component 4B (Chido blood group)
C2	complement component 2
C1R	complement C1r subcomponent
C1S	complement component 1, s subcomponent
C5	complement component 5
C5AR1	complement component 5a receptor 1
C8A	complement component 8 alpha subunit
C6	complement component 6

C9	complement component 9
C7	complement component 7
CLU	clusterin
CR1	complement component 3b/4b receptor 1 (Knops blood group)
CRP	C-reactive protein, pentraxin-related
CD55	CD55 molecule (Cromer blood group)
CFD	complement factor D (adipsin)
CFHR1	complement factor H related 1
CFH	complement factor H
CFI	complement factor I
MBL2	mannose binding lectin 2
CD46	CD46 molecule
CFP	complement factor properdin
MASP1	mannan binding lectin serine peptidase 1
HTRA1	HtrA serine peptidase 1
TIMP3	TIMP metallopeptidase inhibitor 3
VTN	vitronectin
MASP2	mannan binding lectin serine peptidase 2
CFHR3	complement factor H related 3

Complement Alternative Pathway

Name	Description
CFB	complement factor B
C3	complement component 3
C5	complement component 5
C5AR1	complement component 5a receptor 1

C8A	complement component 8 alpha subunit
C6	complement component 6
C9	complement component 9
C7	complement component 7
CR2	complement component 3d receptor 2
CFD	complement factor D (adipsin)
CFH	complement factor H
CFI	complement factor I
CFP	complement factor properdin
C5AR2	complement component 5a receptor 2

Complement Cascade Activation by Pentraxins

Name	Description
APCS	amyloid P component, serum
APP	amyloid beta precursor protein
C1QA	complement component 1, q subcomponent, A chain
C3	complement component 3
C4B	complement component 4B (Chido blood group)
C2	complement component 2
C4BPA	complement component 4 binding protein alpha
C1S	complement component 1, s subcomponent
C5	complement component 5
C9	complement component 9
CRP	C-reactive protein, pentraxin-related

FCGR3A	Fc fragment of IgG receptor IIIa
CFH	complement factor H
MBL2	mannose binding lectin 2
MASP1	mannan binding lectin serine peptidase 1
PTX3	pentraxin 3
SNRNP70	small nuclear ribonucleoprotein U1 subunit 70
SNRPN	small nuclear ribonucleoprotein polypeptide N

Complement Classical Pathway

Name	Description
C3	complement component 3
C4B	complement component 4B (Chido blood group)
C2	complement component 2
C1R	complement C1r subcomponent
C1S	complement component 1, s subcomponent
C3AR1	complement component 3a receptor 1
C5	complement component 5
C5AR1	complement component 5a receptor 1
C8A	complement component 8 alpha subunit
C6	complement component 6
C9	complement component 9
C7	complement component 7
C5AR2	complement component 5a receptor 2

Focal Junction Assembly

Name	Description
ACTN1	actinin alpha 1
CAPN1	calpain 1
DAB2	DAB2, clathrin adaptor protein
DOCK1	dedicator of cytokinesis 1
FN1	fibronectin 1
ILK	integrin linked kinase
ITGA5	integrin subunit alpha 5
ITGB1	integrin subunit beta 1
ITGAV	integrin subunit alpha V
ITGB3	integrin subunit beta 3
LASP1	LIM and SH3 protein 1
LIMS1	LIM zinc finger domain containing 1
PTK2	protein tyrosine kinase 2
PTPN12	protein tyrosine phosphatase, non-receptor type 12
PXN	paxillin
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
TLN1	talin 1
TNS1	tensin 1
VASP	vasodilator-stimulated phosphoprotein
VCL	vinculin
VTN	vitronectin
ZYX	zyxin
ITGB1BP1	integrin subunit beta 1 binding protein 1
BCAR1	BCAR1, Cas family scaffolding protein
ELMO1	engulfment and cell motility 1
DLC1	DLC1 Rho GTPase activating protein
FERMT2	fermitin family member 2

PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase type 1 gamma
FBLIM1	filamin binding LIM protein 1
PARVA	parvin alpha

Glycolysis

Name	Description
ALDOA	aldolase, fructose-bisphosphate A
ALDOB	aldolase, fructose-bisphosphate B
ENO1	enolase 1
ENO3	enolase 3 (beta, muscle)
ENO2	enolase 2 (gamma, neuronal)
GAPDH	glyceraldehyde-3-phosphate dehydrogenase
GCK	glucokinase
GPI	glucose-6-phosphate isomerase
HK2	hexokinase 2
HK3	hexokinase 3
HK1	hexokinase 1
PGAM2	phosphoglycerate mutase 2
PFKM	phosphofructokinase, muscle
PGAM1	phosphoglycerate mutase 1
PGK1	phosphoglycerate kinase 1
PKM	pyruvate kinase, muscle
PKLR	pyruvate kinase, liver and RBC
TPI1	triosephosphate isomerase 1

Histidine-Rich Glycoprotein (HRG)

Name	Description
SERPINC1	serpin family C member 1
CASP3	caspase 3
CD36	CD36 molecule

F12	coagulation factor XII
FGF2	fibroblast growth factor 2
SERPIND1	serpin family D member 1
HRG	histidine rich glycoprotein
IFNG	interferon, gamma
IL2	interleukin 2
SERPINA5	serpin family A member 5
PLG	plasminogen
THBS1	thrombospondin 1
THBS2	thrombospondin 2
HPSE	heparanase
ADAMTSL1	ADAMTS like 1

Lipogenesis Regulation in Adipocytes

Name	Description
ACACA	acetyl-CoA carboxylase alpha
ACACB	acetyl-CoA carboxylase beta
ACLY	ATP citrate lyase
AKT1	v-akt murine thymoma viral oncogene homolog 1
CD36	CD36 molecule
ACSL1	acyl-CoA synthetase long-chain family member 1
FASN	fatty acid synthase
GSK3B	glycogen synthase kinase 3 beta
INS	insulin
INSR	insulin receptor
IRS1	insulin receptor substrate 1
LPL	lipoprotein lipase
PDPK1	3-phosphoinositide dependent protein kinase 1

PPARA	peroxisome proliferator activated receptor alpha
SCD	stearoyl-CoA desaturase (delta-9-desaturase)
SLC2A1	solute carrier family 2 member 1
SLC2A4	solute carrier family 2 member 4
SREBF1	sterol regulatory element binding transcription factor 1
IRS2	insulin receptor substrate 2
DGAT1	diacylglycerol O-acyltransferase 1
AGPAT2	1-acylglycerol-3-phosphate O-acyltransferase 2
LPIN1	lipin 1
DGAT2	diacylglycerol O-acyltransferase 2
GPAT3	glycerol-3-phosphate acyltransferase 3
SLC27A1	solute carrier family 27 member 1

Microtubule Cytoskeleton

Name	Description
DIAPH1	diaphanous related formin 1
DPYSL2	dihydropyrimidinase like 2
STMN1	stathmin 1
MAP2	microtubule associated protein 2
MAP4	microtubule associated protein 4
MAPT	microtubule associated protein tau
CLIP1	CAP-Gly domain containing linker protein 1
AURKB	aurora kinase B
KIF14	kinesin family member 14

KIF2C	kinesin family member 2C
TPPP	tubulin polymerization promoting protein
CLASP1	cytoplasmic linker associated protein 1

Neutrophil Activation via Adherence on Endothelial Cells

Name	Description
ACTN1	actinin alpha 1
BTK	Bruton tyrosine kinase
CD34	CD34 molecule
CDC42	cell division cycle 42
CR1	complement component 3b/4b receptor 1 (Knops blood group)
CYBA	cytochrome b-245 alpha chain
CYBB	cytochrome b-245, beta polypeptide
FCGR2A	Fc fragment of IgG receptor IIa
FPR1	formyl peptide receptor 1
GNAI1	G protein subunit alpha i1
ICAM1	intercellular adhesion molecule 1
ICAM2	intercellular adhesion molecule 2
CXCL8	C-X-C motif chemokine ligand 8
CXCR2	C-X-C motif chemokine receptor 2
ITGB1	integrin subunit beta 1
ITGAM	integrin subunit alpha M
ITGB2	integrin subunit beta 2
ITGA9	integrin subunit alpha 9
ITGAL	integrin subunit alpha L
ITGB3	integrin subunit beta 3

ITPR1	inositol 1,4,5-trisphosphate receptor type 1
MME	membrane metallo-endopeptidase
MMP9	matrix metalloproteinase 9
NCF4	neutrophil cytosolic factor 4
NCF2	neutrophil cytosolic factor 2
NFKBIA	NF- κ B inhibitor alpha
PDPK1	3-phosphoinositide dependent protein kinase 1
PLCG1	phospholipase C gamma 1
PRKCA	protein kinase C alpha
PRKCB	protein kinase C beta
PRKCZ	protein kinase C zeta
PRKCD	protein kinase C delta
MAPK3	mitogen-activated protein kinase 3
MAPK1	mitogen-activated protein kinase 1
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K2	mitogen-activated protein kinase kinase 2
PTK2	protein tyrosine kinase 2
PXN	paxillin
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
SELE	selectin E
SELL	selectin L
SELPLG	selectin P ligand
SELP	selectin P
SYK	spleen tyrosine kinase

TLN1	taln 1
TNS1	tensin 1
VCAM1	vascular cell adhesion molecule 1
VCL	vinculin
VAV1	vav guanine nucleotide exchange factor 1
MADCAM1	mucosal vascular addressin cell adhesion molecule 1
IQGAP1	IQ motif containing GTPase activating protein 1
BCAR1	BCAR1, Cas family scaffolding protein
WASF2	WAS protein family member 2
BAIAP2	BAI1 associated protein 2
PLCB1	phospholipase C beta 1
NCF1	neutrophil cytosolic factor 1

Plasmin Effects in Inflammation

Name	Description
A2M	alpha-2-macroglobulin
AKT1	v-akt murine thymoma viral oncogene homolog 1
ANXA2	annexin A2
RHOA	ras homolog family member A
SERPING1	serpin family G member 1
C1R	complement C1r subcomponent
C1S	complement component 1, s subcomponent
CD40	CD40 molecule
CDC42	cell division cycle 42
ATF2	activating transcription factor 2

ENO1	enolase 1
F2R	coagulation factor II thrombin receptor
F12	coagulation factor XII
FN1	fibronectin 1
FOS	FBJ murine osteosarcoma viral oncogene homolog
GNA15	G protein subunit alpha 15
GNA12	G protein subunit alpha 12
GNAQ	G protein subunit alpha q
IL1B	interleukin 1 beta
IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta
IL1A	interleukin 1 alpha
JAK1	Janus kinase 1
JUN	jun proto-oncogene
KLK1	kallikrein 1
KLKB1	kallikrein B1
KNG1	kininogen 1
MAP3K1	mitogen-activated protein kinase kinase kinase 1
MAP3K11	mitogen-activated protein kinase kinase kinase 11
MMP3	matrix metalloproteinase 3
MMP13	matrix metalloproteinase 13
MMP1	matrix metalloproteinase 1
NFKBIA	NFkB inhibitor alpha
SERPINE1	serpin family E member 1
PDPK1	3-phosphoinositide dependent protein kinase 1

