REVIEWS

SELECTION OF OPTIMAL PROTEIN SETS AS SEROLOGICAL TUMOR MARKER SIGNATURES

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Currently, various potential tumor markers have been proposed for clinical practice. Although some of them are successfully used in diagnostics, and treatment, none of them fully meets the needs of oncology. Therefore, the search for new markers continues. In this context much attention is paid to multiomics technologies such as genomics, transcriptomics, and metabolomics. However, since tumor biomarkers are mainly proteins, proteomics plays a central role in the search of tumor markers. Blood is the most popular source of information about a patient's health and therefore the search is focused on plasma/serum proteins. In order to increase the sensitivity and specificity of the analysis, a very promising approach is to assess the levels of certain sets of relevant proteins rather than individual proteins and this review is devoted to analysis of this problem.

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INTRODUCTION

In a broad sense, tumor biomarkers are certain components that are produced directly or indirectly in the body due to the presence of a tumor. Moreover, these biomarkers can be normal cellular products that are produced in increased quantities by cancer cells, or products of genes that are expressed only during malignant transformation. Thus, a tumor marker present in increased quantities may indicate the presence of cancer.

The marker can exist inside the tumor or enter the blood circulation [1, 2]. This point is fundamentally important, as it suggests a possibility of non-invasive examination and treatment of patients with various malignant neoplasms. The list of known biochemical tumor markers is extensive [2]. Although some of these biomarkers are successfully used in the tumor treatment, none of them can be defined as an "ideal marker", which could be easy and quickly measured, cheap, highly sensitive, specific, and has a high prognostic ability, correlation with the stages of tumor development, and the results of its assay are reproducible [3]. In fact, the ideal tumor marker has not yet been found. Therefore, the search for new tumor biomarkers continues, and since they are mainly proteins, a special role is assigned to proteomics.

From a proteomic viewpoint, the search for protein tumor markers is based on a comparative analysis of proteomes. For this purpose, it is possible to analyze the proteomes of various body fluids (plasma/blood serum, cerebrospinal fluid, saliva, urine, etc.) or tissues. Moreover, human plasma is one of the most popular clinical samples, since it provides a non-invasive express analysis for any type of disease. Therefore, in 2002, a special project aimed at studying the human plasma proteome (HPPP) was launched. Since then, the project has achieved great success in the analysis of plasma proteins [4, 5].

One of the main advantages of using plasma or serum samples is that only a minimally invasive method is required to obtain the samples and this method is widely used for routine blood tests. Such analysis is particularly important for the hematopoietic organs, since the main proteins of human plasma are synthesized mainly in the liver, but also spread to other tissues and even to the brain, which is separated from the circulatory system by the blood-brain barrier. Therefore, the blood plasma proteome should, to a certain degree, reflect changes caused by various diseases, including oncological ones. In the clinical practice, blood tests provide important information about the patient's health. Accordingly, in diagnostics and therapeutic monitoring, analysis the human blood plasma proteome represents a promising approach.

In recent years, recommendations have been developed for the search for biomarkers [6–10]. For this purpose, classical proteomic approaches are used: two-dimensional electrophoresis (2DE), immunodetection, and mass spectrometry (MS), which have many methodological capabilities for high throughput analysis both during independent use or in various combinations. Electrophoretic separation of plasma proteins is a valuable diagnostic tool, as well as a way to monitor clinical progress [11]. MS measures with high accuracy the masses of peptides obtained by specific hydrolysis of proteins. This approach has been used, for example, to detect ovarian cancer (OC) based only on MS spectra [12]. In addition, MS-based proteomics can detect and quantify protein variants, or proteoforms [13]. Ideally, MS-based proteomics can analyze the entire proteome [14–16]. Rapid, reliable, and reproducible shotgun analysis has been developed to obtain “plasma proteome profiles” [14, 17]. Accordingly, there are several directions in the search for ideal tumor markers. First, we can go deep and try to find highly specific proteoforms/tumor markers secreted only by the tumor. Second, we can expand the search and try to select and analyze a panel of several proteins/tumor markers. Third, we can combine these approaches. In this context, examples of using tumor marker panels already exist [18]. This strategy can be applied to solid or liquid biopsy depending on the real situation. Here the question arises of how to select these tumor markers, since the range of their concentrations in plasma is very wide. The plasma proteome is the most complete version of the entire human proteome. In addition to the “classical plasma proteins”, it contains tissue proteins, as well as numerous individual immunoglobulins [19, 20].

If we are going to consider the entire plasma protein panel as a combined tumor biomarker, we need to obtain reliable data on each protein in connection with its response to the malignant process. Blood biochemical tests have long been used to assess human health. The complete set of plasma proteins (proteome) plays a special role in the diagnostics of socially significant diseases, including various types of cancer. Accordingly, it has long been studied which proteins are present in blood plasma, what their concentrations are, and how protein concentrations differ in healthy and sick people [21]. The use of monoclonal antibodies is currently the gold standard for the detection and quantification of proteins in blood plasma. However, this approach has a number of drawbacks, including limited specificity due to antibody cross-reactivity and low potential for multiplex assays.

Qualitative and quantitative assessments of protein markers in blood plasma will significantly improve their diagnostic efficiency. Currently, SOMAscan and Olink are common affinity-based methods that have excellent multiplex potential and are often preferred over (MS) [22, 23]. SOMAscan and Olink are multiplexed aptamer- or antibody-based assays capable of simultaneously measuring thousands of proteins in a wide range of concentrations, from femto- to micromolar ones.

Hence, it follows that it is possible to create assay systems based on sets of specific proteins. Work on the relationship between changes in the levels of major proteins in blood serum or plasma and individual types of cancer began in the 1970s [24]. At that time, protein levels were mainly determined using classical immunological methods — radial immunodiffusion, rocket immunoelectrophoresis, or nephelometric immunoassay. The main attention was paid to acute phase proteins, such as C-reactive protein (CRP_HUMAN), alpha-antitrypsin (A1AT_HUMAN), ceruloplasmin (CERU_HUMAN), haptoglobin (HPT_HUMAN), etc. C-reactive protein was discovered in 1941 [25]. Although the reaction of such proteins to a wide range of factors was observed, the research continued and allowed to accumulate a large array of data on changes in the levels of various acute phase proteins in cancer patients. This allowed to combine such data and try to correlate with different types of cancer. In addition to the indicated acute phase proteins, a number of other tumor markers are currently used in the clinical practice. For example, carcinoembryonic antigen (CEA) (Q13982_HUMAN) belongs to the class of oncoembryonic markers. It is mainly synthesized in the organs of the gastrointestinal tract of the fetus, and after birth its level decreases sharply. It is also found in the tissues of the digestive organs in adults, but in much smaller quantities.

Squamous cell carcinoma antigen (SCCA, SCC), also known as serpin B3 (SPB3_HUMAN), is a 48 kDa glycoprotein known as a marker of squamous cell carcinoma. Normally, a small amount of the antigen is produced inside the epithelial cells of the skin, cervix, and anal canal and is not released into the extracellular space. In SCC, there is an increase in the secretion of the antigen by tumor cells, which may play a role in the processes of invasion and metastasis of carcinoma.

Neuron-specific enolase (NSE) (ENOG_HUMAN, gamma-enolase, ENO2) is one of three members of the enolase family of enzymes involved in glycolysis.

Cancer antigen CA 19-9 is a high-molecular glycoprotein normally produced by epithelial cells of the gastrointestinal tract. Its level increases in almost all patients with tumors of the gastrointestinal tract and especially the pancreatic cancer.

Cancer antigen CA 72-4 is a high-molecular mucin-like glycoprotein produced in many tissues of the fetus and is normally almost undetectable in adults.

SELECTION OF PROTEIN SETS

Using available data on many types of tumor diseases, we have compiled a heat map (Supplementary Materials, Table S1) reflecting changes in the levels of ~160 most abundant plasma/serum proteins in different oncological diseases (Tables 1, 2). The data shown in Supplementary Materials Table S1 were obtained by different research groups and in most cases correlated with each other. In cases, when contradictory results have been

Table 1. Real and proposed oncomarker proteins for the use in the clinical practice

Disease	Markers used	Proposed additional markers
LUNG CANCER (LC), *NSCLC*	Carcinoembryonic antigen (CEA), Squamous cell carcinoma antigen 1 (SCCA-1), CYFRA 21-1 (KRT19), CA125 (MUC16), Carbohydrate antigen 72-4 (CA 72-4)	Alpha-1-acid glycoprotein 1 (*ORM1*), Beta-2-glycoprotein 1 (*APOH*), Cathepsin F (*CTSF*), Complement C1r subcomponent (*C1R*), Fibulin-1 (*FBLN1*), Leucine-rich alpha-2-glycoprotein (*LRG1*), Protein S100-A4 (*S100A4*), Serum amyloid A-1 (*SAA1*)
LUNG CANCER (LC), *SCLC*	Carcinoembryonic antigen (CEA), Squamous cell carcinoma antigen 1 (SCCA-1), Gamma-enolase (ENO2)	Alpha-1-microglobulin (*AMBP*)
COLORECTAL CANCER (CRC)	Carcinoembryonic antigen (CEA), Cancer antigen 19-9 (CA19-9)	Alpha-1-acid glycoprotein 2 (*ORM2*), Alpha-1-antitrypsin (*SERPINA1*), Apolipoprotein C-II (*APOC2*), Leucine-rich alpha-2-glycoprotein (*LRG1*), Mannose-binding protein C (*MBL2*), Protein S100-A8 (*S100A8*), Serum amyloid A-1 (*SAA1*), Albumin (*ALBU*), Adiponectin (*ADIPOQ*), Apolipoprotein E (*APOE*), Fibronectin (*FN1*), Serum paraoxonase/arylesterase (*PON1*), Transthyretin (*TTR*)
BREAST CANCER (BrC)	Carcinoembryonic antigen (CEA), Cancer antigen 15-3 (CA 15-3), CA27-29, Mucin-Like Carcinoma antigen (MCA)	Clusterin (*CLU*), Apolipoprotein A-II (*APOA2*), Heparin Cofactor 2 (*SERPIND1*), Serum amyloid A-1 (*SAA1*), Complement C5 (*C5*)
PROSTATE CANCER (PrC)	PSA. Prostate-specific antigen (KLK3)	Kallistatin (*SERPINA4*), Adiponectin (*ADIPOQ*), Serum amyloid A-1 (*SAA1*)
PANCREATIC CANCER (PCa)	Cancer antigen 19-9 (CA19-9), Carcinoembryonic antigen (CEA), Osteopontin (SPP1), Chitinase-3-like protein 1 (CHI3L1), Ovarian carcinoma antigen CA125 (*MUC16*)	Apolipoprotein A-I (*APOAI*), Apolipoprotein E (*APOE*), Complement C3 (*C3*), Complement C4-A (*C4A*), Plasma gelsolin (*GSN*), Inter-alpha-trypsin inhibitor heavy chain H4 (*ITIH4*), Lumican (*LUM*), Serum amyloid A-1 (*SAA1*), Serum amyloid P-component (*APCS*)
GASTRIC CANCER (GC)	Carbohydrate antigen 72-4 (CA 72-4), Cancer antigen 19-9 (CA19-9), CYFRA 21-1 (*KRT19*), Carcinoembryonic antigen (CEA)	Fibronectin (*FN1*), Protein S100-A9 (*S100A9*), Serum amyloid A-1 (*SAA1*), Sex hormone-binding globulin (*SHBG*), Complement C9 (*C9*)
ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESC)	Squamous cell carcinoma antigen 1 (SCCA-1)	Alpha-1-antichymotrypsin (*SERPINA3*), Alpha-2-HS-glycoprotein (*AHSG*), Leucine-rich alpha-2-glycoprotein (*LRG1*), Serum amyloid A-1 (*SAA1*), Zinc-alpha2-glycoprotein (*AZGP1*), Osteopontin (*SPP1*), Fibrinogen gamma chain (*FGG*), Alpha-1-antitrypsin (*SERPINA1*), Extracellular superoxide dismutase [Cu-Zn] (*SOD3*)
ESOPHAGEAL ADENOCARCINOMA (EA)	Squamous cell carcinoma antigen 1 (SCCA-1), Cancer antigen 19-9 (CA19-9), Pyruvate kinase PKM Isoform M2 (PKM), CYFRA 21-1 (*KRT19*)	Alpha-1-antitrypsin (*SERPINA1*), Extracellular superoxide dismutase [Cu-Zn] (*SOD3*)

Table 1. Real and proposed oncomarker proteins for the use in the clinical practice (continued)

Disease	Markers used	Proposed additional markers
GLIOBLASTOMA (GB)		Apolipoprotein D (*APOD*), Apolipoprotein F (*APOF*), Apolipoprotein M (*APOM*), Complement C4-A (*C4A*), Complement C9 (*C9*), Complement C1q subcomponent subunit C (*C1QC*), Carbonic anhydrase (*CA1*), Ceruloplasmin (*CP*), C-reactive protein (*CRP*), Ferritin light chain (*FTL*), Mannose-binding protein C (*MBL2*), Fetuin-B (*FETUB*), Apolipoprotein A-IV (*APOA4*), Apolipoprotein B-100 (*APOB*), Apolipoprotein C-II (*APOC2*), Apolipoprotein E (*APOE*), Complement C3 (*C3*), Complement C5 (*C5*), Extracellular superoxide dismutase [Cu-Zn] (*SOD3*), Plasma gelsolin (*GSN*), Inter-alpha-trypsin inhibitor heavy chain H1 (*ITIH1*), Inter-alpha-trypsin inhibitor (*ITIH2*), Inter-alpha-trypsin inhibitor heavy chain H4 (*ITIH4*), CD14 antigen (*CD14*), Haptoglobin (*HP*)
LIVER CANCER *HEPATOCARCINOMA (HC)*	Alpha-fetoprotein (AFP), C-reactive protein (*CRP*), PIVKA II (des-gamma carboxyprothrombin)	Afamin (*AFM*), Apolipoprotein A-I (*APOAI*), Apolipoprotein A-II (*APOA2*), Apolipoprotein A-IV (*APOA4*), Complement C2 (*C2*), Complement C3 (*C3*), Complement C7 (*C7*), Complement C9 (*C9*), Ferritin light chain (*FTL*), Serum amyloid A-1 (*SAA1*), Keratin, type II cytoskeletal 1 (*KRT1*), Keratin, type II cytoskeletal 6C (*KRT6C*), Keratin, type I cytoskeletal 9 (*KRT9*), Keratin, type I cytoskeletal 10 (*KRT10*), Interleukin-6 (*IL6*), Serotransferrin (*TF*), Fibronectin (*FN1*), Plasma protease C1 inhibitor (*SERPING1*)
LIVER CANCER *CHOLANGIOCARCINOMA (CCA)*	Alpha-fetoprotein (AFP), Cancer antigen 19-9 (CA19-9), CYFRA 21-1 (*KRT19*)	Alpha-1-antichymotrypsin (*SERPINA3*), Leucine-rich alpha-2-glycoprotein (*LRG1*), Haptoglobin (*HP*), Plasma protease C1 inhibitor (*SERPING1*), Transthyretin (*TTR*)
LIVER CANCER *HEPATOBLASTOMA (HB)*	Alpha-fetoprotein (AFP), Beta-human chorionic gonadotropin (CGB3; CGB5; CGB8)	
KIDNEY CANCER (KC)	C-reactive protein (*CRP*), Pyruvate kinase PKM Isoform M2 (*PKM*), Gamma-enolase (*ENO2*), Ferritin light chain (*FTL*)	Apolipoprotein E (*APOE*), Carbonic anhydrase (*CA1*), Ceruloplasmin (*CP*), Complement C1q subcomponent subunit C (*C1QC*), Complement C3 (*C3*), Complement C4d, Complement C5 (*C5*), Fibronectin (*FN1*), Serum amyloid A-1 (*SAA1*), Matrix metalloproteinase-9 (*MMP9*), Carbonic anhydrase 9 (*CA9*), Complement factor B (*CFB*)
BLADDER CANCER (BC)	CYFRA 21-1 (*KRT19*)	Lumican (*LUM*), Haptoglobin (*HP*), Serum amyloid P component (*APCS*), Alpha-1-acid glycoprotein 1 (*ORM1*)