PLAT	plasminogen activator, tissue type
PLAU	plasminogen activator, urokinase
PLAUR	plasminogen activator, urokinase receptor
PLG	plasminogen
SERPINF2	serpin family F member 2
PRKCE	protein kinase C epsilon
MAPK3	mitogen-activated protein kinase 3
MAPK1	mitogen-activated protein kinase 1
MAP2K3	mitogen-activated protein kinase kinase 3
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K7	mitogen-activated protein kinase kinase 7
MAP2K6	mitogen-activated protein kinase kinase 6
MAP2K2	mitogen-activated protein kinase kinase 2
PXN	paxillin
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
RASGRF1	Ras protein specific guanine nucleotide releasing factor 1
S100A10	S100 calcium binding protein A10
CCL2	C-C motif chemokine ligand 2
CCL20	C-C motif chemokine ligand 20

MAP2K4	mitogen-activated protein kinase kinase 4
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
STAT1	signal transducer and activator of transcription 1
STAT3	signal transducer and activator of transcription 3
TF	transferrin
TGFB1	transforming growth factor beta 1
TNF	tumor necrosis factor
TYK2	tyrosine kinase 2
TFPI2	tissue factor pathway inhibitor 2
BCAR1	BCAR1, Cas family scaffolding protein
RASGRP1	RAS guanyl releasing protein 1
GNA13	G protein subunit alpha 13
SPINK5	serine peptidase inhibitor, Kazal type 5
PLGRKT	plasminogen receptor with a C-terminal lysine

Platelet Activation via Adhesion Molecules

Name	Description
AKT1	v-akt murine thymoma viral oncogene homolog 1
RHOA	ras homolog family member A
BRAF	B-Raf proto-oncogene, serine/threonine kinase
CD40LG	CD40 ligand
CDC42	cell division cycle 42
MAPK14	mitogen-activated protein kinase 14
HBEGF	heparin binding EGF like growth factor

F3	coagulation factor III, tissue factor
PTK2B	protein tyrosine kinase 2 beta
FCER1G	Fc fragment of IgE receptor Ig
FYN	FYN proto-oncogene, Src family tyrosine kinase
GP1BB	glycoprotein Ib platelet beta subunit
GP5	glycoprotein V platelet
GP1BA	glycoprotein Ib platelet alpha subunit
GP9	glycoprotein IX platelet
GRB2	growth factor receptor bound protein 2
ARHGAP35	Rho GTPase activating protein 35
CXCL8	C-X-C motif chemokine ligand 8
IL6	interleukin 6
ITGA6	integrin subunit alpha 6
ITGA2	integrin subunit alpha 2
ITGA2B	integrin subunit alpha 2b
ITGB1	integrin subunit beta 1
ITGB3	integrin subunit beta 3
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
LCP2	lymphocyte cytosolic protein 2
LYN	LYN proto-oncogene, Src family tyrosine kinase
MAP3K1	mitogen-activated protein kinase kinase kinase 1
MYLK	myosin light chain kinase
NOS3	nitric oxide synthase 3
PDPK1	3-phosphoinositide dependent protein kinase 1

PLCG1	phospholipase C gamma 1
PLCG2	phospholipase C gamma 2
PRKCA	protein kinase C alpha
MAPK3	mitogen-activated protein kinase 3
MAPK1	mitogen-activated protein kinase 1
PRKG1	protein kinase, cGMP-dependent, type I
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K6	mitogen-activated protein kinase kinase 6
MAP2K2	mitogen-activated protein kinase kinase 2
PTK2	protein tyrosine kinase 2
PTPRJ	protein tyrosine phosphatase, receptor type J
PXN	paxillin
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
RAP1A	RAP1A, member of RAS oncogene family
ROCK1	Rho associated coiled-coil containing protein kinase 1
SOS1	SOS Ras/Rac guanine nucleotide exchange factor 1
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
STX4	syntaxin 4
SYK	spleen tyrosine kinase
TLN1	talin 1
TNF	tumor necrosis factor

TNS1	tensin 1
VCL	vinculin
VAV1	vav guanine nucleotide exchange factor 1
WAS	Wiskott-Aldrich syndrome
VWF	von Willebrand factor
VAMP8	vesicle associated membrane protein 8
SNAP23	synaptosome associated protein 23kDa
IQGAP1	IQ motif containing GTPase activating protein 1
BCAR1	BCAR1, Cas family scaffolding protein
PIP5K1C	phosphatidylinositol-4-phosphate 5-kinase type 1 gamma
LAT	linker for activation of T-cells
GP6	glycoprotein VI platelet
APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein

Platelet Activation via GPCR Signaling

Name	Description
ADCY3	adenylate cyclase 3
ADORA2A	adenosine A2a receptor
AKT1	v-akt murine thymoma viral oncogene homolog 1
RHOA	ras homolog family member A
BRAF	B-Raf proto-oncogene, serine/threonine kinase
CDC42	cell division cycle 42
F2	coagulation factor II, thrombin
F2R	coagulation factor II thrombin receptor

GNAS	GNAS complex locus
GNAQ	G protein subunit alpha q
HTR2A	5-hydroxytryptamine receptor 2A
ITGA2	integrin subunit alpha 2
ITGB1	integrin subunit beta 1
ITGB3	integrin subunit beta 3
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
MPL	MPL proto-oncogene, thrombopoietin receptor
MYLK	myosin light chain kinase
NOS3	nitric oxide synthase 3
P2RY1	purinergic receptor P2Y1
PDPK1	3-phosphoinositide dependent protein kinase 1
PRKCA	protein kinase C alpha
MAPK3	mitogen-activated protein kinase 3
MAPK1	mitogen-activated protein kinase 1
PRKG1	protein kinase, cGMP-dependent, type I
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K2	mitogen-activated protein kinase kinase 2
PTAFR	platelet activating factor receptor
PTGER4	prostaglandin E receptor 4
PTGIR	prostaglandin I2 (prostacyclin) receptor (IP)
PTGFR	prostaglandin F receptor
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)

RAF1	Raf-1 proto-oncogene, serine/threonine kinase
RAP1A	RAP1A, member of RAS oncogene family
RASGRF1	Ras protein specific guanine nucleotide releasing factor 1
ROCK1	Rho associated coiled-coil containing protein kinase 1
STX4	syntaxin 4
TBXA2R	thromboxane A2 receptor
THPO	thrombopoietin
TLN1	talin 1
WAS	Wiskott-Aldrich syndrome
VAMP8	vesicle associated membrane protein 8
SNAP23	synaptosome associated protein 23kDa
IQGAP1	IQ motif containing GTPase activating protein 1
F2RL3	F2R like thrombin/trypsin receptor 3
RASGRP1	RAS guanyl releasing protein 1
GNA13	G protein subunit alpha 13
PLCB1	phospholipase C beta 1
APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein
P2RY12	purinergic receptor P2Y12

Positive Acute Phase Proteins Synthesis

Name	Description
A2M	alpha-2-macroglobulin
SERPINA3	serpin family A member 3
C3	complement component 3

CEBPB	CCAAT/enhancer binding protein beta
CEBPD	CCAAT/enhancer binding protein delta
CP	ceruloplasmin (ferroxidase)
CRP	C-reactive protein, pentraxin-related
EGR1	early growth response 1
F8	coagulation factor VIII
FN1	fibronectin 1
GHR	growth hormone receptor
GH1	growth hormone 1
GRB2	growth factor receptor bound protein 2
HIF1A	hypoxia inducible factor 1 alpha subunit
HNF4A	hepatocyte nuclear factor 4 alpha
HP	haptoglobin
HPX	hemopexin
IL1B	interleukin 1 beta
IL1RAP	interleukin 1 receptor accessory protein
IL1A	interleukin 1 alpha
IL1R1	interleukin 1 receptor type 1
IL6ST	interleukin 6 signal transducer
IL6R	interleukin 6 receptor
IL6	interleukin 6
IRAK1	interleukin 1 receptor associated kinase 1
JAK1	Janus kinase 1
JAK2	Janus kinase 2
LBP	lipopolysaccharide binding protein
MBL2	mannose binding lectin 2
MYD88	myeloid differentiation primary response 88
NFKBIA	NFkB inhibitor alpha
ORM1	orosomucoid 1
SERPINE2	serpin family E member 2
SERPINA1	serpin family A member 1

PPARA	peroxisome proliferator activated receptor alpha
MAPK8	mitogen-activated protein kinase 8
MAPK1	mitogen-activated protein kinase 1
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K2	mitogen-activated protein kinase kinase 2
PTPN11	protein tyrosine phosphatase, non-receptor type 11
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
SAA1	serum amyloid A1
MAP2K4	mitogen-activated protein kinase kinase 4
SOS1	SOS Ras/Rac guanine nucleotide exchange factor 1
SRF	serum response factor
STAT3	signal transducer and activator of transcription 3
STAT5A	signal transducer and activator of transcription 5A
MAP3K7	mitogen-activated protein kinase kinase kinase 7
TLR4	toll like receptor 4
TNF	tumor necrosis factor
TNFRSF1B	tumor necrosis factor receptor superfamily member 1B
TNFRSF1A	tumor necrosis factor receptor superfamily member 1A
TRAF6	TNF receptor associated factor 6
TRAF2	TNF receptor associated factor 2
TYK2	tyrosine kinase 2
VWF	von Willebrand factor
TRADD	TNFRSF1A associated via death domain
MAPKAPK2	mitogen-activated protein kinase-activated protein kinase 2
IRAK4	interleukin 1 receptor associated kinase 4

Protein Folding

Name	Description
BAG1	BCL2 associated athanogene 1
FKBP4	FK506 binding protein 4
HSPA1A	heat shock protein family A (Hsp70) member 1A
HSP90AA1	heat shock protein 90kDa alpha family class A member 1
HSPA8	heat shock protein family A (Hsp70) member 8
ST13	suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein)
HSP90B1	heat shock protein 90kDa beta family member 1
TOMM70	translocase of outer mitochondrial membrane 70
STUB1	STIP1 homology and U-box containing protein 1
CDC37	cell division cycle 37
HSPBP1	HSPA (heat shock 70kDa) binding protein, cytoplasmic cochaperone 1
HSPA14	heat shock protein family A (Hsp70) member 14
UNC45A	unc-45 myosin chaperone A

Scavenger Receptors in Platelet Activation

Name	Description
RHOA	ras homolog family member A
CD9	CD9 molecule
CD36	CD36 molecule

SCARB1	scavenger receptor class B member 1
MAPK14	mitogen-activated protein kinase 14
FYN	FYN proto-oncogene, Src family tyrosine kinase
GP1BB	glycoprotein Ib platelet beta subunit
GP1BA	glycoprotein Ib platelet alpha subunit
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
LCP2	lymphocyte cytosolic protein 2
LYN	LYN proto-oncogene, Src family tyrosine kinase
MATK	megakaryocyte-associated tyrosine kinase
MAP3K1	mitogen-activated protein kinase kinase kinase 1
PLCG2	phospholipase C gamma 2
PRKCA	protein kinase C alpha
MAPK8	mitogen-activated protein kinase 8
MAP2K6	mitogen-activated protein kinase kinase 6
ROCK1	Rho associated coiled-coil containing protein kinase 1
MAP2K4	mitogen-activated protein kinase kinase 4
SYK	spleen tyrosine kinase
VAV1	vav guanine nucleotide exchange factor 1
YES1	YES proto-oncogene 1, Src family tyrosine kinase
LAT	linker for activation of T-cells