Table 1. Real and proposed oncomarker proteins for the use in the clinical practice (continued)

Disease	Markers used	Proposed additional markers
CERVICAL CANCER (CC)	Squamous cell carcinoma antigen 1 (SCCA-1)	Alpha-1B glycoprotein (*A1BG*), Antithrombin-III (*SERPINC1*), Apolipoprotein C-I (*APOC1*), Complement C3 (*C3*), Plasma gelsolin (*GSN*), Zinc-alpha2-glycoprotein (*AZGP1*), Alpha-1-antitrypsin (*SERPINA1*), Carbohydrate antigen (CA72-4), Mucin-1 (CA15-3), Osteopontin (SPP1)
ENDOMETRIAL CANCER (EC)	Ovarian carcinoma antigen CA125 (*MUC16*), Carcinoembryonic antigen (*CEA*), CA27-29, Squamous cell carcinoma antigen 1 (SCCA-1), Beta-human chorionic gonadotropin (β-hCG)	Protein S100-A8 (*S100A8*), Inter-alpha-trypsin inhibitor (*ITIH2*), Complement C9 (*C9*), Apolipoprotein A-IV (*APOA4*), Apolipoprotein A-I (*APOAI*), Alpha-1-antitrypsin (*SERPINA1*), Albumin (*ALBU*), Carbohydrate antigen 72-4 (CA72-4), Mucin-1 (CA15-3), Clusterin (*CLU*), Inter-alpha-trypsin inhibitor heavy chain H4 (*ITIH4*), Antithrombin-III (*SERPINC1*), Complement C1r subcomponent (*C1R*)
OVARIAN CANCER (OC)	Ovarian carcinoma antigen CA125 (*MUC16*), Carbohydrate antigen 72-4 (CA 72-4), Serotransferrin (*TF*), Transthyretin (*TTR*), Apolipoprotein A-I (*APOAI*), Beta-2-microglobulin (*B2M*), HE4, Follicle stimulating hormone (FSH)	
THYROID CANCER (TC)	Thyroglobulin (*TG*), Calcitonin (*CALCA*), Thyroid-stimulating hormone (*TSH*), Carcinoembryonic antigen (*CEA*)	CD 166 antigen (*ALCAM*), Complement factor H-related protein 1 (*CFHR1*), Apolipoprotein A-IV (*APOA4*), Apolipoprotein A-I (*APOAI*), Gamma-glutamyl hydrolase (*GGH*), Amyloid beta A-4 protein (*APP*)
SKIN CANCER	Protein S100-B (*S100B*)	Transthyretin (*TTR*), Angiotensinogen (*AGT*), Matrix metalloproteinase-9 (*MMP9*), Vitamin D-binding protein (*GC*), Matrix metalloproteinase-1 (*MMP1*), Osteopontin (*SPP1*)
HEMATOLOGICAL CANCER *MULTIPLE MYELOMA*	M-protein (IgG, IgA)	Fibronectin (*FN1*), Urokinase Plasminogen Activator Receptor (*PLAUR*), Fibulin-1 (*FBLN1*),
HEMATOLOGICAL CANCER *MALIGNANT LYMPHOMA*	Beta-2-microglobulin (*B2M*)	Haptoglobin-related protein (*HPR*), Protransforming growth factor alpha (*TGFA*)
NASOPHARYNGEAL CANCER (NPC)	Cathepsin-B (*CTSB*), Cathepsin-D (*CTSD*)	Apolipoprotein E (*APOE*), Ferritin light chain (*FTL*)
ORAL CAVITY AND OROPHARYNGEAL CANCERS (OCOPC)	Squamous cell carcinoma antigen 1 (SCCA-1), CYFRA 21-1 (*KRT19*)	Beta-2-microglobulin (*B2M*), Extracellular superoxide dismutase [Cu-Zn] (*SOD3*)
LARYNGEAL CANCER	Squamous cell carcinoma antigen 1 (SCCA-1), CYFRA 21-1 (*KRT19*)	Protein S100A8 (*S100A8*)
BONE CANCER	Ovarian carcinoma antigen CA125 (*MUC16*), Cancer antigen 19-9 (CA19-9), Lactate dehydrogenase (LDH), Alkaline phosphatase (ALP)	

Table 2. Plasma proteins with altered content charactetized by association with oncological diseases considered in Supplementary Materials Table S1

#	UniProt	ID (Uniprot)	Name (*gene*)	Oncology (reference)
1	P02763	A1AG1_HUMAN	Alpha-1-acid glycoprotein 1 (*ORM1*)	[18, 40–50]
2	P19652	A1AG2_HUMAN	Alpha-1-acid glycoprotein 2 (*ORM2*)	[18, 38, 51, 53, 54]
3	P01009	A1AT_HUMAN	Alpha-1-antitrypsin (*SERPINA1*)	[18, 27, 28, 38, 42, 43, 52, 55–65]
4	P04217	A1BG_HUMAN	Alpha-1B glycoprotein (*A1BG*)	[18, 38, 65–68]
5	P01023	A2MG_HUMAN	Alpha-2-macroglobulin (*A2M*)	[27, 32, 38, 41, 69–71]
6	P08697	A2AP_HUMAN	Alpha-2-antiplasmin (*SERPINF2*)	[72, 73]
7	P02750	A2GL_HUMAN	Leucine-rich alpha-2-glycoprotein (*LRG1*)	[18, 50, 59, 63, 66, 74–81]
8	P05067	A4_HUMAN	Amyloid beta A4 protein (*APP*)	[82]
9	P01011	AACT_HUMAN	Alpha-1-antichymotrypsin (*SERPINA3*)	[18, 32, 59, 79, 82–86]
10	Q15848	ADIPO_HUMAN	Adiponectin (*ADIPOQ*)	[18, 26, 87–89]
11	P43652	AFAM_HUMAN	Afamin (*AFM*)	[18, 38, 90–94]
12	P02768	ALBU_HUMAN	Albumin (*ALBU*)	[59, 78, 95–99]
13	P02760	AMBP_HUMAN	Protein AMBP (*AMBP*) Alpha-1-microglobulin (*AMBP*) Bikunin (*AMBP*)	[27, 100, 101]
14	P15144	AMPN_HUMAN	Aminopeptidase N (*ANPEP*)	[82]
15	P01019	ANGT_HUMAN	Angiotensinogen (*AGT*)	[37, 102]
16	P01008	ANT3_HUMAN	Antithrombin-III (*SERPINC1*)	[38, 58, 65, 103–106]
17	P02647	APOA1_HUMAN	Apolipoprotein A-I (*APOAI*)	[18, 31, 32, 80, 82, 107–113]
18	P02652	APOA2_HUMAN	Apolipoprotein A-II (*APOA2*)	[32, 36, 38, 54, 82, 94, 107, 114–119]
19	P06727	APOA4_HUMAN	Apolipoprotein A-IV (*APOA4*)	[37, 38, 41, 53, 82, 86, 92, 105, 111, 119]
20	P04114	APOB_HUMAN	Apolipoprotein B-100 (*APOB*)	[32, 67, 78, 93, 120]
21	P02654	APOC1_HUMAN	Apolipoprotein C-I (*APOC1*)	[18, 32–36, 121–124]
22	P02655	APOC2_HUMAN	Apolipoprotein C-II (*APOC2*)	[77, 78, 125]
23	P02656	APOC3_HUMAN	Apolipoprotein C-III (*APOC3*)	[18, 32, 42, 54, 77, 93, 115, 121, 123]
24	P05090	APOD_HUMAN	Apolipoprotein D (*APOD*)	[78, 126]
25	P02649	APOE_HUMAN	Apolipoprotein E (*APOE*)	[18, 80, 93, 126–131]
26	Q13790	APOF_HUMAN	Apolipoprotein F (*APOF*)	[18, 78, 119, 132]
27	P02749	APOH_HUMAN	Beta-2-glycoprotein 1 (*APOH*)	[31, 53, 133–136]
28	O95445	APOM_HUMAN	Apolipoprotein M (*APOM*)	[78, 137]
29	P61769	B2MG_HUMAN	Beta-2-microglobulin (*B2M*)	[138, 139]
30	Q16790	CAH9_HUMAN	CA-9 carbonic anhydrase 9 (*CA9*)	[78, 140]
31	P02747	C1QC_HUMAN	Complement C1q subcomponent subunit C (*C1QC*)	[42, 141]
32	P00736	C1R_HUMAN	Complement C1r subcomponent (*C1R*)	[32, 142–144]
33	P09871	C1S_HUMAN	Complement C1s subcomponent (*C1S*)	[18, 32, 38, 145, 146]
34	P04003	C4BPA_HUMAN	C4b-binding protein alpha chain (*C4BP*)	[78, 82]
35	P07858	CATB_HUMAN	Cathepsin-B (*CTSB*)	[147]
36	P07339	CATD_HUMAN	Cathepsin-D (*CTSD*)	[147]
37	Q9UBX1	CATF_HUMAN	Cathepsin-F (*CTSF*)	[148]
38	P06731	CEAM5_HUMAN	CEA (carcinoembryonic antigen) Carcinoembryonic antigen-related cell adhesion molecule 5 (*CEACAM5*)	[29, 149–153]
39	P05156	CFAI_HUMAN	Complement factor I (*CFI*)	[59, 82, 154]
40	P00751	CFAB_HUMAN	Complement factor B (*CFB*)	[18, 32, 73, 93, 155–158]
41	P00746	CFAD_HUMAN	Complement factor D (*CFD*)	[159]

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#	UniProt	ID (Uniprot)	Name (*gene*)	Oncology (reference)
42	P08603	CFAH_HUMAN	Complement factor H (*CFH*)	[32, 160–162]
43	P06681	CO2_HUMAN	Complement C2 (*C2*)	[18, 32, 38, 52]
44	P01024	CO3_HUMAN	Complement C3 (*C3*) Cleaved into 12 chains Complement C3a	[32, 38, 41, 53, 68, 73, 78–80, 144, 155, 163–167]
45	P0C0L4	CO4A_HUMAN	Complement C4-A (*C4A*)	[42, 50, 53, 67, 78, 80, 157, 165, 166]
46	P0C0L5	CO4B_HUMAN	Complement C4-B (*C4B*)	[18, 42, 59, 165, 166]
47	P0C0L5	CO4B_HUMAN	Complement C4d a degradation product of C4b (*C4B*)	[168, 169]
48	P01031	CO5_HUMAN	Complement C5 (*C5*) Cleaved into 4 chains Complement C5a	[18, 32, 38, 50, 78, 93, 169, 170]
49	P13671	CO6_HUMAN	Complement C6 (*C6*)	[18, 67, 144]
50	P10643	CO7_HUMAN	Complement C7 (*C7*)	[32, 38, 78, 93, 171]
51	P02748	CO9_HUMAN	Complement C9 (*C9*)	[18, 32, 36, 38, 50, 172, 173]
52	P00915	CAH1_HUMAN	Carbonic anhydrase (*CA1*)	[18, 78, 174, 175]
53	P01258	CALC_HUMAN	Calcitonin (*CALCA*)	[176]
54	P15169	CBPN_HUMAN	Carboxypeptidase N catalytic chain (*CPN1*)	[38, 54, 77, 78, 177]
55	P36222	CH3L1_HUMAN	Chitinase-3-like protein 1 (*CHI3L1*)	[178]
56	P08571	CD14_HUMAN	Monocyte differentiation antigen CD14 (*CD14*) urinary form	[38, 179]
57	P16070	CD44_HUMAN	CD44 antigen (*CD44*)	[180]
58	Q13740	CD166_HUMAN	CD 166 antigen (*ALCAM*)	[82]
59	P0DN86	CGB3_HUMAN	Beta-human chorionic gonadotropin (*CGB3; CGB5; CGB8*)	[181]
60	P00450	CERU_HUMAN	Ceruloplasmin (*CP*)	[18, 43, 69, 144, 182–187]
61	P06276	CHLE_HUMAN	Cholinesterase (*BCHE*)	[188, 189]
62	P10909	CLUS_HUMAN	Clusterin (*CLU*)	[32, 54, 67, 73, 93, 167, 190–195]
63	Q96KN2	CNDP1_HUMAN	Beta-Ala-His dipeptidase (*CNDP1*)	[78, 196–198]
64	Q12860	CNTN1_HUMAN	Contactin-1 (*CNTN1*)	[82]
65	P02741	CRP_HUMAN	C-reactive protein (*CRP*) C-reactive protein (1–205)	[77, 78, 86, 199–202]
66	Q16610	ECM1_HUMAN	Extracellular matrix protein 1 (*ECM1*)	[203–205]
67	P09104	ENOG_HUMAN	Gamma-enolase (*ENO2*)	[149, 206, 207]
68	P00742	FA10_HUMAN	Coagulation factor X (*F10*)	[82]
69	P23142	FBLN1_HUMAN	Fibulin-1 (*FBLN1*)	[148, 208–212]
70	O00602	FCN1_HUMAN	Ficolin-1 (*FCN1*)	[213]
71	Q15485	FCN2_HUMAN	Ficolin-2 (*FCN2*)	[213]
72	O75636	FCN3_HUMAN	Ficolin-3 (*FCN3*)	[79, 102, 214–217]
73	P02771	FETA_HUMAN	Alpha-fetoprotein (*AFP*) Glycosylated form of AFP-L3	[218–220]
74	P02765	FETUA_HUMAN	Alpha-2-HS-glycoprotein (*AHSG*)	[29, 30, 38, 41, 221, 222]
75	Q9UGM5	FETUB_HUMAN	Fetuin-B (*FETUB*)	[78, 223]
76	Q03591	FHR1_HUMAN	Complement factor H-related protein 1 (*CFHR1*)	[82]
77	P02671	FIBA_HUMAN	Fibrinogen alpha chain (*FGA*)	[52, 93, 224, 225]
78	P02675	FIBB_HUMAN	Fibrinogen beta chain (*FGB*)	[41, 54, 225, 226]
79	P02679	FIBG_HUMAN	Fibrinogen gamma chain (*FGG*)	[93, 227–230]