Scavenger Receptors in Platelet Aggregation

Name	Description
RHOA	ras homolog family member A
CD68	CD68 molecule
GNAQ	G protein subunit alpha q
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
OLR1	oxidized low density lipoprotein receptor 1
P2RY1	purinergic receptor P2Y1
PDPK1	3-phosphoinositide dependent protein kinase 1
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)
ROCK1	Rho associated coiled-coil containing protein kinase 1
TLN1	talin 1
IQGAP1	IQ motif containing GTPase activating protein 1
PLCB1	phospholipase C beta 1
APBB1IP	amyloid beta precursor protein binding family B member 1 interacting protein

TAM Receptors in Platelet Aggregation

Name	Description
AKT1	v-akt murine thymoma viral oncogene homolog 1
AXL	AXL receptor tyrosine kinase

GAS6	growth arrest specific 6
PDPK1	3-phosphoinositide dependent protein kinase 1
PROS1	protein S (alpha)
TYRO3	TYRO3 protein tyrosine kinase
VWF	von Willebrand factor
MERTK	MER proto-oncogene, tyrosine kinase

Vascular Endothelial Cell Activation by Blood Coagulation Factors

Name	Description
AKT1	v-akt murine thymoma viral oncogene homolog 1
BDKRB2	bradykinin receptor B2
CDH5	cadherin 5
CTGF	connective tissue growth factor
HBEGF	heparin binding EGF like growth factor
F2	coagulation factor II, thrombin
F2RL2	coagulation factor II thrombin receptor like 2
F2RL1	F2R like trypsin receptor 1
F2R	coagulation factor II thrombin receptor
F10	coagulation factor X
F7	coagulation factor VII
FOS	FBJ murine osteosarcoma viral oncogene homolog
GNA15	G protein subunit alpha 15
GNA11	G protein subunit alpha 11
GNAQ	G protein subunit alpha q
CXCL2	C-X-C motif chemokine ligand 2
ICAM1	intercellular adhesion molecule 1
CYR61	cysteine rich angiogenic inducer 61
IL1B	interleukin 1 beta

CXCL8	C-X-C motif chemokine ligand 8
IL6	interleukin 6
IRAK1	interleukin 1 receptor associated kinase 1
ITPR1	inositol 1,4,5-trisphosphate receptor type 1
JAK2	Janus kinase 2
JUN	jun proto-oncogene
KNG1	kininogen 1
MYD88	myeloid differentiation primary response 88
NFKBIA	NFKB inhibitor alpha
YBX1	Y-box binding protein 1
PDPK1	3-phosphoinositide dependent protein kinase 1
PLCB3	phospholipase C beta 3
PRKCA	protein kinase C alpha
MAPK3	mitogen-activated protein kinase 3
MAPK1	mitogen-activated protein kinase 1
MAP2K1	mitogen-activated protein kinase kinase 1
MAP2K2	mitogen-activated protein kinase kinase 2
PROC	protein C, inactivator of coagulation factors Va and VIIIa
PROS1	protein S (alpha)
RAF1	Raf-1 proto-oncogene, serine/threonine kinase
RASGRF1	Ras protein specific guanine nucleotide releasing factor 1
CCL2	C-C motif chemokine ligand 2
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
STAT1	signal transducer and activator of transcription 1
STAT3	signal transducer and activator of transcription 3
TFPI	tissue factor pathway inhibitor
TLR4	toll like receptor 4
TNF	tumor necrosis factor

TRAF6	TNF receptor associated factor 6
TYK2	tyrosine kinase 2
VCAM1	vascular cell adhesion molecule 1
VEGFA	vascular endothelial growth factor A
F2RL3	F2R like thrombin/trypsin receptor 3
RASGRP1	RAS guanyl releasing protein 1
PROCR	protein C receptor
PLCB1	phospholipase C beta 1
IRAK4	interleukin 1 receptor associated kinase 4
OCLN	occludin

WHAT IS CLAIMED IS:

1. A method for screening, monitoring and/or treating a gastrointestinal (GI) cancer patient, the method comprising:
obtaining a sample from the patient,
isolating glycosylated proteins from the sample,
grouping the isolated glycosylated proteins into a profile of pathways, and
matching the obtained profile at least partially with at least one profile selected from the group of profiles of Tables 1, 2, 3, 4, 5, 6, 7, 8, and any combination thereof.
2. The method of claim 1, wherein the GI cancer is selected from the group consisting of colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer.
3. The method of claim 1, wherein the sample is selected from the group consisting of a human tissue biopsy or biosample including pancreas biopsy sample, gastrointestinal sample, blood sample, plasma sample, serum sample, circulating tumor cells sample, tear sample, saliva sample, sperm sample, urine sample, fecal sample and hair sample.
4. The method of claim 1, wherein the sample is analyzed using one or more techniques selected from the group consisting of chromatography, gas chromatography, liquid chromatography, mass spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay.
5. The method of claim 1, wherein the sample is analyzed using a combination of a detection techniques of nucleic acids and proteins or peptides.
6. The method of claim 1, wherein biomarkers of Tables 1, 2, 3, 4, 5, 6, and 7 are immobilized on a solid support.

7. The method of claim 1, wherein the matching is conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 1, 2, 3, 4, 5, 6 or 7.
8. The method of claim 1, wherein the matching is conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 1, 2, 3, 4, 5, 6 or 7.
9. A panel comprising a profile of biomarkers selected from the group consisting of Table 1, 2, 3, 4, 5, 6, 7, 8, and any combination thereof.
10. A kit comprising the panel of claim 9.
11. A method for detecting or monitoring a disorder of the pancreas, the method comprising obtaining a sample from a patient and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9.
12. The method of claim 11, wherein the disorder of the pancreas is selected from the group consisting of acute pancreatitis, chronic pancreatitis, hereditary pancreatitis, pancreatic neoplasm, and pancreatic cancer.
13. The method of claim 11, wherein the sample is selected from the group consisting of a human tissue biopsy or biosample including pancreas biopsy sample, gastrointestinal sample, blood sample, plasma sample, serum sample, circulating tumor cells sample, tear sample, saliva sample, sperm sample, urine sample, fecal sample and hair sample.
14. The method of claim 11, wherein the sample is analyzed using one or more techniques selected from the group consisting of chromatography, gas chromatography, liquid chromatography, mass spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a

multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay.

15. The method of claim 11, wherein the sample is analyzed using a combination of a detection techniques of nucleic acids and proteins or peptides.
16. The method of claim 11, wherein at least one biomarker and/or glycobiomarker of Tables is immobilized on a solid support.
17. The method of claim 11, wherein the testing is conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9.
18. The method of claim 11, wherein the testing is conducted by reacting the patient's sample with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9.
19. The method of claim 11, wherein the testing is conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 5A, 5, 6A, 6 and 9.
20. A method for treating a disorder of the pancreas, the method comprising obtaining a sample from a mammal in need of the treatment and testing the sample for at least one or more biomarker and/or glycobiomarker selected from Tables 5A, 5, 6A, 6 and 9.
21. A method for screening, monitoring and/or treating a gastrointestinal (GI) cancer patient selected from the group consisting of colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer, the method comprising:
 - obtaining a blood or plasma sample from the patient,
 - isolating glycosylated proteins from the sample, and
 - analyzing the isolated glycosylated proteins for the presence of biomarkers listed in Tables 1A, 2A, 3A, 4A, 5A, 6A, 7A, and any combination thereof.

22. The method of claim 21, wherein the sample is analyzed using one or more techniques selected from the group consisting of chromatography, gas chromatography, liquid chromatography, mass spectrometry, ELISA, antibody linkage, immunoassay, biochip assay, microarray, nanoassay, spectroscopy, a multiplex molecular assay or techniques which utilize a fluorescent, enzyme, radioactive, metallic, biotin, chemiluminescent, bioluminescent molecule assay.
23. The method of claim 21, wherein the sample is analyzed using a combination of a detection techniques of nucleic acids and proteins or peptides.
24. The method of claim 21, wherein biomarkers of Tables 1A, 2A, 3A, 4A, 5A, 6A, and 7A are immobilized on a solid support.
25. The method of claim 1, wherein the matching is conducted by reacting the patient's sample with at least one antibody or protein chemistry based reagent specific to at least one biomarker and/or glycobiomarker of Tables 1A, 2A, 3A, 4A, 5A, 6A or 7A.
26. The method of claim 1, wherein the matching is conducted by reacting the patient's sample with a synthetic compound or probe which react with at least one protein specific to at least one biomarker and/or glycobiomarker of Tables 1A, 2A, 3A, 4A, 5A, 6A or 7A.
27. A panel comprising a profile of biomarkers selected from the group consisting of Table 1A, 2A, 3A, 4A, 5A, 6A, 7A, and any combination thereof.
28. A kit comprising the panel of claim 27.