Table 2. Plasma proteins with altered content charactetized by association with oncological diseases considered in Supplementary Materials Table S1 (continued)

#	UniProt	ID (Uniprot)	Name (*gene*)	Oncology (reference)
80	P02751	FINC_HUMAN	Fibronectin (*FN1*)	[38, 42, 50, 58, 82, 120, 231–236]
81	P02792	FRIL_HUMAN	Ferritin light chain (*FTL*)	[78, 237–239]
82	P06396	GELS_HUMAN	Plasma gelsolin (*GSN*)	[38, 41, 82, 86, 216, 240, 241]
83	Q92820	GGH_HUMAN	Gamma-glutamyl hydrolase (*GGH*)	[82]
84	P22352	GPX3_HUMAN	Glutathione peroxidase 3 (*GPX3*)	[242–244]
85	P07492	GRP_HUMAN	Gastrin-releasing peptide (*GRP*)	[150]
86	P69905	HBA_HUMAN	Hemoglobin subunit alpha (*HBA1*)	[18, 38, 59, 69, 119]
87	P68871	HBB_HUMAN	Hemoglobin subunit beta (*HBB*)	[18, 38, 42, 69, 78, 245]
88	P02790	HEMO_HUMAN	Hemopexin (*HPX*)	[78, 105, 144, 229, 246–248]
89	P05546	HEP2_HUMAN	Heparin Cofactor 2 (*SERPIND1*)	[38, 73, 248–251]
90	P00738	HPT_HUMAN	Haptoglobin (Zonulin) (*HP*) Haptoglobin alpha 1 chain Haptoglobin alpha 2 chain Haptoglobin beta chain	[18, 31, 33, 38, 41, 42, 53, 63, 78, 79, 105, 123, 144, 167, 216, 252–259]
91	P00739	HPTR_HUMAN	Haptoglobin-related protein (*HPR*)	[260, 261]
92	P04196	HRG_HUMAN	Histidine-rich glycoprotein (*HRG*)	[262, 263]
93	P05155	IC1_HUMAN	Plasma protease C1 inhibitor (*SERPING1*)	[18, 38, 93, 264, 265]
94	P05231	IL6_HUMAN	Interleukin-6 (*IL6*)	[266–268]
95	P19827	ITIH1_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H1 (*ITIH1*)	[18, 38, 269–274]
96	P19823	ITIH2_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H2 (*ITIH2*)	[38, 77, 78]
97	Q06033	ITIH3_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H3 (*ITIH3*)	[270]
98	Q14624	ITIH4_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H4 (*ITIH4*)	[41, 80, 131, 270, 273, 274]
99	P04264	K2C1_HUMAN	Keratin, type II cytoskeletal 1 (*KRT1*)	[38]
100	P48668	K2C6C_HUMAN	Keratin, type II cytoskeletal 6C (*KRT6C*)	[38]
101	P35527	K1C9_HUMAN	Keratin, type I cytoskeletal 9 (*KRT9*)	[38]
102	P13645	K1C10_HUMAN	Keratin, type I cytoskeletal 10 (*KRT10*)	[38]
103	P08727	K1C19_HUMAN	Keratin, type I cytoskeletal 19, CYFRA 21-1 (*KRT19*)	[150, 275–278]
104	P29622	KAIN_HUMAN	Kallistatin (*SERPINA4*)	[77, 279, 280]
105	P06870	KLK1_HUMAN	Kallikrein-1 (*KLK1*)	[38, 281]
106	P07288	KLK3_HUMAN	PSA. Prostate-specific antigen (*KLK3*)	[282]
107	P01042	KNG1_HUMAN	Kininogen 1 (*KNG1*)	[38, 61, 283, 284]
108	P14618	KPYM_HUMAN	Pyruvate kinase PKM Isoform M2 (*PKM*)	[285, 286]
109	P51884	LUM_HUMAN	Lumican (*LUM*)	[38, 216, 287–289]
110	P11226	MBL2_HUMAN	Mannose-binding protein C (*MBL2*)	[158, 223, 261, 290]
111	P03956	MMP1_HUMAN	Matrix metalloproteinase-1 (*MMP1*)	[291]
112	P14780	MMP9_HUMAN	Matrix metalloproteinase-9 (*MMP9*)	[285, 291]
113	P15941	MUC1_HUMAN	Mucin-1, Cancer antigen 15-3 (CA 15-3) (*MUC1*) CA27-29 glycoform of MUC1 MCA, Mucin-Like Carcinoma Antigen	[152, 292]
114	Q8WXI7	MUC16_HUMAN	Mucin-16, Ovarian carcinoma antigen CA125 (*MUC16*)	[79, 92, 149, 150, 178, 293, 294]
115	P10451	OSTP_HUMAN	Osteopontin (*SPP1*)	[178, 295–297]
116	P05121	PAI1_HUMAN	Plasminogen activator inhibitor-1 (*SERPINE1*)	[78, 298, 299]
117	P36955	PEDF_HUMAN	Pigment epithelium-derived factor (*SERPINF1*)	[119, 300]
118	Q96PD5	PGRP2_HUMAN	N-acetylmuramoyl-L-alanine amidase (*PGLYRP2*)	[18, 38, 77, 223, 301]

Table 2. Plasma proteins with altered content charactetized by association with oncological diseases considered in Supplementary Materials Table S1 (continued)

#	UniProt	ID (Uniprot)	Name (*gene*)	Oncology (reference)
119	P21810	PGS1_HUMAN	Biglycan (*BGN*)	[289, 302]
120	P80108	PHLD_HUMAN	Phosphatidylinositol-glycan-specific phospholipase D (*GPLD1*)	[303, 304]
121	P00747	PLMN_HUMAN	Plasminogen (*PLG*) Plasmin heavy chain A Angiostatin Plasmin heavy chain A, short form Plasmin light chain	[77, 305, 306]
122	P27169	PON1_HUMAN	Serum paraoxonase/arylesterase 1 (*PON1*)	[54, 104, 151, 307–311]
123	Q15166	PON3_HUMAN	Serum paraoxonase/lactonase (*PON3*)	[54]
124	P13686	PPA5_HUMAN	Tartrate-resistant acid phosphatase type 5 (*ACP5*)	[312]
124	P27918	PROP_HUMAN	Properdin (*CFP*)	[18, 313]
125	P07225	PROS_HUMAN	Vitamin K-dependent protein S (*PROS1*)	[77, 314]
126	P02753	RET4_HUMAN	Plasma retinol-binding protein 4 (*PRBP*)	[38, 54, 80, 102, 315–317]
127	P0DJI8	SAA1_HUMAN	Serum amyloid A-1 (*SAA1*)	[18, 43, 77, 105, 167, 202, 318–324]
128	P35542	SAA4_HUMAN	Serum amyloid A-4 (*SAA4*)	[74]
129	P02743	SAMP_HUMAN	Serum amyloid P-component (*APCS*)	[78–80, 298, 325]
130	P04278	SHBG_HUMAN	Sex hormone-binding globulin (*SHBG*)	[18, 229, 326, 327]
131	P26447	S10A4_HUMAN	Protein S100 A4 (*S100A4*)	[33]
132	P05109	S10A8_HUMAN	Protein S100-A8 (*S100A8*)	[42, 328–332]
133	P06702	S10A9_HUMAN	Protein S100-A9 (*S100A9*)	[18, 328, 331–333]
134	P04271	S100B_HUMAN	Protein S100-B (*S100B*)	[332, 334, 335]
135	P08294	SODE_HUMAN	Extracellular superoxide dismutase [Cu-Zn] (*SOD3*)	[77, 78, 336]
137	P29508	SPB3_HUMAN	Squamous cell carcinoma antigen 1 (*SCCA-1*), Serpin B3 (*SERPINB3*)	[337, 338]
138	Q9BXU1	STK31_HUMAN	Serine/threonine-protein kinase 31 (*STK31*)	[209]
139	P05452	TETN_HUMAN	Tetranectin (*CLEC3B*)	[339, 340]
140	P01135	TGFA_HUMAN	Protransforming growth factor alpha (*TGFA*)	[341, 342]
141	P05543	THBG_HUMAN	Thyroxine-binding globulin (*SERPINA7*)	[18, 343, 344]
142	P00734	THRB_HUMAN	Prothrombin, PIVKA II, des-gamma carboxyprothrombin (*F2*)	[41, 78, 345–347]
143	P02787	TRFE_HUMAN	Serotransferrin (*TF*)	[38, 41, 348]
144	P02766	TTHY_HUMAN	Transthyretin (*TTR*)	[52, 80, 102, 121, 229, 349–353]
145	P01266	THYG_HUMAN	Thyroglobulin (*TG*)	[176]
146	Q03405	UPAR_HUMAN	Urokinase Plasminogen Activator Receptor, uPAR, CD87 (*PLAUR*)	[212]
147	Q14508	WFDC2_HUMAN	HE4, WAP four-disulfide core domain protein 2 (Epididymal secretory protein E4) (*WFDC2*)	[293, 354, 355]
148	P02774	VTDB_HUMAN	Vitamin D-binding protein (*GC*)	[38, 50, 53, 102, 356, 357]
149	P04004	VTNC_HUMAN	Vitronectin (*VTN*)	[32, 38, 41, 67, 78, 82, 358]
150	P15692	VEGFA_HUMAN	Vascular endothelial growth factor A, long form (*VEGFA*)	[293]
151	P25311	ZA2G_HUMAN	Zinc-alpha2-glycoprotein (*AZGP1*)	[38, 41, 359–362]
152	N/A	N/A	Carbohydrate antigen 72-4, CA 72-4	[363, 364]
153	N/A	N/A	Cancer-associated antigen CA-549	[365, 366]
154	N/A	N/A	Cancer antigen 19-9, CA19-9	[63, 151, 178, 367]

Normal protein concentrations are available in the PeptideAtlas database [39]. In the column "Oncology" references, in which changes in the protein levels associated with certain diseases, are given.

obtained for some proteins, they were marked in green. For example, some authors reported about increased levels of adiponectin in gastric cancer (GC) [18], while others found a decrease in the adiponectin level [26]. A similar situation is observed for alpha-1-antitrypsin (AAT) (*SERPINA1*) in non-small cell lung cancer (NSCLC) [27, 28], for alpha-2-HS-glycoprotein (*AHSG*) in colorectal cancer (CRC) [29, 30], for apolipoprotein A-I (*APOA1*) in NSCLC [31, 32], for apolipoprotein C-I (*APOC1*) in NSCLC [32, 33], breast cancer (BrC) [34, 35], and gastric cancer (GC) [18, 36], for apolipoprotein A-IV (*APOA4*) in hepatocarcinoma (HC) [37, 38], etc. However, from all the collected data (Supplementary Materials, Table S1) it follows that for many proteins there is a reproducible increase or decrease in their levels depending on the presence of a specific oncological disease. Interestingly, the only exception is serum albumin; its level never increases in a tumor, but only decreases in most cases.

It should be noted that the changes in the levels of individual proteins depending on the presence of a particular oncological disease in the patient can be quite specific, as follows from the presented heat map (Supplementary Materials, Table S1). Accordingly, based on this heat map, it is possible to consider in detail the possibilities of development of biomarker protein signatures for each tumor. Below we consider data on various oncological diseases depending on tumor localization in a particular organ. However, the complexity here is added by the fact that almost all organs consist of different types of cells (more than 230 cell types are known in humans), and, therefore, the tumors formed in them can have different natures. In total, more than 100 types of tumors are known, but we tried to provide data on the most common ones.

1. LUNG CANCER (LC)

LC ranks first in the world in terms of the number of all cases and mortality among cancer diseases. The main oncological diseases implied by the name lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Moreover, the term NSCLC combines adenocarcinoma, which is recognized in half of all cases, large cell and squamous cell carcinoma, and undifferentiated cancer. SCLC accounts for approximately one fifth of all clinical cases and is characterized by an extremely rapid and aggressive course. During the early stages, SCLC has no characteristic symptoms and is very poorly diagnosed. SCLC differs from NSCLC in that it has neuroendocrine features and is characterized by an increased level of neuron-specific enolase (NSE), which is highly sensitive (up to 87%) and specific for SCLC. Therefore, it is used to differentiate LC, as well as to assess the course of treatment [368]. Currently, in addition to NSE, cancer embryonic antigen (CEA), squamous cell carcinoma antigen (SCCA), cytokeratin 19 (CYFRA 21-1), and CA-125 are also used as markers for diagnosing LC [149, 277, 338]. Elevated levels of NSE and CEA may indicate the presence of SCLC. Based on the levels of SCCA, CYFRA 21-1, and CEA, conclusions are made about squamous cell lung cancer [338]. CYFRA 21-1 and CA-125 are elevated in adenocarcinoma. Elevated levels of CYFRA 21-1, SCCA or CEA may indicate the large cell form of lung cancer [277, 338].

The level of CA 72-4 is used as an additional LC marker, as it is nonspecific and its level is elevated in many cancer patients, especially in gastric cancer and ovarian cancer. Based on the literature data shown in Table 1, we can propose the following proteins for the NSCLC marker signature: CEA, SCC, CYFRA 21-1, CA-125, CA 72-4, alpha-1-acid glycoprotein (*ORM1*), beta-2-glycoprotein 1 (*APOH*), cathepsin F (*CTSF*), complement C1r/C1s, leucine-rich alpha-2-glycoprotein (*LRG1*), protein S100-A4 (*S100A4*), serum amyloid A-1 (*SAA1*). (They all have increased levels.) For SCLC, NSE and alpha-microglobulin/bicunin (*AMBP*) should be added [27, 31, 32, 66, 150].

2. COLORECTAL CANCER (CRC)

CRC is the third most common cancer in the world. The most sensitive marker for it is CEA, in combination with CA19-9 [151, 209]. In addition to them, the following proteins listed in Table 1 could be added to the biomarker protein signature: alpha-1-acid glycoprotein 2 (orosomucoid 2, *ORM2*), alpha-1-antitrypsin (*SERPINA1*), apolipoprotein A-I (*APOA1*), apolipoprotein C-II (*APOCII*), extracellular matrix protein (*ECM1*), leucine-rich alpha-2-glycoprotein (*LRG1*), mannose-binding lectin 2 (*MBL2*), S100 protein (*S100A8* and *S100A*), serum amyloid A-1 (*SAA1*) as markers with an increased level in CRC. A number of proteins whose content is decreased could be also used. These include, in addition to the well-known albumin, adiponectin (*ADIPOQ*), apolipoprotein E (*APOE*), fibronectin (*FN1*), inter-alpha-trypsin inhibitor (*ITIH4*), paraoxonase/arylesterase (*PON1*), and some other proteins (Table 1) [26, 50, 51, 57, 77, 331].

3. BREAST CANCER (BrC)

Breast cancer is the most common oncological disease in women. CEA, CA15.3, and CA27-29 are commonly used in the diagnostics and treatment of BrC [152]. In the USA, a combination of CA 15-3, CA 27.29, and MCA (MUC) is recommended for the BC diagnosis [292]. Based on the data presented in Table 1, clusterin (*CLU*), apolipoprotein A-II (*APOA2*), heparin cofactor 2 (*SERPIND1*), serum amyloid A-1 (*SAA1*), and complement C5a (*C5*) can be added to the BrC marker signature. Their levels are significantly elevated in BrC (Supplementary Materials, Table S1) [54, 170, 195, 322].

4. PROSTATE CANCER (PrC)

In men, PrC is only slightly inferior to LC in terms of the number of cases worldwide. Prostate-specific antigen (PSA) is the most important marker in the diagnostics and monitoring of PrC patients at various stages of the disease [282]. PSA is a serine protease (a glycoprotein belonging to the kallikrein family), which is an important component of the prostate gland secretion, reducing the viscosity of sperm. PSA is found in large quantities in seminal fluid (up to 3 mg/ml) and is therefore tested in forensic biological examination to determine traces of sperm. Normally, the blood PSA level of men is below 4 ng/ml. However, its elevated level does not necessarily indicate PrC, but may be associated with other various problems of the prostate gland. Therefore, in addition to PSA, candidates for inclusion in the signature of PrC markers are callistatin (*SERPINA4*), adiponectin (*ADIPOQ*) (lowered level), serum amyloid A-1 (*SAA1*) (increased level) (Supplementary Materials, Table S1) [89, 321].

5. PANCREATIC CANCER (PCa)

PCa is characterized by the complexity of diagnostics, which leads to its late detection and high mortality due to the aggressiveness of the disease. CA19-9 is most often used to monitor this disease. Its level is elevated in PC and depends on the stage of the disease. However, the level of CA19-9 can also be elevated in other cases, for example, in CRC [151]. Another marker is CEA; although it distinguishes benign pancreatic tumors from malignant ones, the CEA test is also not very specific. Therefore, the combination of CEA with CA19-9 has diagnostic value, as in the case of CRC [368]. A combination of thrombospondin-2 with CA19-9 is also promising [367]. In addition, the effectiveness of a set of osteopontin (*SPP1*), CA19-9, and chitinase-3-like protein 1 (*CHI3L1*), as well as CA125 with CEA has also been shown [178]. The marker signature may also include apolipoprotein A-I (*APOA1*), complement C3 (*C3*), complement C4-A (*C4A*), gelsolin (*GSN*), inter-alpha-trypsin inhibitor (*ITIH4*), lumican (*LUM*), serum amyloid A-1 (*SAA1*), and serum amyloid component P (*APCS*); their levels are elevated in PCa (Supplementary Materials, Table S1) [80, 128, 288, 323].

6. GASTRIC CANCER (GCa)

GC ranks fifth in the world in terms of both incidence and mortality. In clinical practice, CA72.4, CA19.9, CYFRA 21-1, and CEA are used as tumor markers for GCa [153, 275, 364]. However, none of them has absolute specificity or sensitivity for GCa, although initial diagnostis based on these markers is possible. Adding markers to the signature, for example, such proteins as fibronectin (*FN1*), S100-A9 protein (*S100A9*), serum amyloid A-1 (*SAA1*), sex hormone binding globulin (*SHBG*), and complement C9 (*C9*) (their levels of which are elevated in GCa), can help improve diagnostics [18, 36, 231, 332].

7. ESOPHAGEAL CANCER

7.1. Esophageal Squamous Cell Carcinoma (ESC)

ESC accounts for approximately 90% of esophageal cancer cases worldwide [369]. It is one of the most aggressive oncopathologies, and men are affected 2–3 times more often than women. SCCA is currently used as a ESC marker [268]. However, it is not suitable for detecting ESC in the early, asymptomatic stages. Candidates for addition to the marker signature include alpha-1-antichymotrypsin (*SERPINAIII*), alpha-2-HS-glycoprotein (*AHSG*), leucine-rich alpha-2-glycoprotein (*LRG1*), serum amyloid A-1 (*SAA1*), zinc-alpha2-glycoprotein (*AZGP1*), osteopontin (*SPP1*); their levels are significantly increased in ESC, while the levels of fibrinogen gamma chain (*FGG*), alpha-1-antitrypsin (*SERPINA1*), superoxide dismutase (*SOD3*) decrease in this disease (Supplementary Materials, Table S1) [59, 62, 268, 295, 320, 336].

7.2. Esophageal Adenocarcinoma (EA)

EA is one of the most aggressive types of cancer (mortality is about 80%). In the USA, EA is even more common than ESC, and mainly affects white men. Survival is possible only with radical treatment at the initial stage of the disease [370]. However, the problem is that in the early stages, EA does not cause symptoms, which appear only when the disease is actively progressing. SCCA, CA19-9, pyruvate kinase M2 (*PKM*), CYFRA 21-1 are used in the diagnostics of EA [268, 276]. In addition, alpha-1-antitrypsin (*SERPINA1*), demonstrating increased levels in EA (in ESC it is decreased), and decreased levels of superoxide dismutase [Cu-Zn] (*SOD3*) (Supplementary Materials, Table S1) [62] could be added to the marker protein signature.

8. GLIOBLASTOMA (GB)

Primary glioblastoma multiforme (GB) is a fast-growing and very aggressive tumor. The term “multiforme” was introduced in 1926 due to its cytological diversity [371]. The same term is also used to describe the high degree of molecular heterogeneity of GB [372]. Standard therapy for GB, surgery followed by radio- and chemotherapy, does not completely remove tumor cells and provides only a limited therapeutic effect with a median survival of less than 2 years [373]. The problem is that in GB, the tumor consists of at least two cell populations: tumor cells and tumor stem cells (TSCs). Moreover, the division of TSCs restores the tumor and leads to relapses, as TSCs are resistant to radiation and chemotherapy [374]. An exact definition of TSCs has not yet been developed, and standard molecular markers are absent. In practical use, there are no biomarkers yet for early GB diagnostics and monitoring of the patient's response to treatment, and GB is usually diagnosed at a late stage. Potential participants in the tumor marker signature could be apolipoprotein D (*APOD*), apolipoprotein F (*APOF*), apolipoprotein M (*APOM*), complement C4-A (*C4A*), complement C7 (*C7*), complement C9 (*C9*), complement C1q subcomponent subunit C (*C1QC*), as well as carbonic anhydrase (*CA1*), C-reactive protein (*CRP*), haptoglobin (zonulin) (*HP*), ferritin light chain (*FTL*), mannose-binding lectin 2 (*MBL2*), and fetuin B (*FETUB*), the levels of which are elevated in HD, as well as apolipoprotein A-IV (*APOA4*), apolipoprotein B-100 (*APOB*), apolipoprotein C-II (*APOCII*), apolipoprotein E (*APOE*), complement C3 (*C3*), complement C5 (*C5*), superoxide dismutase (*SOD3*), gelsolin (*GSN*), and inter-alpha-trypsin inhibitor (*ITIH1*, *ITIH2*, *ITIH4*); their levels are reduced in GB (Table 1) [78, 86, 158, 258].

9. LIVER CANCER

The most common form of primary liver cancer in adults (90%) is hepatocarcinoma (HC) or hepatocellular carcinoma, followed by cholangiocarcinoma (CCA) (~10%) and sarcoma (~1%). Hepatoblastoma (HB) can develop in children [375].

9.1. Hepatocarcinoma (HC)

HC is associated with elevated AFP values in 80–90% of cases [218, 219]. In Russia, AFP is used in combination with the inflammation marker CRP to monitor HC treatment [201]. In foreign clinics, in addition to AFP, more specific markers are also used for diagnostics of HC and its monitoring; these include the glycosylated form of AFP (AFP-L3) and des-gamma-carboxyprothrombin (DGP) [347]. Using such combination of biomarkers it is possible to achieve sensitivity of 94% and specificity of more than 97% [219, 220, 347]. It should be noted that many other additional candidates for inclusion in the serological signature of HC tumor markers exist. This is apparently due to the fact that the liver is the main producer of plasma proteins, which are included in the list of tumor markers (Table 2). Naturally, neoplastic changes in the liver will be influence levels of these putative markers. For example, in addition to the markers already used, it is reasonable to include in the biomarker signature afamin (AFM) (its level is elevated in HC, and lowered in other oncologies) [38]. The levels of apolipoprotein A-I (*APOA1*), apolipoprotein A-II (*APOA2*), complement C2 (*C2*), complement C7 (*C7*), complement C9 (*C9*), serum amyloid A-1 (*SAA1*), cytokeratins (1,6,9,10), interleukin (*IL6*) are increased, while the level of serotransferrin (*TF*), fibronectin (*FN1*) and plasma protease inhibitor C1 (*SERPING1*) decreased (Supplementary Materials, Table S1) [38, 201, 266, 267, 347].

9.2. Cholangiocarcinoma (CCA)

In contrast to HC, CCA is rarely accompanied by an increase in the AFP levels, but is almost always positive for CA19-9 [63, 367]. In the mixed type (CCA-HC), the levels of both markers, AFP and CA19-9, are elevated. In addition, in CCA, tests for CYFRA 21-1 and CA19-9 are used [376]. According to Table 1, the biomarker signature can also include alpha-1-antichymotrypsin (*AACT*), alpha-1-antitrypsin (*SERPINA1*), leucine-rich alpha-2-glycoprotein (*LRG1*), haptoglobin (*HB*) (their levels are increased in CCA), as well as plasma protease inhibitor C1 (*SERPING1*) and transthyretin (*TTR*) (their levels are decreased in CCA) [63, 93, 352]. In sarcomas, these markers do not work.

9.3. Hepatoblastoma (HB)

HB is a malignant low-differentiated liver tumor of embryonic origin, developing from hepatocyte precursors, hepatoblasts. HB is the most common primary malignant liver tumor in children aged 0–4 years [377]. HB is associated with significantly elevated AFP levels in 80–90% of cases, in addition, the β-subunit of human chorionic gonadotropin (β-hCG) is detected in approximately 20% of patients (Supplementary Materials, Table S1) [181].

10. KIDNEY CANCER (KC)

In the early stages, KC is often asymptomatic and is diagnosed by chance during an ultrasound examination for another disease. Men are affected by KC approximately twice as often as women. In the early stages, KC can be successfully treated. The main treatment method is kidney removal (nephrectomy). The list of clinical markers of KC includes C-reactive protein (*CRP*), pyruvate kinase M2 (*PKM*), neuron-specific enolase (*ENOG*), and ferritin (*FTL*) are used as markers for RP diagnostics [202, 207, 239, 285]. In addition to these proteins, the tumor marker signature could contain several complements (C1q, C4d, D, 1), fibronectin (*FN1*), SAA, characterized by increased levels in this disease, as well as matrix metalloproteinase-9 (*MMP9*) and complement factor B (*CFB*); their levels are decreased (Supplementary Materials, Table S1) [140, 145, 202, 207, 285].

11. BLADDER CANCER (BC)

In the early stages, this oncology does not manifest itself. Only as the tumor grows, the first sign is the presence of blood in the urine. In this case, a urine test is even more effective than a blood test. The most widely used tumor marker for BC is the UBC (Urine Blood Cancer) test, including the measurement of cytokeratins 8 and 18 levels, as well as CYFRA 21.1 (cytokeratin 19) [278, 378]. Determination of these tumor markers in urine is the best non-invasive method for BC diagnostics and can be used in addition to cystoscopy. Tumor marker levels at the beginning of treatment also have prognostic value, since the choice of treatment depends on their levels. In addition, there are several other candidates for inclusion in the BC tumor marker signature. For example, the levels of lumican (*LUM*) and haptoglobin (*HPT*) are increased in BC, and the level of serum amyloid component P (*APCS*) decreased (Supplementary Materials, Table S1) [144, 289, 298].

12. GYNECOLOGICAL CANCER

12.1. Cervical Cancer (CC)

Cervical cancer (CC) is one of the most common oncological diseases. Moreover, it is the only malignant tumor with known causes this disease (infection with human papillomaviruses). There are two main types of CC — squamous cell carcinoma (80%) and adenocarcinoma (20%). At an early stage, the disease does not manifest itself, and it can only be detected using laboratory diagnostics. First of all, this is an analysis for the human papillomavirus (HPV). SCCA is used as a protein marker. However, SCCA is not a marker specific for CC. Specificity and sensitivity would be increased by adding to the biomarker signature (in addition to SCCA) such proteins as alpha-1-acid glycoprotein (*ORM1*), alpha-1B glycoprotein (*A1BG*), antithrombin III (*SERPINC1*), apolipoprotein C-I (*APOC1*), complement C3 (*C3*), gelsolin 1 (*GSN*), zinc-alpha2-glycoprotein (*AZGP1*); their levels are increased in CC, while the levels of leucine-rich alpha-2-glycoprotein (*LRG1*), alpha-1-antitrypsin (*SERPINA1*) decrease in this disease (Table 1) [65, 68, 124, 297].

12.2. Endometrial Cancer (EC)

There are no tumor markers with sufficient sensitivity and specificity suitable for screening early endometrial cancer, and tumor markers make insignificant contribution to the diagnostics of this disease. For monitoring of EC patients, the best marker is CA125 (mucin-16); its elevated levels were observed in approximately 60% of patients [294]. In addition, there is an example of constructing an EC proteomic signature based on analysis of elevated serum levels of clusterin (*CLU*), ITIH4 (*ITIH4*), antithrombin-III (*SERPINC1*), and complement subcomponent C1r (*C1R*) in patients detected by means of 2DE; the authors even constructed a mathematical model for detecting EC [274].