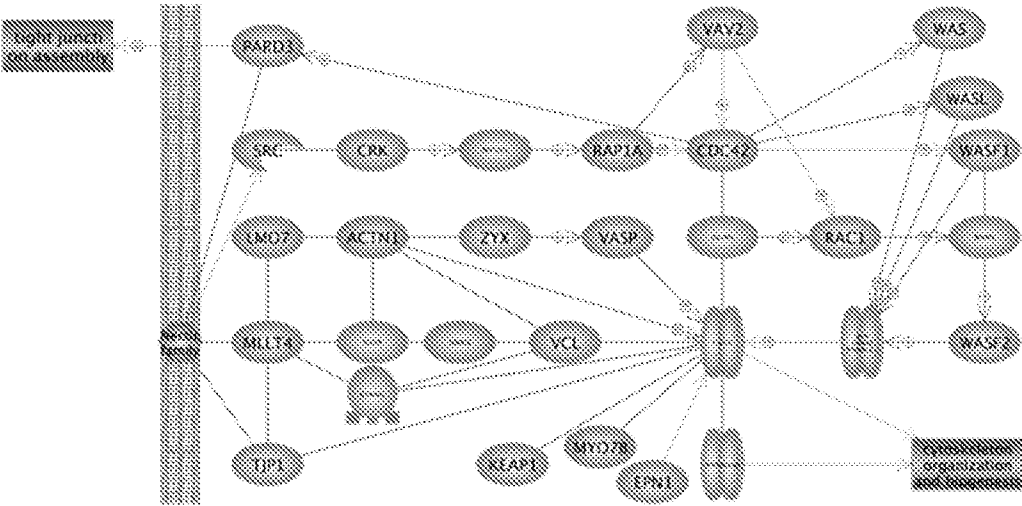


FIG. 1

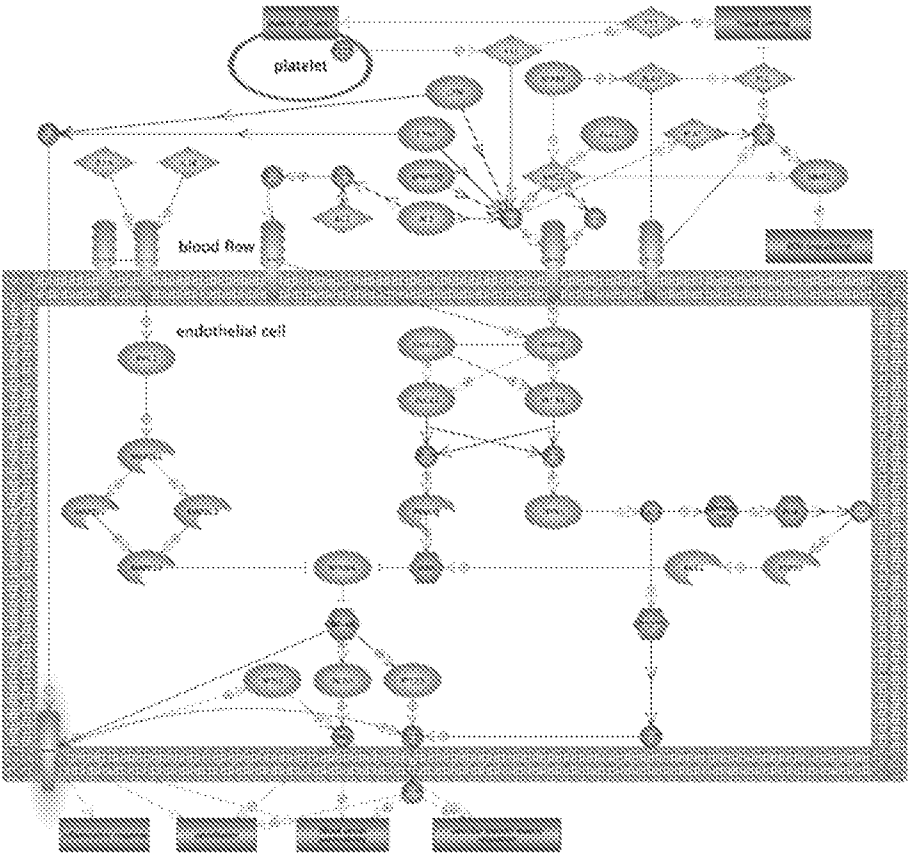


FIG. 2

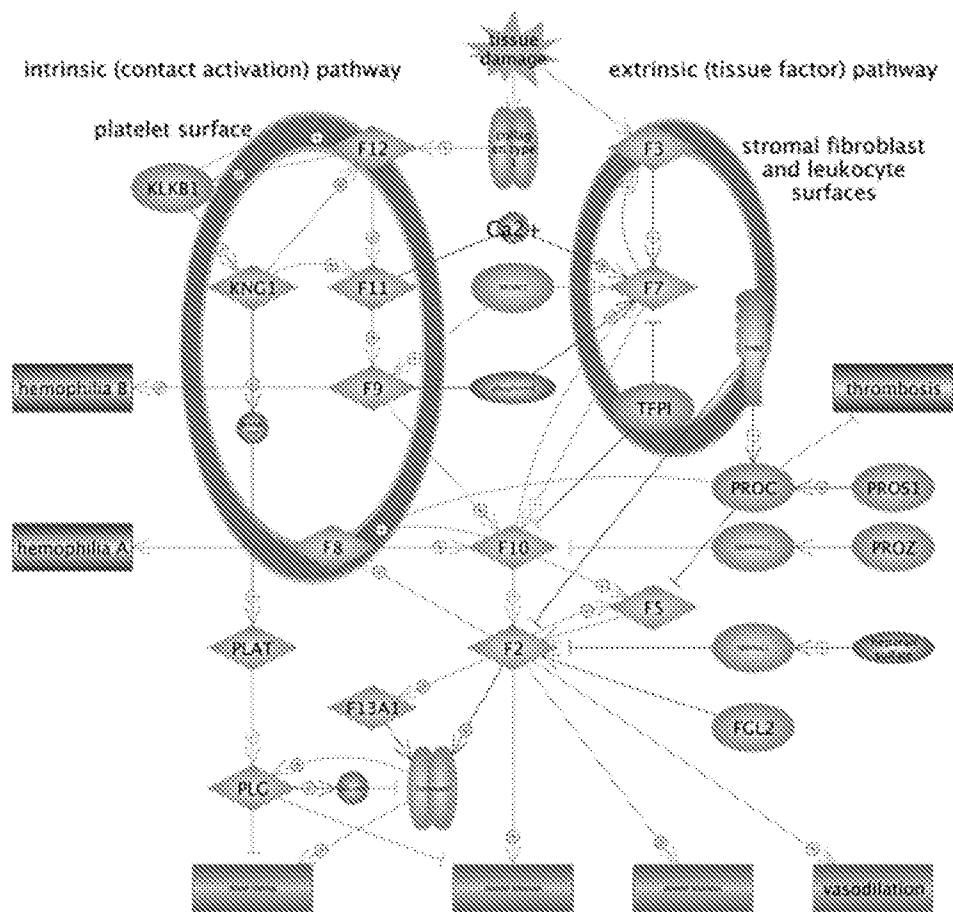


FIG. 3

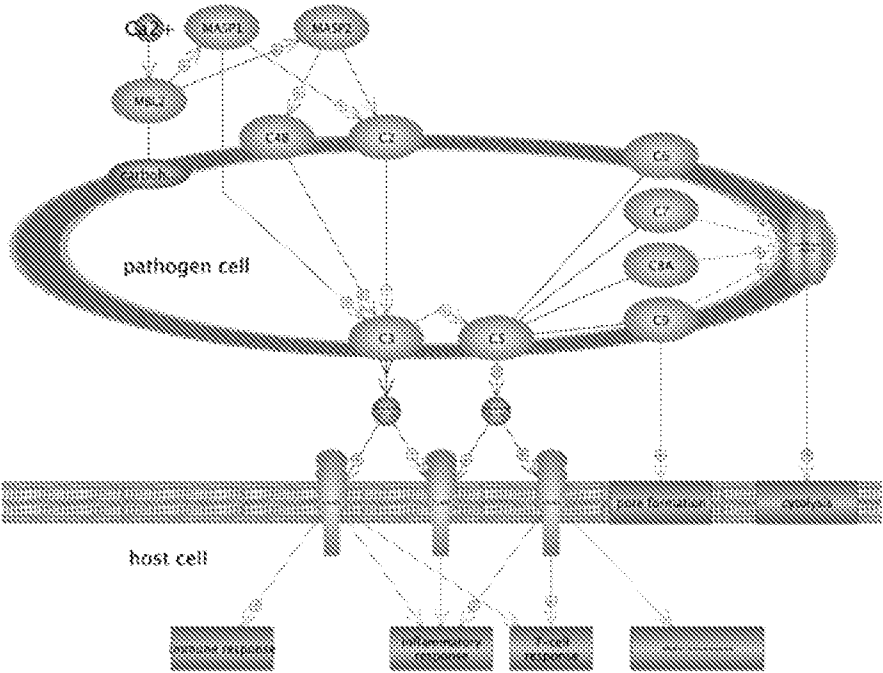


FIG. 4

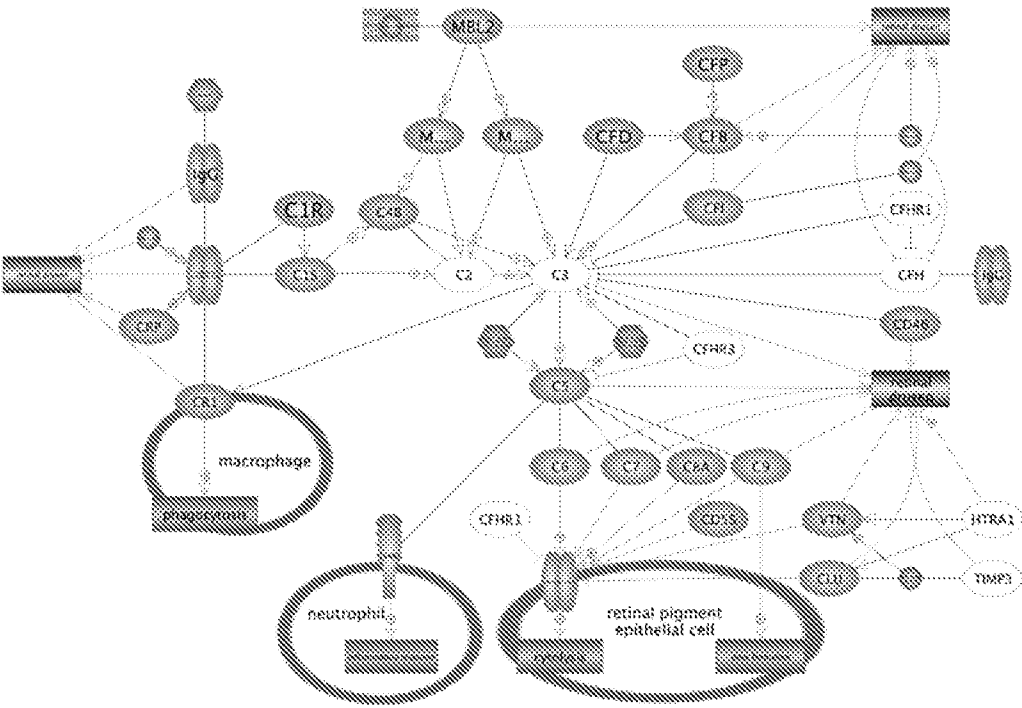


FIG. 5

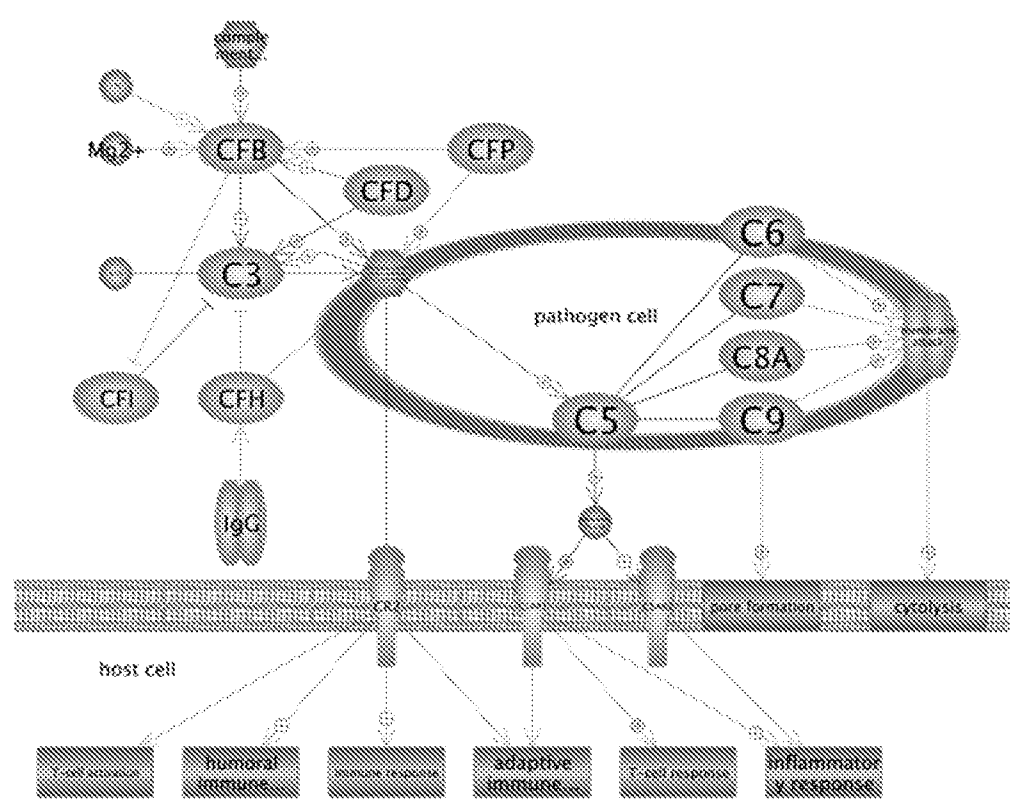


FIG. 6

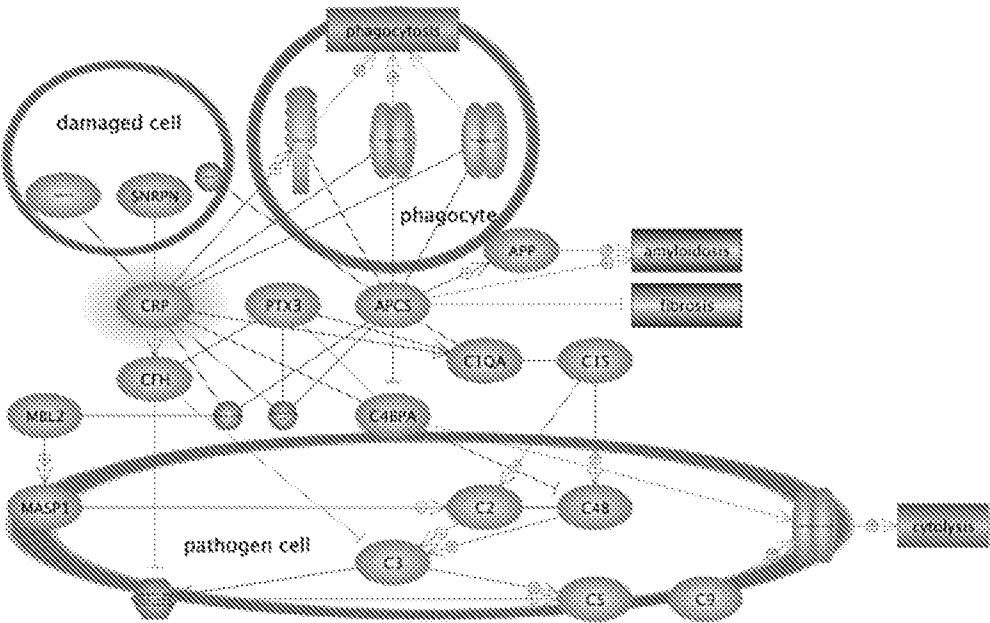


FIG. 7

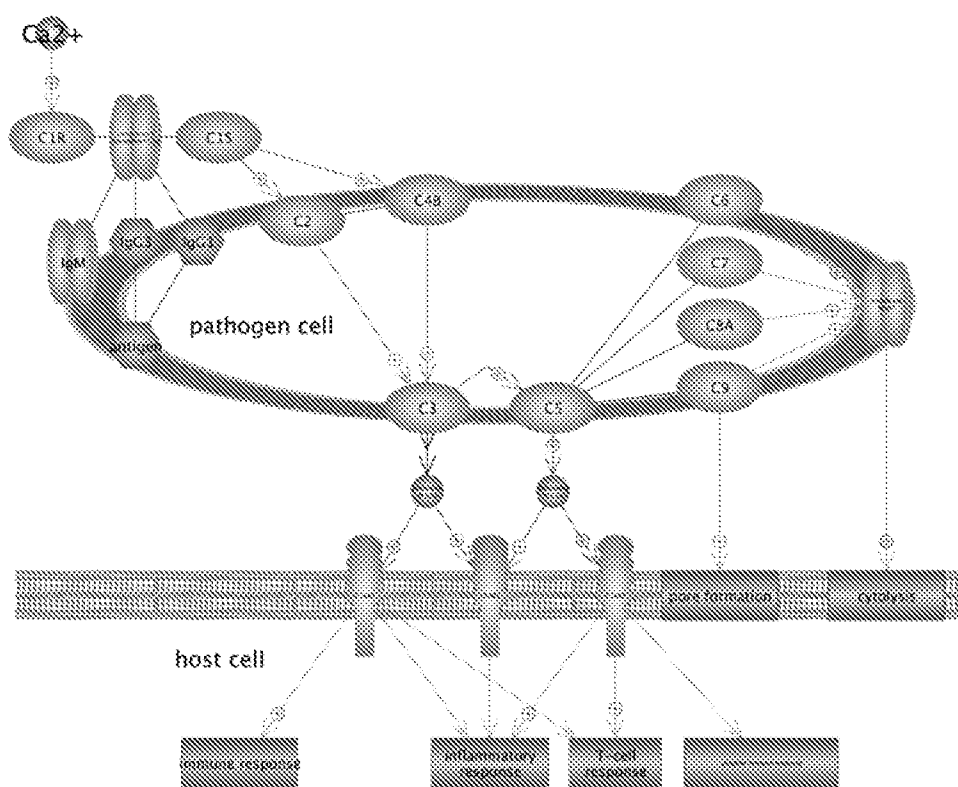


FIG. 8

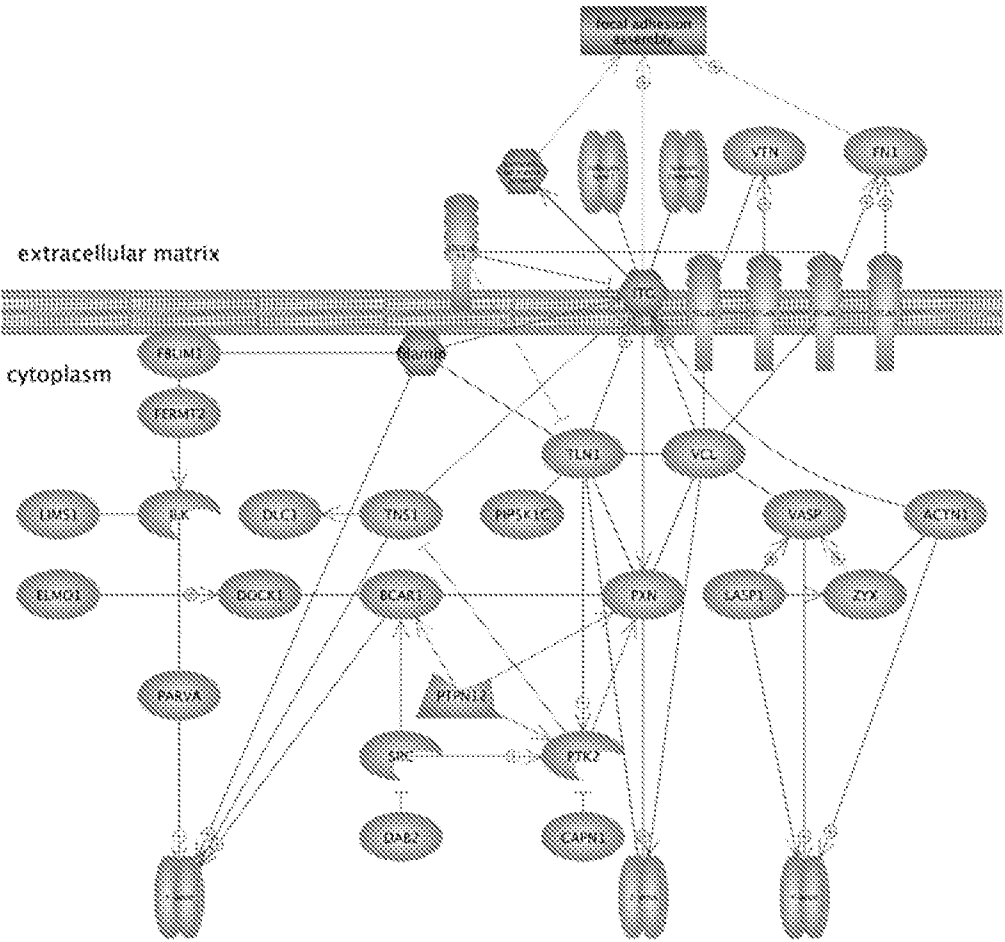


FIG. 9

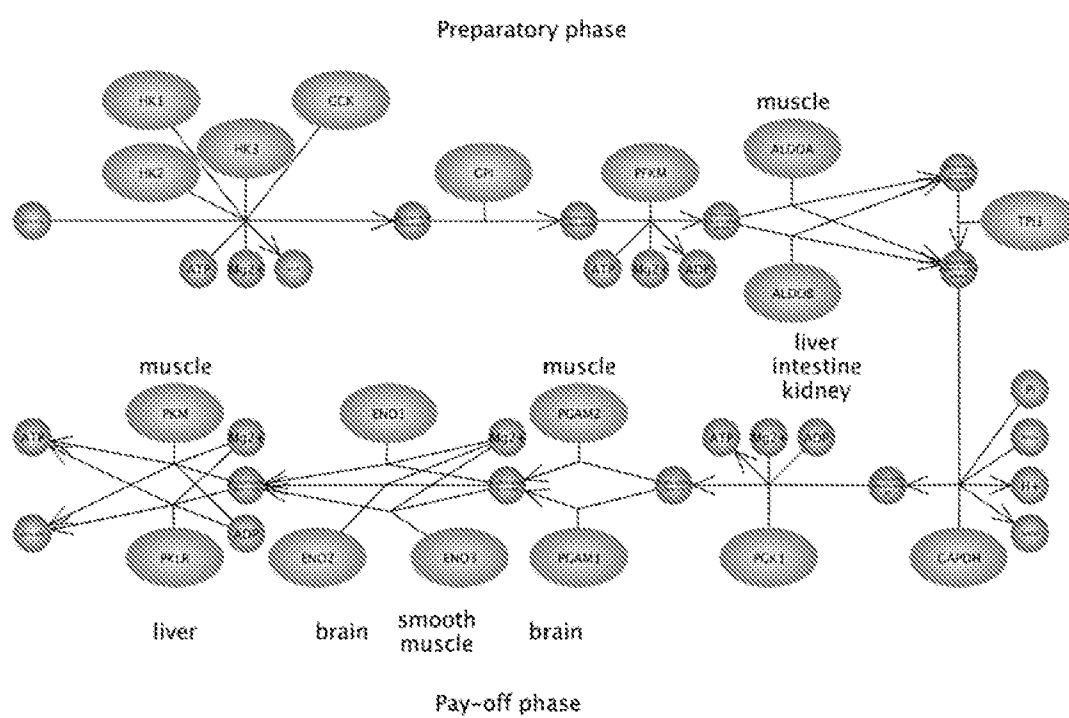


FIG. 10

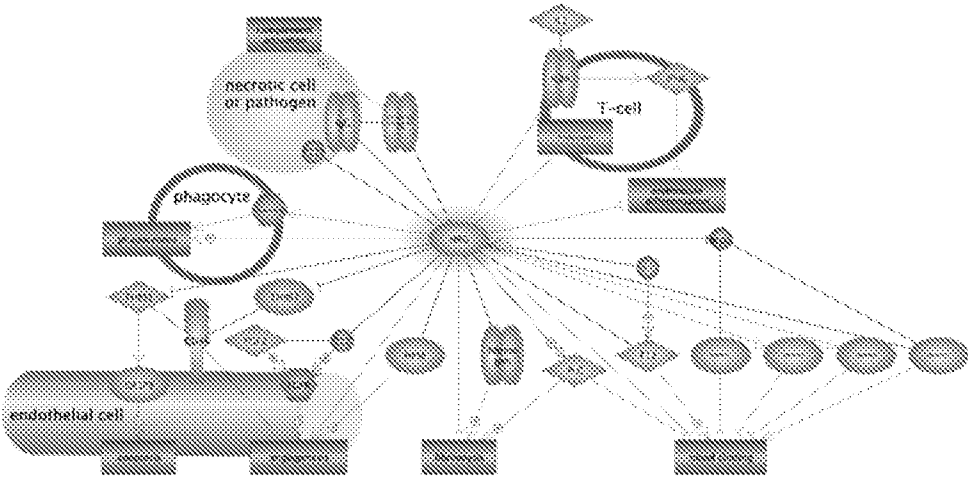


FIG. 11

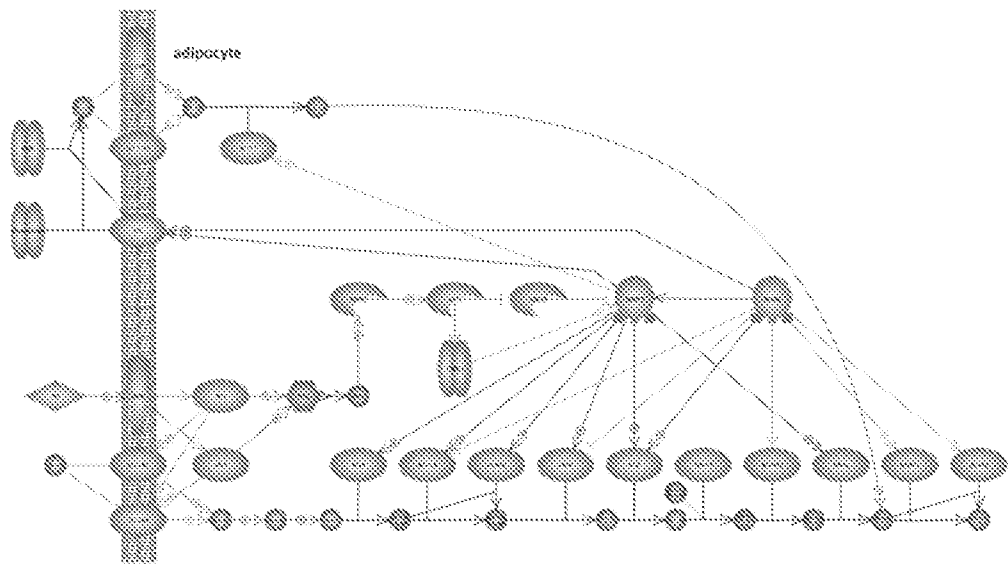


FIG. 12

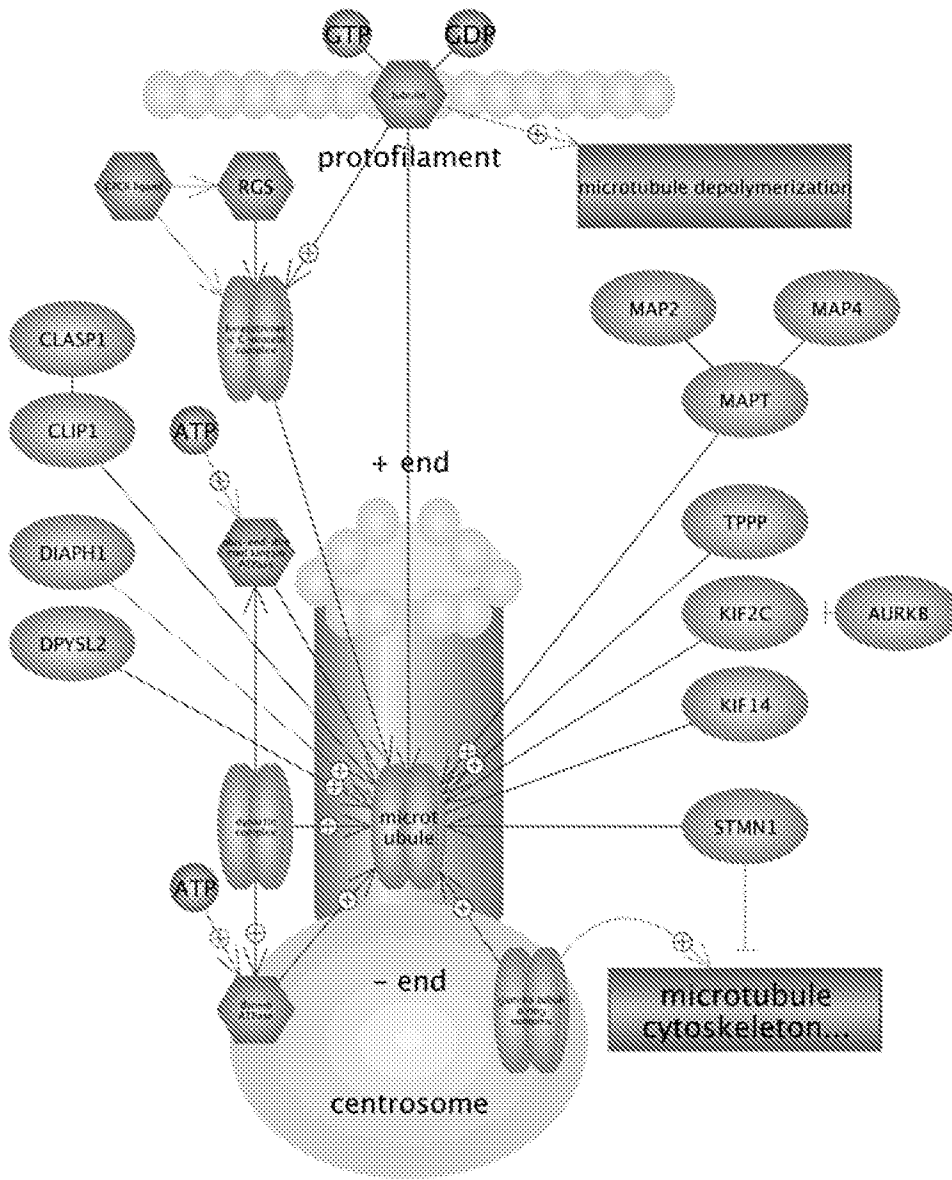


FIG. 13

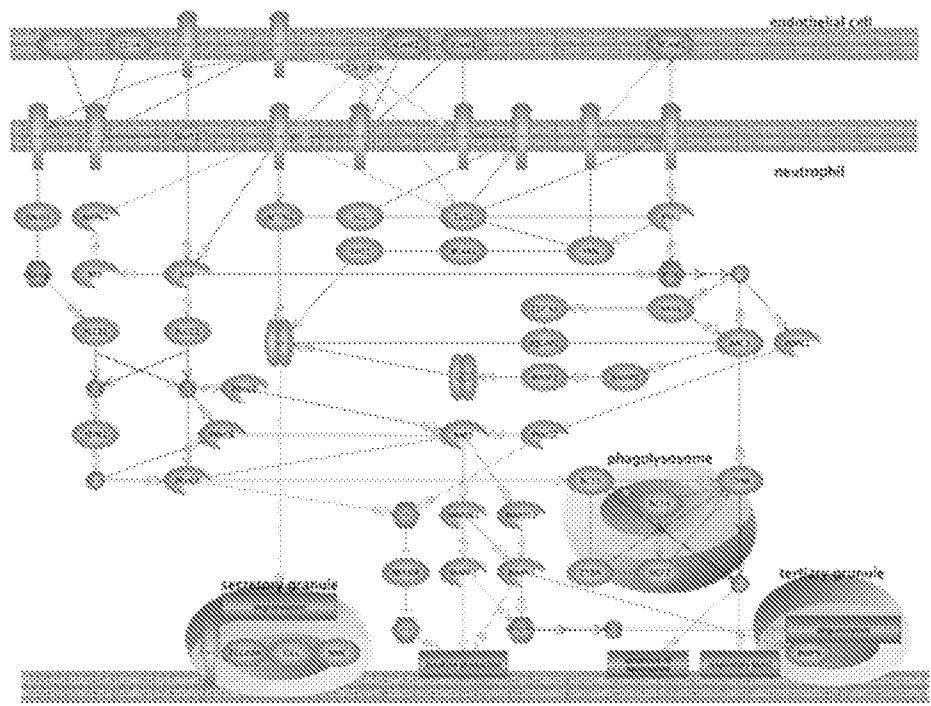


FIG. 14

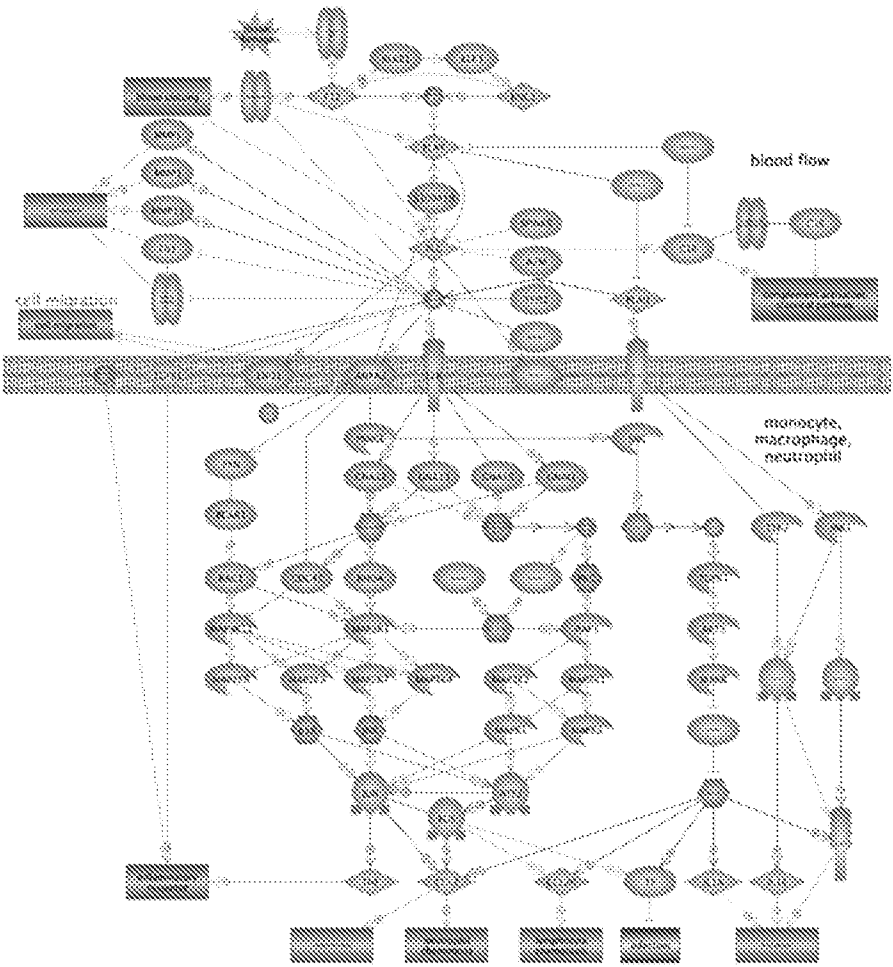


FIG. 15

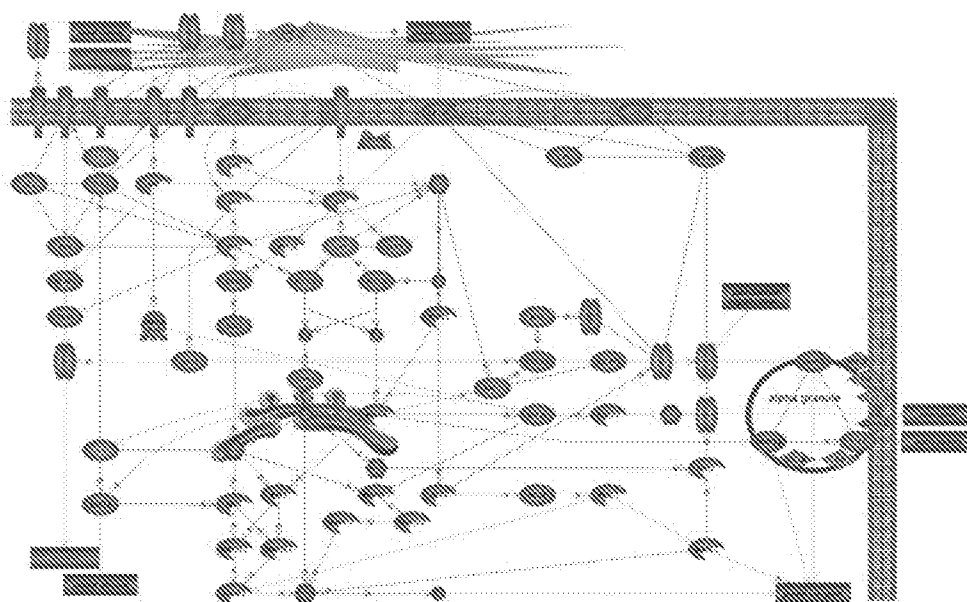


FIG. 16

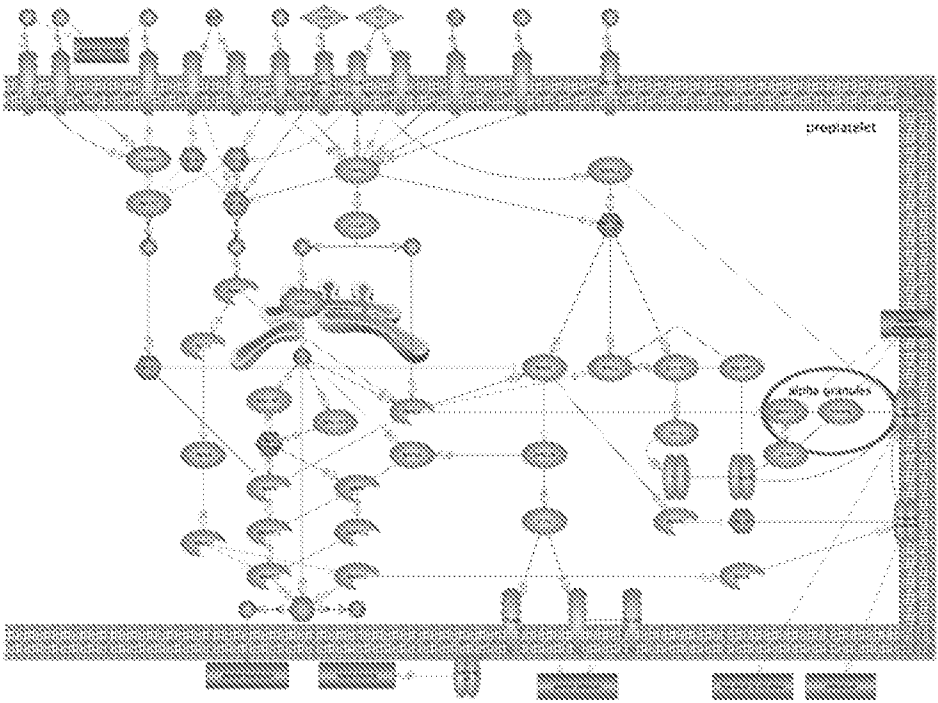


FIG. 17

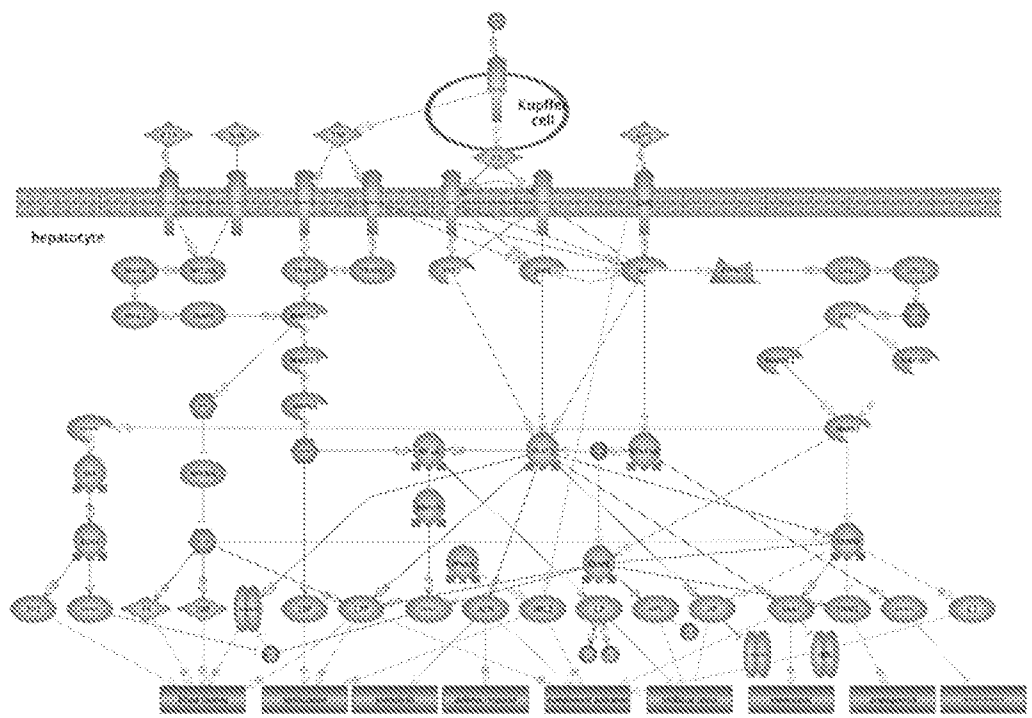


FIG. 18

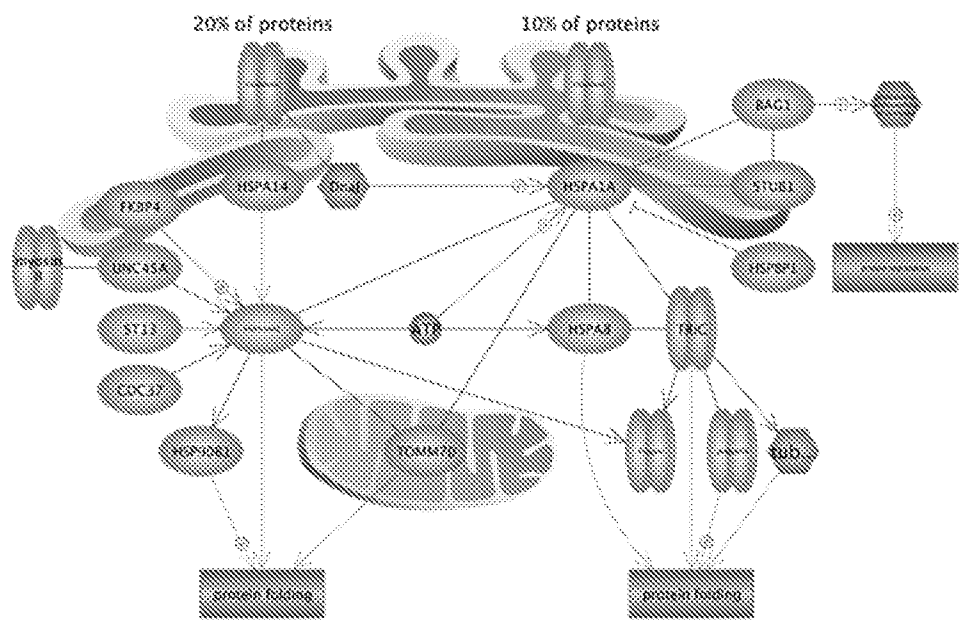


FIG. 19

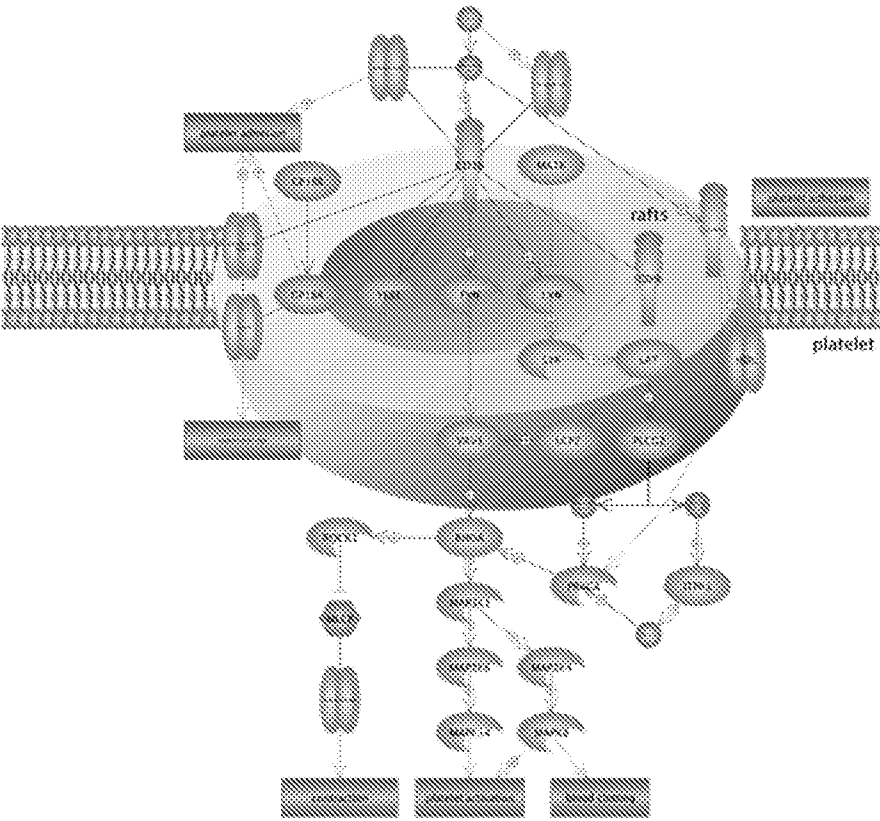


FIG. 20

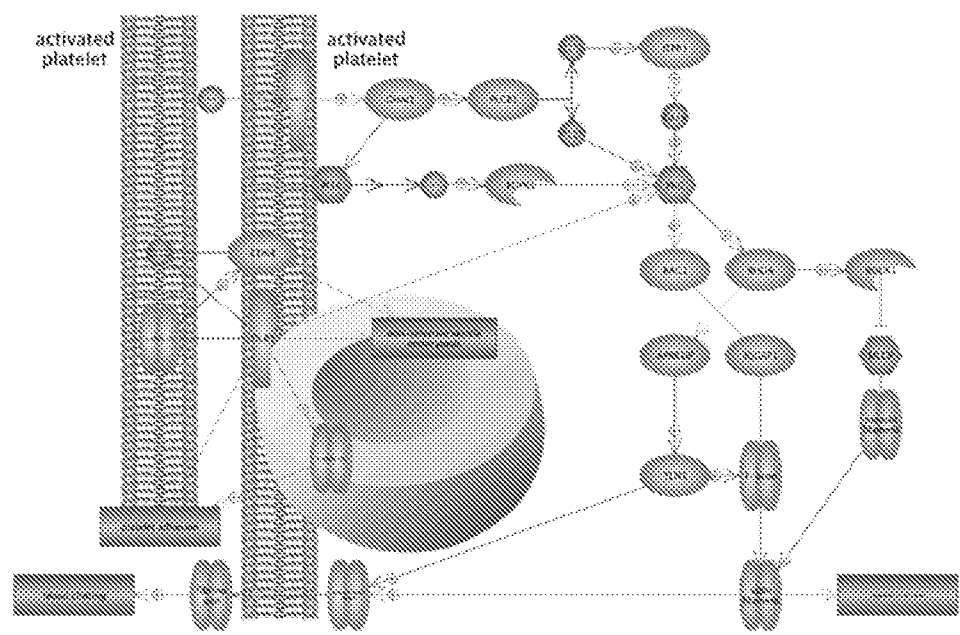


FIG. 21

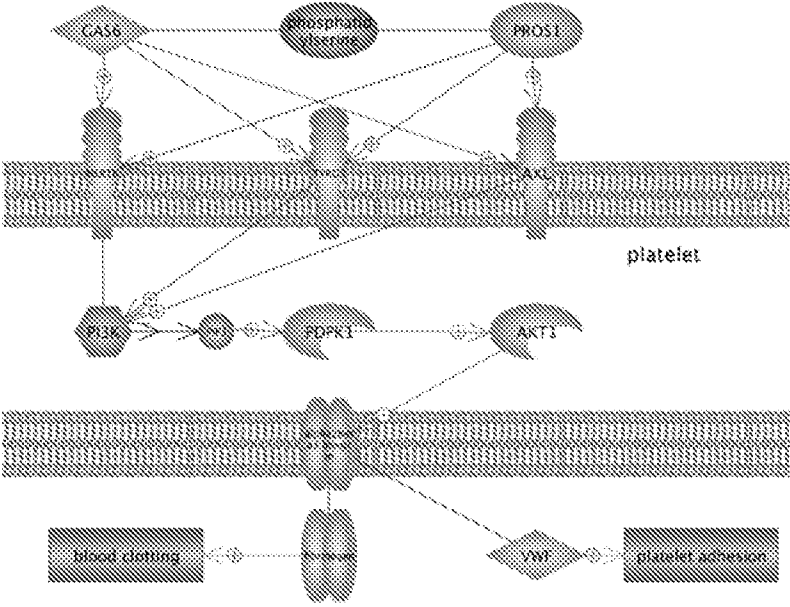


FIG. 22

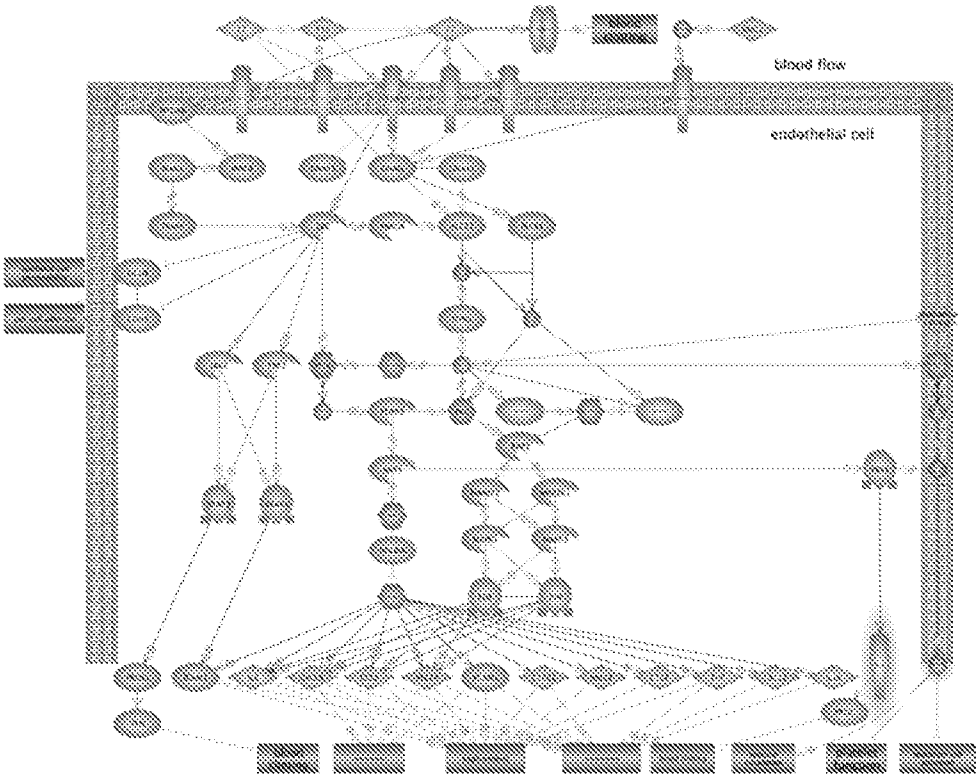


FIG. 23

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/27196

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - G01N 33/50, G01N 33/577, G01N 33/574 (2017.01)
 CPC - G01N 33/6842, G01N 2333/924

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2007/032876 A2 (UNIVERSITY OF IOWA RESEARCH FOUNDATION) 22 March 2007 (22.03.2007) para [0001]; [0033]; [0037]; [0078]	1-10