Taking into consideration the data presented in Table 1, the EC signature may also include leucine-rich alpha-2-glycoprotein (*LRG1*) and S100-A8 (*S100A8*), characterized by increased levels in EC, as well as zinc-alpha2-glycoprotein (*AZGP1*), kininogen 1 (*KING1*), inter-alpha-trypsin inhibitor (*ITIH2*), complement component C9 (*C9*), apolipoprotein A-IV (*APOA4*), apolipoprotein A-I (*APOA1*), alpha-1-antitrypsin (AAT) (*SERPINA1*), and albumin (*ALBU*) (their levels of are reduced in EC) (Supplementary Materials, Table S1) [65, 274].

12.3. Ovarian Cancer (OC)

This tumor can be either primary or secondary. The primary tumor is carcinoma (~70% of all OCs). With early diagnosis of OC, the five-year survival rate is more than 90%. In most cases, radical surgical intervention is sufficient. However, due to the lack of specific symptoms and tests for early detection, no more than 20 percent of all cases are detected at the early stage. Treatment at later stages gives much worse survival of OC patients [368].

Determination of tumor markers is one of the effective methods for OC diagnostics. In this context, such non-specific tumor markers as CA125 (mucin-16) and CA 72-4 (TAG-72) are used and their combination increases specificity and sensitivity [379]. In addition, several FDA-approved broader kits are already used abroad. For example, OVA1 is a blood test that measures the levels of five proteins (CA125, transferrin, transthyretin, apolipoprotein A-I, and beta-2-microglobulin). A complex mathematical formula (multivariate index analysis) is used to evaluate and combine the plasma levels of these proteins to provide an OC risk score. Using this approach, OVA1 can detect OC at an early stage with a specificity of 98% [380, 381]. Another kit, OVA2, is used to estimate the risk of malignancy in women; it employs assay of the following five proteins: apolipoprotein A-I (*APOA1*), HE4 (*HE4*), CA-125, follicle-stimulating hormone (*FSH*), and transferrin (*TF*) [302]. In addition, there is also a test ROMA (The Risk of Ovarian Malignancy Algorithm), which includes CA125 and HE4 assays [355]. But this test also takes into account information about the menopausal status of the examined women [354].

13. THYROID CANCER (TC)

TC accounts for about 1.5%. all oncopathologies Among patients, women over 40 years of age predominate; in this age category TC occurs almost 5 times more often than in men. TC is classified according to pathohistological characteristics and the following variants are distinguished: papillary thyroid cancer (up to 75%), follicular thyroid cancer (up to 15%), medullary thyroid cancer (up to 8%), anaplastic thyroid cancer (less than 5%), and others: thyroid lymphoma, squamous cell thyroid carcinoma, various types of thyroid sarcomas. The tumor has a significant impact on the hormonal balance, therefore, in the case of TC, hormones such as thyroid stimulating hormone (*TSH*) or calcitonin (*CT*) are tested first [176, 382]. Among the protein markers, thyroglobulin (*THYG*), which is a precursor of the thyroid hormones thyroxine and triiodothyronine, as well as CEA are used in the clinical practice [176, 383]. The TC tumor marker signature can include CD166, complement factor H-related protein (*CFHR1*), gamma-glutamyl hydrolase (*GGH*), characterized by elevated levels in TC, as well as serum amyloid protein A4 (*SAA4*), apolipoprotein A-IV (*APOA4*), apolipoprotein A-I (*APOA1*), characterized by reduced levels in TC, and also some other proteins (Supplementary Materials, Table S1) [53, 82].

14. SKIN CANCER

Skin cancer is one of the most common oncological diseases, apparently due to the fact that the skin is the largest human organ. The main types of skin cancer are: squamous cell cancer (aggressive, forms in the epithelial layer); basal cell cancer (basalioma), which is characterized by a slow progression, can grow into the deep layers of the skin, reaching bone tissue, looks like a thickening or ulcer, can bleed and peel; metatypical cancer (spinocellular carcinoma), which is similar to basalioma, complicating the diagnostics, especially at the initial stage; melanoma occurs in pigment cells melanocytes, it looks like a birthmark at the first stage, but as the disease progresses, the color becomes uneven, and the edges of the tumor become heterogeneous and unclear.

Blood tests usually include analysis of S-100B, which is the most well-known biomarker of melanoma and its level correlates with the stage of the disease [335, 384]. Transthyretin (*TTR*), angiotensinogen (*AGT*), matrix metalloproteinase 9 (*MMP9*) (elevated level), as well as vitamin D-binding protein (*GC*), osteopontin (*SPP1*) (decreased level) (Supplementary Materials, Table S1) can also be candidates for inclusion in the skin cancer tumor marker panel [102, 291, 296].

15. HEMATOLOGIC CANCER

Hematological cancer or hemoblastoses are oncological diseases that affect the cells of the blood, lymph, and bone marrow. They are divided into leukemias, which do not have a specific localization, and lymphosarcomas. Leukemias can be acute, in which immature hematopoietic cells (blasts) are affected, and chronic, when mature cells are involved. This leads to the appearance of a large number of immature leukocytes, thus explaining why the disease is called "leukemia". Clinical blood analysis and molecular genetic methods play a leading role, and there is no particular need for additional protein markers. Acute leukemia (AL) is divided into myeloblastic (affected precursors of platelets, erythrocytes or leukocytes) and lymphoblastic, in which T- and B-form lymphocyte precursors are affected. Chronic leukemia (CL) can be lymphocytic (affects B-lymphocytes) and myelocytic (affects leukocytes of the granulocytic lineage).

Lymphomas, on the contrary, arise in extraosseous cells. Most often, these are lymph nodes. There are two types of lymphomas: Hodgkin's lymphoma (HL), which usually does not proceed aggressively, and lymphosarcoma (non-Hodgkin's lymphoma, NHL), a group of tumors with varying degrees of aggressiveness.

There are also paraproteinemic hemoblastoses (PH), when all tumor cells produce some one, often functionally defective immunoglobulin, a paraprotein, which may even be normal, but is still harmful due to its quantity, because the synthesis of other immunoglobulins is reduced and this causes immunological failure of the body. The PG group includes multiple myeloma (MM), Waldenstrom's macroglobulinemia, and heavy chain disease. The most common in this group is MM, where M-protein (monoclonal immunoglobulin, most often IgG or IgA) is usually diagnosed [385]. In addition, fibronectin (*FN1*), urokinase receptor (uPAR, CD87) (*PLAUR*), and fibulin-1 (*FBLN1*) (Supplementary Materials, Table S1) can be included in the tumor marker signature of this disease [212, 236].

It should be noted that in the case of severe forms of hematological oncology, it is difficult to distinguish between them. In this case, accurate diagnostics requires bone marrow and cerebrospinal fluid analyses. In addition to the general blood test, beta-2-microglobulin (*B2M*) can be used in hemoblastoses; this is an oncomarker of process activity in some types of immunopathology and lymphoid tumors [138]. In addition, as follows from Table 1, in malignant lymphoma, the levels of haptoglobin-related protein (HRP) and transforming growth factor alpha (TGFα) are greatly increased [260, 342].

16. HEAD AND NECK CANCER (HNC)

HNC is not the most common oncological pathology, but it has a high mortality rate, and even with successful treatment it greatly affects the quality of life of patients. As in the case of other oncological diseases, late diagnosis is one of the main reasons for unfavorable outcomes. The group "HNC" includes several types of diseases that can develop in the head and neck area [386]. These are cancer of the oral cavity, tongue, gums and lips, vocal apparatus, throat, salivary glands, nose and paranasal sinuses. Men suffer from this pathology twice as often as women. Most often, squamous cell carcinoma develops, adenocarcinoma is less often [387].

16.1. Cancer of the Nasal Cavity and Paranasal Sinuses

These tumors develop from the epithelium lining the nasal cavity and the surrounding paranasal sinuses. As a rule, this is squamous cell carcinoma, but adenocarcinoma may also be present. Currently, there are no recommendations for the use of protein tumor markers for this disease.

16.2. Nasopharyngeal Cancer (NPC)

In the clinical practice, the main approach to screening for the potential occurrence of NPC is the PCR test for Epstein-Barr virus DNA [368]. Additionally, cathepsin-B (*CTSB*) and cathepsin-D (*CTSD*) tests can detect the presence of a tumor at an early stage of the disease [147]. The tumor marker signature can also include CEA, NSE, apolipoprotein E (*APOE*), and ferritin (*FTL*) (Supplementary Materials, Table S1) [129, 238].

16.3. Oral Cavity and Oropharyngeal Cancers (OCOPC)

The oral cavity includes the mouth and tongue. The oropharynx includes the middle of the throat, from the tonsils to the tip of the voice box. Throat cancer develops in the throat and adjacent structures (tonsils, vocal cords, epiglottis). It is usually squamous cell carcinoma, and SCCA and CYFRA 21-1 levels are examined; however, they do not have sufficient specificity for OCOPC [240, 388]. Greater specificity can be achieved by analyzing the same markers not in plasma/serum, but in saliva [389]. In addition, beta-2-microglobulin (*B2M*) can be included in the tumor marker signature (Supplementary Materials, Table S1) [139].

16.4. Laryngeal Cancer and Hypopharyngeal Cancer

The larynx is a part of the vocal apparatus. This tubular organ in the neck is used for breathing, speaking, and swallowing. It is located in the upper part of the windpipe, or trachea. The hypopharynx (esophagus) is the lower part of the throat surrounded by the larynx. In 90% of cases, laryngeal cancer is squamous cell carcinoma (markers SCCA and CYFRA 21-1). It is possible to add the protein S100-A8 (*S100A8*) to the signature [390].

16.5. Salivary Gland Cancer

Adenocarcinoma can develop from the cells of the salivary glands. Here, as in the case of OCOPC, much greater specificity and sensitivity can be achieved by analyzing saliva rather than plasma/serum [391].

17. BONE CANCER

Bone cancer is a malignant tumor of bone and cartilage tissue, which most often affects the tubular bones of the arms and legs. Bone cancer is formed from connective tissue cells, and the main part is of secondary origin, caused by metastases. Based on histological analysis, the following types of bone cancer are determined: osteogenic sarcoma (osteosarcoma), chondrosarcoma (arises in cartilage tissue), Ewing's sarcoma, and metastatic bone cancer (has characteristics of the original pathology). Non-metastatic bone cancer occurs mainly in adolescence, and more often in men than in women.

Tartrate-resistant acid phosphatase (TRACP 5b) is used as a marker for diagnosing metastases of BC and PrC; it is also used in other diseases, and not only oncological, where osteoclasts actively produce TRACP 5b, for example, Paget's disease, osteoporosis, and other bone tissue lesions [312]. A test for lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) is also applicable because levels of these proteins can be significantly increased in bone cancer. CA125 and CA19-9 are used as additional markers.

CONCLUSIONS

The use of panels of serological markers for diagnostics of oncological diseases is very attractive from all viewpoints: it is associated with minimal risk of intervention, simple performance and takes little time. It is important that many examples of such diagnostics already exist. For example, association between inflammation and clinical manifestations is described using the modified Glasgow Prognostic Score (mGPS), which includes CRP and albumin levels [392]. The combination of an elevated CRP level (>10 mg/l) and a decrease in albumin (<35 g/l) corresponds to a higher mGPS level, which correlates with systemic inflammation and poor cancer treatment outcomes [393, 394]. Other major plasma proteins are also used in the above-mentioned OC tests. The OVA1 test includes CA125, transferrin, transthyretin, apolipoprotein A-I, and beta-2-microglobulin. The ROMA test includes CA125 and HE4 [354]. The OVERA (OVA2) test includes apolipoprotein A-I, HE4, CA125, follicle-stimulating hormone (*FSH*), and transferrin [395]. Analysis of clusterin (*CLU*), ITIH4 (*ITIH4*), antithrombin-III (SERPINC1), and C1r (*C1R*) complement subcomponent is used to detect OC [274].

Selecting appropriate panels (proteomic signatures) of plasma tumor markers, it is possible to develop tests for the detection and monitoring of various types of cancer. The main thing in this case is to select a suitable set of proteins/tumor markers (Table 1) and develop an algorithm that will take into account the time course of all possible changes in these proteins (level, PTM, etc.) associated with the occurrence and course of a particular cancer disease.

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COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any research involving humans or the use of animals as objects.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Supplementary materials are available in the electronic version at the journal site (pbmc.ibmc.msk.ru).

REFERENCES

1. *Bhatt A.N., Mathur R., Farooque A., Verma A., Dwarakanath B.S.* (2010) Cancer biomarkers — current perspectives. Indian J. Med. Res., **132**(2), 129–149.
2. *Polanski M., Anderson N.L.* (2006) A list of candidate cancer biomarkers for targeted proteomics. Biomarker Insights, **1**, 1–48. DOI: 10.1177/117727190600100001
3. *Malati T.* (2007) Tumour markers: An overview. Indian J. Clin. Biochem., **22**(2), 17–31. DOI: 10.1007/BF02913308
4. *Paik Y.-K., Kim H., Lee E.-Y., Kwon M.-S., Cho S.Y.* (2008) Overview and introduction to clinical proteomics. Methods Mol. Biol., **428**, 1–31. DOI: 10.1007/978-1-59745-117-8_1
5. *Nanjappa V., Thomas J.K., Marimuthu A., Muthusamy B., Radhakrishnan A., Sharma R., Ahmad Khan A., Balakrishnan L., Sahasrabuddhe N.A., Kumar S., Jhaveri B.N., Sheth K.V., Kumar Khatana R., Shaw P.G., Srikanth S.M., Mathur P.P., Shankar S., Nagaraja D., Christopher R,. Mathivanan S., Raju R., Sirdeshmukh R., Chatterjee A., Simpson R.J., Harsha H.C., Pandey A., Prasad T.S.* (2014) Plasma Proteome Database as a resource for proteomics research: 2014 update. Nucleic Acids Res., **42**(Database issue), D959-D965. DOI: 10.1093/nar/gkt1251
6. *Luque-Garcia J.L., Neubert T.A.* (2007) Sample preparation for serum/plasma profiling and biomarker identification by mass spectrometry. J. Chromatogr. A, **1153**(1–2), 259–276. DOI: 10.1016/j.chroma.2006.11.054
7. *Paulovich A.G., Whiteaker J.R., Hoofnagle A.N., Wang P.* (2008) The interface between biomarker discovery and clinical validation: the tar pit of the protein biomarker pipeline. Proteomics Clin. Appl., **2**(10–11), 1386–1402. DOI: 10.1002/prca.200780174
8. *Omenn G.S., States D.J., Adamski M., Blackwell T.W., Menon R., Hermjakob H., Apweiler R., Haab B.B., Simpson R.J., Eddes J.S., Kapp E.A., Moritz R.L., Chan D.W., Rai A.J., Admon A., Aebersold R., Eng J., Hancock W.S., Hefta S.A., Meyer H., Paik Y.-K., Yoo J.-S., Ping P., Pounds J., Adkins J., Qian X., Wang R., Wasinger V., Wu C.Y., Zhao X., Zeng R., Archakov A., Tsugita A., Beer I., Pandey A., Pisano M., Andrews P., Tammen H., Speicher D.W., Hanash S.M.* (2005) Overview of the HUPO Plasma Proteome Project: results from the pilot phase with 35 collaborating laboratories and multiple analytical groups, generating a core dataset of 3020 proteins and a publicly-available database. Proteomics, **5**(13), 3226–3245. DOI: 10.1002/pmic.200500358
9. *Surinova S., Schiess R., Hüttenhain R., Cerciello F., Wollscheid B., Aebersold R.* (2011) On the development of plasma protein biomarkers. J. Proteome Res., **10**(1), 5–16. DOI: 10.1021/pr1008515
10. *Parker C.E., Borchers C.H.* (2014) Mass spectrometry based biomarker discovery, verification, and validation — quality assurance and control of protein biomarker assays. Mol. Oncol., **8**(4), 840–858. DOI: 10.1016/j.molonc.2014.03.006
11. *Hochstrasser D.F., Sanchez J.-C., Appel R.D.* (2002) Proteomics and its trends facing nature’s complexity. Proteomics, **2**(2), 807–812. DOI: 10.1002/1615-9861(200207)2:7<807::AID-PROT807>3.0.CO;2-4
12. *Petricoin E.F., Ardekani A.M., Hitt B.A., Levine P.J., Fusaro V.A., Steinberg S.M., Mills G.B., Simone C., Fishman D.A., Kohn E.C., Liotta L.A.* (2002) Use of proteomic patterns in serum to identify ovarian cancer. Lancet, **359**(9306), 572–577. DOI: 10.1016/S0140-6736(02)07746-2
13. *Schiess R., Wollscheid B., Aebersold R.* (2009) Targeted proteomic strategy for clinical biomarker discovery. Mol. Oncol., **3**(1), 33–44. DOI: 10.1016/j.molonc.2008.12.001
14. *Geyer P.E., Kulak N.A., Pichler G., Holdt L.M., Teupser D., Mann M.* (2016) Plasma proteome profiling to assess human health and disease. Cell Systems, **2**(3), 185–195. DOI: 10.1016/j.cels.2016.02.015
15. *Geyer P.E., Holdt L.M., Teupser D., Mann M.* (2017) Revisiting biomarker discovery by plasma proteomics. Mol. Syst. Biol., **13**(9), 942. DOI: 10.15252/msb.20156297
16. *Farrah T., Deutsch E.W., Omenn G.S., Campbell D.S., Sun Z., Bletz J.A., Mallick P., Katz J.E., Malmström J., Ossola R., Watts J.D., Lin B., Zhang H., Moritz R.L., Aebersold R.* (2011) A high-confidence human plasma proteome reference set with estimated concentrations in PeptideAtlas. Mol. Cell. Proteomics, **10**(9), M110.006353. DOI: 10.1074/mcp.M110.006353
17. *Cox J., Hein M.Y., Luber C.A., Paron I., Nagaraj N., Mann M.* (2014) Accurate proteome-wide label-free quantification by delayed normalization and maximal peptide ratio extraction, termed MaxLFQ. Mol. Cell. Proteomics, **13**(9), 2513–2526. DOI: 10.1074/mcp.M113.031591
18. *Abramowicz A., Wojakowska A., Gdowicz-Klosok A., Polanska J., Rodziewicz P., Polanowski P., Namysl-Kaletka A., Pietrowska M., Wydmanski J., Widlak P.* (2015) Identification of serum proteome signatures

of locally advanced and metastatic gastric cancer: a pilot study. J. Transl. Med., **13**, 304. DOI: 10.1186/s12967-015-0668-9

19. *Anderson N.L., Anderson N.G.* (2002) The human plasma proteome: history, character, and diagnostic prospects. Mol. Cell. Proteomics, **1**(11), 845–867. DOI: 10.1074/mcp.R200007-MCP200
20. *Hortin G.L., Sviridov D., Anderson N.L.* (2008) High-abundance polypeptides of the human plasma proteome comprising the top 4 logs of polypeptide abundance. Clin. Chem., **54**(10), 1608–1616. DOI: 10.1373/clinchem.2008.108175
21. *Skates S.J., Gillette M.A., la Baer J., Carr S.A., Anderson L., Liebler D.C., Ransohoff D., Rifai N., Kondratovich M., Težak Ž., Mansfield E., Oberg A.L., Wright I., Barnes G., Gail M., Mesri M., Kinsinger C.R., Rodriguez H., Boja E.S.* (2013) Statistical design for biospecimen cohort size in proteomics-based biomarker discovery and verification studies. J. Proteome Res., **12**(12), 5383–5394. DOI: 10.1021/pr400132j
22. *Candia J., Cheung F., Kotliarov Y., Fantoni G., Sellers B., Griesman T., Huang J., Stuccio S., Zingone A., Ryan B.M., Tsang J.S., Biancotto A.* (2017) Assessment of variability in the SOMAscan assay. Sci. Rep., **7**, 14248. DOI: 10.1038/s41598-017-14755-5
23. *Cui M., Cheng C., Zhang L.* (2022) High-throughput proteomics: a methodological mini-review. Lab. Invest., **102**(11), 1170–1181. DOI: 10.1038/s41374-022-00830-7
24. *Pang W.W., Abdul-Rahman P.S., Wan-Ibrahim W.I., Hashim O.H.* (2010) Can the acute-phase reactant proteins be used as cancer biomarkers? Int. J. Biol. Markers, **25**(1), 1–11. DOI: 10.1177/172460081002500101
25. *Abernethy T.J., Avery O.T.* (1941) The occurrence during acute infections of a protein not normally present in the blood: I. Distribution of the reactive protein in patient's sera and the effect of calcium on the flocculation reaction with C polysaccharide of pneumococcus. J. Exp. Med., **73**(2), 173–182. DOI: 10.1084/jem.73.2.173
26. *Nagaraju G.P., Aliya S., Alese O.B.* (2015) Role of adiponectin in obesity related gastrointestinal carcinogenesis. Cytokine Growth Factor Rev., **26**(1), 83–93. DOI: 10.1016/j.cytogfr.2014.06.007
27. *Boccellino M., Pinto F., Ieluzzi V., Giovane A., Quagliuolo L., Fariello C., Coppola M., Carlucci A., Santini M., Ferati K., Bexheti-Ferati A., Giordano A., di Domenico M.* (2019) Proteomics analysis of human serum of patients with non-small-cell lung cancer reveals proteins as diagnostic biomarker candidates. J. Cell. Physiol., **234**(12), 23798–23806. DOI: 10.1002/jcp.28948
28. *Ercetin E., Richtmann S., Delgado B.M., Gomez-Mariano G, Wrenger S., Korenbaum E., Liu B., de Luca D., Kühnel M.P., Jonigk D., Yuskaeva K., Warth A., Muley T., Winter H., Meister M., Welte T., Janciauskiene S., Schneider M.A.* (2019) Clinical significance of *SERPINA1* gene and its encoded alpha1-antitrypsin protein in NSCLC. Cancers, **11**(9), 1306. DOI: 10.3390/cancers11091306
29. *Fan N., Kang R., Ge X., Li M., Liu Y., Chen H., Gao C.* (2014) Identification alpha-2-HS-glycoprotein precursor and tubulin beta chain as serology diagnosis biomarker of colorectal cancer. Diagn. Pathol., **9**, 53. DOI: 10.1186/1746-1596-9-53
30. *Bertuzzi M., Marelli C., Bagnati R., Colombi A., Fanelli R., Saieva C., Ceroti M., Bendinelli B., Caini S., Airoldi L., Palli D.* (2015) Plasma clusterin as a candidate pre-diagnosis marker of colorectal cancer risk in the Florence cohort of the European Prospective Investigation into Cancer and Nutrition: a pilot study. BMC Cancer, **15**, 56. DOI: 10.1186/s12885-015-1058-7
31. *Pietrowska M., Jelonek K., Michalak M., Roś M., Rodziewicz P., Chmielewska K., Polański K., Polańska J., Gdowicz-Kłosok A., Giglok M., Suwiński R., Tarnawski R., Dziadziuszko R., Rzyman W., Widłak P.* (2014) Identification of serum proteome components associated with progression of non-small cell lung cancer. Acta Biochim. Pol., **61**(2), 325–331.
32. *Zhao P., Wu J., Lu F., Peng X., Liu C., Zhou N., Ying M.* (2019) The imbalance in the complement system and its possible physiological mechanisms in patients with lung cancer. BMC Cancer, **19**, 201. DOI: 10.1186/s12885-019-5422-x
33. *Yang Y., Zhao S., Fan Y., Zhao F., Liu Q., Hu W., Liu D., Fan K., Wang J., Wang J.* (2009) Detection and identification of potential biomarkers of non-small cell lung cancer. Technol. Cancer Res. Treat., **8**(6), 455–466. DOI: 10.1177/153303460900800607
34. *Song D., Yue L., Zhang J., Ma S., Zhao W., Guo F., Fan Y., Yang H., Liu Q., Zhang D., Xia Z., Qin P., Jia J., Yue M., Yu J., Zheng S., Yang F., Wang J.* (2016) Diagnostic and prognostic significance of serum apolipoprotein C-I in triple-negative breast cancer based on mass spectrometry. Cancer Biol. Ther., **17**(6), 635–647. DOI: 10.1080/15384047.2016.1156262
35. *Lee H.-B., Kang U.-B., Moon H.-G., Lee J., Lee K.-M., Yi M., Park Y.S., Lee J.W., Yu J.-H., Choi S.H., Cho S.H., Lee C., Han W., Noh D.-Y.* (2015) Development and validation of a novel plasma protein signature for breast cancer diagnosis by using multiple reaction monitoring-based mass spectrometry. Anticancer Res., **35**(11), 6271–6279.
36. *Chong P.-K., Lee H., Loh M.C.S., Choong L.-Y., Lin Q., So J.B.Y., Lim K.H., Soo R.A., Yong W.P., Chan S.P., Smoot D.T., Ashktorab H., Yeoh K.G., Lim Y.P.* (2010) Upregulation of plasma C9 protein in gastric cancer patients. Proteomics, **10**(18), 3210–3221. DOI: 10.1002/pmic.201000127
37. *Bharali D., Banerjee B.D., Bharadwaj M., Husain S.A., Kar P.* (2018) Expression analysis of apolipoproteins AI & AIV in hepatocellular carcinoma: a protein-based hepatocellular carcinoma-associated study. Indian J. Med. Res., **147**(4), 361–368. DOI: 10.4103/ijmr.IJMR_1358_16
38. *Guo J., Jing R., Zhong J.-H., Dong X., Li Y.-X., Liu Y.-K., Huang T.-R., Zhang C.-Y.* (2017) Identification of CD14 as a potential biomarker of hepatocellular carcinoma using iTRAQ quantitative proteomics. Oncotarget, **8**(37), 62011–62028. DOI: 10.18632/oncotarget.18782
39. *Deutsch E.W., Omenn G.S., Sun Z., Maes M., Pernemalm M., Palaniappan K.K., Letunica N., Vandenbrouck Y., Brun V., Tao S.C., Yu X., Geyer P.E., Ignjatovic V., Moritz R.L., Schwenk J.M.* (2021) Advances and utility of the human plasma proteome. J. Proteome Res., **20**(12), 5241–5263. DOI: 10.1021/acs.jproteome.1c00657
40. *Abramson F.P., Jenkins J., Ostchega Y.* (1982) Effects of cancer and its treatments on plasma concentration of alpha 1-acid glycoprotein and propranolol binding. Clin. Pharmacol. Ther., **32**(5), 659–663. DOI: 10.1038/clpt.1982.218
41. *Ciereszko A., Dietrich M.A., Słowińska M., Nynca J., Ciborowski M., Kisluk J., Michalska-Falkowska A., Reszec J., Sierko E., Nikliński J.*(2019) Identification of protein changes in the blood plasma of lung cancer patients subjected to chemotherapy using a 2D-DIGE approach. PLOS One, **14**(10), e0223840. DOI: 10.1371/journal.pone.0223840