Y	US 2011/0256560 A1 (DIAMANDIS et al.) 20 October 2011 (20.10 2011) para [0005]; [0080]; [0148]; [0197]; [0198]; Table 3	1-10
Y	US 2014/0154710 A1 (UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.) 5 June 2014 (5.06.2014) para [0008-0009]; [0057]; [0066], [0084],[0086]; [0131]; [0150]; [0239]; Tables 4, 10	1-8

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
 15 August 2017

Date of mailing of the international search report

01 SEP 2017

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 Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/27196

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

-----Please see continuation in first extra sheet-----

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10 limited to glycosylated proteins CFB, CFI, C2, C1R, C1S, C1QC, C9, CRP, VTN, CLU

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 17/27196

Continuation of Box III Lack of Unity

Group I+: Claims 1-28, directed to a method for screening, monitoring and/or treating a gastrointestinal (GI) cancer patient, the method comprising: providing profiles of glycosylated proteins pathways or biomarkers; and a panel or a kit comprising the same. The method will be searched to the extent that the profile of glycosylated proteins pathways encompasses pathway "Complement Activation in Macular Degeneration" comprising glycosylated proteins CFB, CFI, C2, C1R, C1S, C1QC, C9, CRP, VTN, CLU (see instant Specification, pg 13, Table 1). It is believed that claims 1-10 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass "Complement Activation in Macular Degeneration" pathway. Additional pathways or biomarkers will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected pathways or biomarkers. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be a method for detecting or monitoring a disorder of the pancreas, the method comprising testing the sample for biomarker and/or glycobiomarker comprising Actin, cytoplasmic (Table 5A) (Claims 11-20). Another exemplary election would be a method for screening, monitoring and/or treating a gastrointestinal (GI) cancer, comprising detecting the biomarker and/or glycobiomarker comprising 14-3-3 protein sigma (Table 1A) (claims 21-28).

The inventions listed as Group I+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

The technical feature of each of the inventions listed as Group I+ is the glycosylated proteins pathways or biomarkers, recited therein. Each invention of Group I+ requires a specific pathways or biomarkers, not required by any of the other inventions.

Common Technical Features

The inventions of Group I+ share the technical feature of a method for screening, monitoring and/or treating a GI cancer patient by obtaining a sample from the patient, isolating glycoproteins from the sample, and analyzing the profile of glycosylated proteins pathway and or biomarkers, including use of panels of biomarkers. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is made obvious by US 2014/0154710 A1 to UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC. (hereinafter 'Univ Georgia').