42. *Verathamjamras C., Chantaraamporn J., Sornprachum T., Mutapat P., Chokchaichamnankit D., Mingkwan K., Luevisadpibul V., Srisomsap C., Chutipongtanate S., Svasti J., Champattanachai V.* (2023) Label-free quantitative proteomics reveals aberrant expression levels of LRG, C9, FN, A1AT and AGP1 in the plasma of patients with colorectal cancer. Clin. Proteomics, **20**(1), 15. DOI: 10.1186/s12014-023-09407-y
43. *Janciauskiene S., Wrenger S., Günzel S., Gründing A.R., Golpon H., Welte T.* (2021) Potential roles of acute phase proteins in cancer: why do cancer cells produce or take up exogenous acute phase protein alpha1-antitrypsin? Front. Oncol., **11**, 622076. DOI: 10.3389/fonc.2021.622076
44. *Elpek G.O.* (2021) Orosomucoid in liver diseases. World J. Gastroenterol., **27**(45), 7739–7747. DOI: 10.3748/wjg.v27.i45.7739
45. *Fischer K., Kettunen J., Würtz P., Haller T., Havulinna A.S., Kangas A.J., Soininen P., Esko T., Tammesoo M.-L., Mägi R., Smit S., Palotie A., Ripatti S., Salomaa V., Ala-Korpela M., Perola M., Metspalu A.* (2014) Biomarker profiling by nuclear magnetic resonance spectroscopy for the prediction of all-cause mortality: an observational study of 17,345 persons. PLOS Med., **11**(2), e1001606. DOI: 10.1371/journal.pmed.1001606
46. *Ayyub A., Saleem M., Fatima I., Tariq A., Hashmi N., Musharraf S.G.* (2016) Glycosylated alpha-1-acid glycoprotein 1 as a potential lung cancer serum biomarker. Int. J. Biochem. Cell Biol., **70**, 68–75. DOI: 10.1016/j.biocel.2015.11.006
47. *Jabir R.S., Ho G.F., Annuar M.A.B.A., Stanslas J.* (2018) Plasma alpha-1-acid glycoprotein as a potential predictive biomarker for non-haematological adverse events of docetaxel in breast cancer patients. Biomarkers, **23**(2), 142–146. DOI: 10.1080/1354750X.2017.1334152
48. *Balmaña M., Giménez E., Puerta A., Llop E., Figueras J., Fort E., Sanz-Nebot V., de Bolós C., Rizzi A., Barrabés S., de Frutos M., Peracaula R.* (2016) Increased α1-3 fucosylation of α-1-acid glycoprotein (AGP) in pancreatic cancer. J. Proteomics, **132**, 144–154. DOI: 10.1016/j.jprot.2015.11.006
49. *Tanabe K., Kitagawa K., Kojima N., Iijima S.* (2016) Multifucosylated alpha-1-acid glycoprotein as a novel marker for hepatocellular carcinoma. J. Proteome Res., **15**(9), 2935–2944. DOI: 10.1021/acs.jproteome.5b01145
50. *Chantaraamporn J., Champattanachai V., Khongmanee A., Verathamjamras C., Prasongsook N., Mingkwan K., Luevisadpibul V., Chutipongtanate S., Svasti J.* (2020) Glycoproteomic analysis reveals aberrant expression of complement C9 and fibronectin in the plasma of patients with colorectal cancer. Proteomes, **8**(3), 26. DOI: 10.3390/proteomes8030026
51. *Gao F., Zhang X., Whang S., Zheng C.* (2014) Prognostic impact of plasma ORM2 levels in patients with stage II colorectal cancer. Ann. Clin. Lab. Sci., **44**(4), 388–393.
52. *El-Akawi Z.J., Al-Hindawi F.K., Bashir N.A.* (2008) Alpha-1 antitrypsin (alpha1-AT) plasma levels in lung, prostate and breast cancer patients. Neuro Endocrinol. Lett., **29**(4), 482–484.
53. *Farrokhi Yekta R., Arefi Oskouie A., Rezaei Tavirani M., Mohajeri-Tehrani M.R., Soroush A.R.* (2018) Decreased apolipoprotein A4 and increased complement component 3 as potential markers for papillary thyroid carcinoma: a proteomic study. Int. J. Biol. Markers, **33**(4), 455–462. DOI: 10.1177/1724600818787752
54. *Lobo M.D.P., Moreno F.B.M.B., Souza G.H.M.F., Verde S.M.M.L., Moreira R.A., Monteiro-Moreira A.C.D.* (2017) Label-free proteome analysis of plasma from patients with breast cancer: stage-specific protein expression. Front. Oncol., **7**, 14. DOI: 10.3389/fonc.2017.00014
55. *Pérez-Holanda S., Blanco I., Menéndez M., Rodrigo L.* (2014) Serum concentration of alpha-1 antitrypsin is significantly higher in colorectal cancer patients than in healthy controls. BMC Cancer, **14**, 355. DOI: 10.1186/1471-2407-14-355
56. *Liang Y., Ma T., Thakur A., Yu H., Gao L., Shi P., Li X., Ren H., Jia L., Zhang S., Li Z., Chen M.* (2015) Differentially expressed glycosylated patterns of α-1-antitrypsin as serum biomarkers for the diagnosis of lung cancer. Glycobiology, **25**(3), 331–340. DOI: 10.1093/glycob/cwu115
57. *Jaberie H., Hosseini S.V., Naghibalhossaini F.* (2020) Evaluation of alpha 1-antitrypsin for the early diagnosis of colorectal cancer. Pathol. Oncol. Res., **26**(2), 1165–1173. DOI: 10.1007/s12253-019-00679-0
58. *Repetto O., de Re V., Mussolin L., Tedeschi M., Elia C., Bianchi M., Buffardi S., Sala A., Burnelli R., Mascarin M.* (2020) Proteomic profiles and biological processes of relapsed vs. non-relapsed pediatric Hodgkin lymphoma. Int. J. Mol. Sci., **21**(6), 2185. DOI: 10.3390/ijms21062185
59. *Zhao J., Fan Y.-X., Yang Y., Liu D.-L., Wu K., Wen F.-B., Zhang C.-Y., Zhu D.-Y., Zhao S.* (2015) Identification of potential plasma biomarkers for esophageal squamous cell carcinoma by a proteomic method. Int. J. Clin. Exp. Pathol., **8**(2), 1535–1544.
60. *Wu C.-C., Lu Y.-T., Yeh T.-S., Chan Y.-H., Dash S., Yu J.-S.* (2021) Identification of fucosylated SERPINA1 as a novel plasma marker for pancreatic cancer using lectin affinity capture coupled with iTRAQ-based quantitative glycoproteomics. Int. J. Mol. Sci. **22**(11), 6079. DOI: 10.3390/ijms22116079
61. *Wang W., Wang S., Zhang M.* (2020) Evaluation of kininogen 1, osteopontin and α-1-antitrypsin in plasma, bronchoalveolar lavage fluid and urine for lung squamous cell carcinoma diagnosis. Oncol. Lett., **19**(4), 2785–2792. DOI: 10.3892/ol.2020.11376
62. *Shah A.K., Hartel G., Brown I., Winterford C., Na R., Cao K.-A.L., Spicer B.A., Dunstone M.A., Phillips W.A., Lord R.V., Barbour A.P., Watson D.I., Joshi V., Whiteman D.C., Hill M.M.* (2018) Evaluation of serum glycoprotein biomarker candidates for detection of esophageal adenocarcinoma and surveillance of Barrett's esophagus. Mol. Cell. Proteomics, **17**(12), 2324–2334. DOI: 10.1074/mcp.RA118.000734
63. *Sandanayake N.S., Sinclair J., Andreola F., Chapman M.H., Xue A., Webster G.J., Clarkson A., Gill A., Norton I.D., Smith R.C., Timms J.F., Pereira S.P.* (2011) A combination of serum leucine-rich α-2-glycoprotein 1, CA19-9 and interleukin-6 differentiate biliary tract cancer from benign biliary strictures. Br. J. Cancer, **105**(9), 1370–1378. DOI: 10.1038/bjc.2011.376
64. *Brkic S., Salkic A., Nuhbegovic S., Brkic F., Umihanic S.* (2011) Influence of surgical therapy on serum values of alpha 1-antitrypsin in patients with head and neck tumors. Medicinski Arhiv, **65**(2), 99–101.
65. *Abdul-Rahman P.S., Lim B.-K., Hashim O.H.* (2007) Expression of high-abundance proteins in sera of patients with endometrial and cervical cancers: analysis using 2-DE with silver staining and lectin detection methods. Electrophoresis, **28**(12), 1989–1996. DOI: 10.1002/elps.200600629

66. *Liu Y., Luo X., Hu H., Wang R., Sun Y., Zeng R., Chen H.* (2012) Integrative proteomics and tissue microarray profiling indicate the association between overexpressed serum proteins and non-small cell lung cancer. PLOS One, **7**(12), e51748. DOI: 10.1371/journal.pone.0051748
67. *Kopylov A.T., Stepanov A.A., Malsagova K.A., Soni D., Kushlinsky N.E., Enikeev D.V., Potoldykova N.V., Lisitsa A.V., Kaysheva A.L.* (2020) Revelation of proteomic indicators for colorectal cancer in initial stages of development. Molecules, **25**(3), 619. DOI: 10.3390/molecules25030619
68. *Canales N.A.G., Marina V.M., Castro J.S., Jiménez A.A., Mendoza-Hernández G., McCarron E.L., Roman M.B., Castro-Romero J.I.* (2014) A1BG and C3 are overexpressed in patients with cervical intraepithelial neoplasia III. Oncol. Lett., **8**(2), 939–947. DOI: 10.3892/ol.2014.2195
69. *Kim J.H., Kim Y.-W., Kim I.-W., Park D.C., Kim Y.W., Lee K.-H., Jang C.K., Ahn W.S.* (2013) Identification of candidate biomarkers using the Experion™ automated electrophoresis system in serum samples from ovarian cancer patients. Int. J. Oncol., **42**(4), 1257–1262. DOI: 10.3892/ijo.2013.1803
70. *Gaziev U.M., Kit O.I., Frantsiyants E.M., Kozlova L., Mezentsev S.S.* (2016) Alpha-2-macroglobulin as the marker for pancreatic cancer process direction. J. Clin. Oncol., **34**(15_suppl), e15686–e15686. DOI: 10.1200/jco.2016.34.15_suppl.e15686
71. *Opstal-van Winden A.W.J., Krop E.J.M., Kåredal M.H., Gast M.-C.W., Lindh C.H., Jeppsson M.C., Jönsson B.A.G., Grobbee D.E., Peeters P.H.M., Beijnen J.H., van Gils C.H., Vermeulen R.C.H.* (2011) Searching for early breast cancer biomarkers by serum protein profiling of pre-diagnostic serum; a nested case-control study. BMC Cancer, **11**, 381. DOI: 10.1186/1471-2407-11-381
72. *Taguchi O., Gabazza E.C., Yoshida M., Yamakami T., Kobayashi H., Shima T.* (1996) High plasma level of plasmin-alpha 2-plasmin inhibitor complex is predictor of poor prognosis in patients with lung cancer. Clin. Chim. Acta, **244**(1), 69–81. DOI: 10.1016/0009-8981(95)06196-7
73. *Cavalcante M.S., Torres-Romero J.C., Lobo M.D.P., Moreno F.B.M.B., Bezerra L.P., Lima D.S., Matos J.C., Moreira R.A., Monteiro-Moreira A.C.O.* (2016) A panel of glycoproteins as candidate biomarkers for early diagnosis and treatment evaluation of B-cell acute lymphoblastic leukemia. Biomarker Res., **4**, 1. DOI: 10.1186/s40364-016-0055-6
74. *Ivancic M.M., Megna B.W., Sverchkov Y., Craven M., Reichelderfer M., Pickhardt P.J., Sussman M.R., Kennedy G.D.* (2020) Noninvasive detection of colorectal carcinomas using serum protein biomarkers. J. Surg. Res., **246**, 160–169. DOI: 10.1016/j.jss.2019.08.004
75. *Guldvik I.J., Zuber V., Braadland P.R., Grytli H.H., Ramberg H., Lilleby W., Thiede B., Zucknick M., Saatcioglu F., Gislefoss R., Kvåle R., George A., Grönberg H., Wiklund F., Neal D.E., Gnanapragasam V.J., Taskén K.A., Mills I.G.* (2020) Identification and validation of leucine-rich α-2-glycoprotein 1 as a noninvasive biomarker for improved precision in prostate cancer risk stratification. Eur. Urol. Open Sci., **21**, 51–60. DOI: 10.1016/j.euros.2020.08.007
76. *Zhang Q., Huang R., Tang Q., Yu Y., Huang Q., Chen Y., Wang G., Wang X.* (2018) Leucine-rich alpha-2-glycoprotein-1 is up-regulated in colorectal cancer and is a tumor promoter. OncoTargets Ther., **11**, 2745–2752. DOI: 10.2147/OTT.S153375
77. *Holm M., Saraswat M., Joenväärä S., Ristimäki A., Haglund C., Renkonen R.* (2018) Colorectal cancer patients with different C-reactive protein levels and 5-year survival times can be differentiated with quantitative serum proteomics. PLOS One, **13**(4), e0195354. DOI: 10.1371/journal.pone.0195354
78. *Gautam P., Nair S.C., Gupta M.K., Sharma R., Polisetty R.V., Uppin M.S., Sundaram C., Puligopu A.K., Ankathi P., Purohit A.K., Chandak G.R., Harsha H.C., Sirdeshmukh R.* (2012) Proteins with altered levels in plasma from glioblastoma patients as revealed by iTRAQ-based quantitative proteomic analysis. PLOS One, **7**(9), e46153. DOI: 10.1371/journal.pone.0046153
79. *Andersen J.D., Boylan K.L., Jemmerson R., Geller M.A., Misemer B., Harrington K.M., Weivoda S., Witthuhn B.A., Argenta P., Vogel R.I., Skubitz A.P.* (2010) Leucine-rich alpha-2-glycoprotein-1 is upregulated in sera and tumors of ovarian cancer patients. J. Ovarian Res., **3**, 21. DOI: 10.1186/1757-2215-3-21
80. *Kakisaka T., Kondo T., Okano T., Fujii K., Honda K., Endo M., Tsuchida A., Aoki T., Itoi T., Moriyasu F., Yamada T., Kato H., Nishimura T., Todo S., Hirohashi S.* (2007) Plasma proteomics of pancreatic cancer patients by multi-dimensional liquid chromatography and two-dimensional difference gel electrophoresis (2D-DIGE): up-regulation of leucine-rich alpha-2-glycoprotein in pancreatic cancer. J. Chromatogr. B Analyt. Technol. Biomed. Life Sci., **852**(1–2), 257–267. DOI: 10.1016/j.jchromb.2007.01.029
81. *Zhou Y., Zhang X., Zhang J., Fang J., Ge Z., Li X.* (2017) LRG1 promotes proliferation and inhibits apoptosis in colorectal cancer cells via RUNX1 activation. PLOS One, **12**(4), e0175122. DOI: 10.1371/journal.pone.0175122
82. *Li D., Zhou L., Ma C., Chen W., Zhang Y., Yu S., Wang D., Zou Y., Wu J., Qiu L.* (2019) Comparative analysis of the serum proteome profiles of thyroid cancer: an initial focus on the lipid profile. Oncol. Lett., **18**(3), 3349–3357. DOI: 10.3892/ol.2019.10655
83. *Stenman U.H., Leinonen J., Alfthan H., Rannikko S., Tuhkanen K., Alfthan O.* (1991) A complex between prostate-specific antigen and alpha 1-antichymotrypsin is the major form of prostate-specific antigen in serum of patients with prostatic cancer: assay of the complex improves clinical sensitivity for cancer. Cancer Res., **51**(1), 222–226.
84. *Jin Y., Wang W., Wang Q., Zhang Y., Zahid K.R., Raza U., Gong Y.* (2022) Alpha-1-antichymotrypsin as a novel biomarker for diagnosis, prognosis, and therapy prediction in human diseases. Cancer Cell Int., **22**(1), 156. DOI: 10.1186/s12935-022-02572-4
85. *Jin Y., Wang J., Ye X., Su Y., Yu G., Yang Q., Liu W., Yu W., Cai J., Chen X., Liang Y., Chen Y., Wong B.H.C., Fu X., Sun H.* (2016) Identification of GlcNAcylated alpha-1-antichymotrypsin as an early biomarker in human non-small-cell lung cancer by quantitative proteomic analysis with two lectins. Br. J. Cancer, **114**(5), 532–544. DOI: 10.1038/bjc.2015.348
86. *Miyauchi E., Furuta T., Ohtsuki S., Tachikawa M., Uchida Y., Sabit H., Obuchi W., Baba T., Watanabe M., Terasaki T., Nakada M.* (2018) Identification of blood biomarkers in glioblastoma by SWATH mass spectrometry and quantitative targeted absolute proteomics. PLOS One, **13**(3), e0193799. DOI: 10.1371/journal.pone.0193799