Univ Georgia teaches glycoprotein biomarkers specific for gastrointestinal cancers (para [0008] "The present invention is directed to cancer biomarkers, particularly glycoprotein biomarkers. A preferred cancer biomarker according to the invention is a cancer-specific glycoform of a glycoprotein. The present invention additionally provides methods for identifying glycoproteins possessing a cancer-specific glycoform ... Preferred cancer biomarkers are specific for ... colorectal cancer, pancreatic cancer and liver cancer. [i.e., gastrointestinal cancers]"), for screening, monitoring, and treating cancers (para [0042] "The cancer-specific biomarkers of the invention can be used to detect or monitor the progression of cancer or precancerous conditions, as well as to distinguish cancerous or precancerous conditions from each other and from benign (noncancerous) disease states." para [0126] "the invention may include a method for treating a subject having cancer or a precancerous condition, wherein the glycan moiety present on the cancer-specific glycoform of the glycoprotein is a targeting moiety."), including panels of glycoprotein markers (para [0115] "a panel of glycoform-specific (glycospecific) binding molecules (binding elements), such as lectins, glycospecific antibodies, or glycospecific aptamers, can be used to assay the biological sample for the presence or absence of cancer-specific glycoform biomarkers."), and analyzing the profile of glycosylated proteins pathway in specific cancers (para [0140] "During oncogenesis, distinct signal transduction pathways are altered, leading to the differential expression of numerous genes", para [0131] "We have developed a procedure ... to identify potential biomarkers for the early detection of breast carcinoma. We have characterized the media from the invasive breast cancer cell line MBAMB231 for L-PHA-reactive proteins... Our results identified proteins participating in the urokinase plasminogen activator pathway and the TGFb pathway."). Univ Georgia does not expressly recite pathways associated with glycoproteins specific to gastric cancers, however, it would have been obvious to an artisan of ordinary skill to use the methods of Univ Georgia to investigate pathways affected in any cancer taught by Univ Georgia, because the methodology could be applied to any cancer for which glycosylated biomarkers are known. Univ Georgia does not recite the use of kits to market the compositions (e.g. panels of biomarkers), however, it would have been obvious to an artisan of ordinary skill to package and market compositions and panels of biomarkers in kit form, because said kits are a preferred method of selling therapeutic products.

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the inventions.

Group I+ therefore lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.