87. *Li H., Sun L., Chen L., Kang Z., Hao G., Bai F.* (2022) Effects of adiponectin, plasma D-dimer, inflammation and tumor markers on clinical characteristics and prognosis of patients with ovarian cancer. J. Med. Biochem., **41**(1), 71–78. DOI: 10.5937/jomb0-26452
88. *Yildirim A., Bilici M., Cayir K., Yanmaz V., Yildirim S., Tekin S.B.* (2009) Serum adiponectin levels in patients with esophageal cancer. Jpn. J. Clin. Oncol., **39**(2), 92–96. DOI: 10.1093/jjco/hyn143
89. *Goktas S., Yilmaz M.I., Caglar K., Sonmez A., Kilic S., Bedir S.* (2005) Prostate cancer and adiponectin. Urology, **65**(6), 1168–1172. DOI: 10.1016/j.urology.2004.12.053
90. *Dieplinger H., Dieplinger B.* (2015) Afamin — a pleiotropic glycoprotein involved in various disease states. Clin. Chim. Acta, **446**, 105–110. DOI: 10.1016/j.cca.2015.04.010
91. *Melmer A., Fineder L., Lamina C., Kollerits B., Dieplinger B., Braicu I., Sehouli J., Cadron I., Vergote I., Mahner S., Zeimet A.G., Castillo-Tong D.C., Ebenbichler C.F., Zeillinger R., Dieplinger H.* (2013) Plasma concentrations of the vitamin E-binding protein afamin are associated with overall and progression-free survival and platinum sensitivity in serous ovarian cancer — a study by the OVCAD consortium. Gynecol. Oncol., **128**(1), 38–43. DOI: 10.1016/j.ygyno.2012.09.032
92. *Dieplinger H., Ankerst D.P., Burges A., Lenhard M., Lingenhel A., Fineder L., Buchner H., Stieber P.* (2009) Afamin and apolipoprotein A-IV: novel protein markers for ovarian cancer. Cancer Epidemiol. Biomarkers Prev., **18**(4), 1127–1133. DOI: 10.1158/1055-9965.EPI-08-0653
93. *Chang T.-T., Ho C.-H.* (2020) Plasma proteome atlas for differentiating tumor stage and post-surgical prognosis of hepatocellular carcinoma and cholangiocarcinoma. PLOS One, **15**(8), e0238251. DOI: 10.1371/journal.pone.0238251
94. *Humphries J.M., Penno M.A.S., Weiland F., Klingler-Hoffmann M., Zuber A., Boussioutas A., Ernst M., Hoffmann P.* (2014) Identification and validation of novel candidate protein biomarkers for the detection of human gastric cancer. Biochim. Biophys. Acta, **1844**(5), 1051–1058. DOI: 10.1016/j.bbapap.2014.01.018
95. *Oñate-Ocaña L.F., Aiello-Crocifoglio V., Gallardo-Rincón D., Herrera-Goepfert R., Brom-Valladares R., Carrillo J.F., Cervera E., Mohar-Betancourt A.* (2007) Serum albumin as a significant prognostic factor for patients with gastric carcinoma. Ann. Surg. Oncol., **14**(2), 381–389. DOI: 10.1245/s10434-006-9093-x
96. *Lis C.G., Grutsch J.F., Vashi P.G., Lammersfeld C.A.* (2003) Is serum albumin an independent predictor of survival in patients with breast cancer? J. Parenter. Enteral Nutr., **27**(1), 10–15. DOI: 10.1177/014860710302700110
97. *Boonpipattanapong T., Chewatanakornkul S.* (2006) Preoperative carcinoembryonic antigen and albumin in predicting survival in patients with colon and rectal carcinomas. J. Clin. Gastroenterol., **40**(7), 592–595. DOI: 10.1097/00004836-200608000-00006
98. *Suh B., Park S., Shin D.W., Yun J.M., Keam B., Yang H.-K., Ahn E., Lee H., Park J.H., Cho B.* (2014) Low albumin-to-globulin ratio associated with cancer incidence and mortality in generally healthy adults. Ann. Oncol., **25**(11), 2260–2266. DOI: 10.1093/annonc/mdu274
99. *Fujii T., Tokuda S., Nakazawa Y., Kurozumi S., Obayashi S., Yajima R., Shirabe K.* (2020) Implications of low serum albumin as a prognostic factor of long-term outcomes in patients with breast cancer. In Vivo, **34**(4), 2033–2036. DOI: 10.21873/invivo.12003
100. *Cohen A., Wang E., Chisholm K.A., Kostyleva R., O'Connor-McCourt M., Pinto D.M.* (2013) A mass spectrometry-based plasma protein panel targeting the tumor microenvironment in patients with breast cancer. J. Proteomics, **81**, 135–147. DOI: 10.1016/j.jprot.2012.11.004
101. *Pugia M.J., Valdes R., Jortani S.A.* (2007) Bikunin (urinary trypsin inhibitor): structure, biological relevance, and measurement. Adv. Clin. Chem., **44**, 223–245. DOI: 10.1016/s0065-2423(07)44007-0
102. *Greco M., de Mitri M., Chiriacò F., Leo G., Brienza E., Maffia M.* (2009) Serum proteomic profile of cutaneous malignant melanoma and relation to cancer progression: association to tumor derived alpha-N-acetylgalactosaminidase activity. Cancer Lett., **283**(2), 222–229. DOI: 10.1016/j.canlet.2009.04.001
103. *Lu Z., Wang F., Liang M.* (2017) SerpinC1/Antithrombin III in kidney-related diseases. Clin. Sci., **131**(9), 823–831. DOI: 10.1042/CS20160669
104. *Cao X., Cao Z., Ou C., Zhang L., Chen Y., Li Y., Zhu B., Shu H.* (2021) Combination of serum paraoxonase/arylesterase 1 and antithrombin-III is a promising non-invasion biomarker for discrimination of AFP-negative HCC versus liver cirrhosis patients. Clin. Res. Hepatol. Gastroenterol., **45**(5), 101583. DOI: 10.1016/j.clinre.2020.11.013
105. *Dowling P., O'Driscoll L., Meleady P., Henry M., Roy S., Ballot J., Moriarty M., Crown J., Clynes M.* (2007) 2-D difference gel electrophoresis of the lung squamous cell carcinoma versus normal sera demonstrates consistent alterations in the levels of ten specific proteins. Electrophoresis, **28**(23), 4302–4310. DOI: 10.1002/elps.200700246
106. *Dabrowska M., Prokopowicz J., Kemona H., Kretowska J., Kulik S., Głuszczak M.* (1988) Serum antithrombin III and alpha-2-antiplasmin concentration in patients with lung carcinoma. Folia Haematologica, **115**(5), 641–646.
107. *Ren L., Yi J., Li W., Zheng X., Liu J., Wang J., Du G.* (2019) Apolipoproteins and cancer. Cancer Med., **8**(16), 7032–7043. DOI: 10.1002/cam4.2587
108. *Georgila K., Vyrla D., Drakos E.* (2019) Apolipoprotein A-I (ApoA-I), immunity, inflammation and cancer. Cancers, **11**(8), 1097. DOI: 10.3390/cancers11081097
109. *Cheng T., Dai X., Zhou D.-L., Lv Y., Miao L.-Y.* (2015) Correlation of apolipoprotein A-I kinetics with survival and response to first-line platinum-based chemotherapy in advanced non-small cell lung cancer. Med. Oncol., **32**(1), 407. DOI: 10.1007/s12032-014-0407-8
110. *Chang H., Wei J.-W., Chen K., Zhang S., Han F., Lu L.-X., Xiao W.-W., Gao Y.-H.* (2018) Apolipoprotein A-I is a prognosticator of nasopharyngeal carcinoma in the era of intensity-modulated radiotherapy. J. Cancer, **9**(4), 702–710. DOI: 10.7150/jca.22836
111. *Chang S.-C., Lin W.-L., Chang Y.-F., Lee C.-T., Wu J.-S., Hsu P.-H., Chang C.-F.* (2019) Glycoproteomic identification of novel plasma biomarkers for oral cancer. J. Food Drug Anal., **27**(2), 483–493. DOI: 10.1016/j.jfda.2018.12.008
112. *Wang X.-P., Li X.-H., Zhang L., Lin J.-H., Huang H., Kang T., Mao M.-J., Chen H., Zheng X.* (2016) High level of serum apolipoprotein A-I is a favorable prognostic factor for overall survival in esophageal squamous cell carcinoma. BMC Cancer, **16**, 516. DOI: 10.1186/s12885-016-2502-z
113. *Shi C., Gong S., Wu A., Yang S., Zou D., Zhang Y., Wu N., Ma C., Shi S., Chen Y., Wu Y., Zheng X., Huang Z., Ding J., Ouyang G., Mu Q.* (2022) Decreased serum

apolipoprotein A1 level predicts poor prognosis of patients with *de novo* myelodysplastic syndromes. BMC Cancer, **22**, 127. DOI: 10.1186/s12885-022-09248-2

114. *Hachem H., Favre G., Ghalim N., Puchois P., Fruchart J.C., Soula G.* (1987) Quantitative abnormalities of lipoprotein particles in multiple myeloma. J. Clin. Chem. Clin. Biochem., **25**(10), 675–679. DOI: 10.1515/cclm.1987.25.10.675
115. *Honda K., Okusaka T., Felix K., Nakamori S., Sata N., Nagai H., Ioka T., Tsuchida A., Shimahara T., Shimahara M., Yasunami Y., Kuwabara H., Sakuma T., Otsuka Y., Ota N., Shitashige M., Kosuge T., Büchler M.W., Yamada T.* (2012) Altered plasma apolipoprotein modifications in patients with pancreatic cancer: protein characterization and multi-institutional validation. PLOS One, **7**(10), e46908. DOI: 10.1371/journal.pone.0046908
116. *Liu Y., Sogawa K., Sunaga M., Umemura H., Satoh M., Kazami T., Yoshikawa M., Tomonaga T., Yokosuka O., Nomura F.* (2014) Increased concentrations of apo A-I and apo A-II fragments in the serum of patients with hepatocellular carcinoma by magnetic beads-assisted MALDI-TOF mass spectrometry. Am. J. Clin. Pathol., **141**(1), 52–61. DOI: 10.1309/AJCPBLFBNAP6N2UN
117. *Malik G, Ward M.D., Gupta S.K., Trosset M.W., Grizzle W.E., Adam B.-L., Diaz J.I., Semmes O.J.* (2005) Serum levels of an isoform of apolipoprotein A-II as a potential marker for prostate cancer. Clin. Cancer Res, **11**(3), 1073–1085.
118. *de Bont J.M., den Boer M.L., Reddingius R.E., Jansen J., Passier M., van Schaik R.H.N., Kros J.M., Sillevis Smitt P.A.E., Luider T.H., Pieters R.* (2006) Identification of apolipoprotein A-II in cerebrospinal fluid of pediatric brain tumor patients by protein expression profiling. Clin. Chem., **52**(8), 1501–1509. DOI: 10.1373/clinchem.2006.069294
119. *Gómez B.B., López-Cortés R., Casas-Nebra F.J., Vázquez-Estévez S., Pérez-Fentes D., Chantada-Vázquez M.D.P., Bravo S.B., Núñez C.* (2021) Detection of circulating serum protein biomarkers of non-muscle invasive bladder cancer after protein corona-silver nanoparticles analysis by SWATH-MS. Nanomaterials, **11**(9), 2384. DOI: 10.3390/nano11092384
120. *Li B., An H.J., Kirmiz C., Lebrilla C.B., Lam K.S., Miyamoto S.* (2008) Glycoproteomic analyses of ovarian cancer cell lines and sera from ovarian cancer patients show distinct glycosylation changes in individual proteins. J. Proteome Res., **7**(9), 3776–3788. DOI: 10.1021/pr800297u
121. *Wang M., Wang J., Jiang H.* (2019) Diagnostic value of apolipoprotein C-I, transthyretin and apolipoprotein C-III in gastric cancer. Oncol. Lett., **17**(3), 3227–3232. DOI: 10.3892/ol.2019.9957
122. *Yi J., Ren L., Wu J., Li W., Zheng X., Du G., Wang J.* (2019) Apolipoprotein C1 (APOC1) as a novel diagnostic and prognostic biomarker for gastric cancer. Ann. Transl. Med., **7**(16), 380. DOI: 10.21037/atm.2019.07.59
123. *Fan Y., Shi L., Liu Q., Dong R., Zhang Q., Yang S., Fan Y., Yang H., Wu P., Yu J., Zheng S., Yang F., Wang J.* (2009) Discovery and identification of potential biomarkers of papillary thyroid carcinoma. Mol. Cancer, **8**, 79. DOI: 10.1186/1476-4598-8-79
124. *Fu T., Zhou Y., Mao S.* (2023) The expression and clinical significance of apolipoprotein C1 in cervix cancer. Eur. J. Gynaecol. Oncol., **44**(6), 67–73. DOI: 10.22514/ejgo.2023.100
125. *Dufresne J., Bowden P., Thavarajah T., Florentinus-Mefailoski A., Chen Z.Z., Tucholska M., Norzin T., Ho M.T., Phan M., Mohamed N., Ravandi A., Stanton E., Slutsky A.S., dos Santos C.C., Romaschin A., Marshall J.C., Addison C., Malone S., Heyland D., Scheltens P., Killestein J., Teunissen C., Diamandis E.P., Siu K.W.M., Marshall J.G.* (2019) The plasma peptides of breast versus ovarian cancer. Clin. Proteomics, **16**, 43. DOI: 10.1186/s12014-019-9262-0
126. *Zhou Y., Luo G.* (2020) Apolipoproteins, as the carrier proteins for lipids, are involved in the development of breast cancer. Clin. Transl. Oncol., **22**(11), 1952–1962. DOI: 10.1007/s12094-020-02354-2
127. *Zhao Z., Zou S., Guan X., Wang M., Jiang Z., Liu Z., Li C., Lin H., Liu X., Yang R., Gao Y., Wang X.* (2018) *Apolipoprotein E* overexpression is associated with tumor progression and poor survival in colorectal cancer. Front. Genet., **9**, 650. DOI: 10.3389/fgene.2018.00650
128. *Kemp S.B., Carpenter E.S., Steele N.G., Donahue K.L., Nwosu Z.C., Pacheco A., Velez-Delgado A., Menjivar R.E., Lima F., The S., Espinoza C.E., Brown K., Long D., Lyssiotis C.A., Rao A., Zhang Y., Pasca di Magliano M., Crawford H.C.* (2021) Apolipoprotein E promotes immune suppression in pancreatic cancer through NF-κB-mediated production of CXCL1. Cancer Res., **81**(16), 4305–4318. DOI: 10.1158/0008-5472.CAN-20-3929
129. *Xue Y., Huang S., Huang J., Li S., Zhang C., Zhou X.* (2020) Identification of apolipoprotein E as a potential diagnostic biomarker of nasopharyngeal carcinoma. Cancer Manag. Res., **12**, 8943–8950. DOI: 10.2147/CMAR.S239479
130. *Xu X., Wan J., Yuan L., Ba J., Feng P., Long W., Huang H., Liu P., Cai Y., Liu M., Luo J., Li L.* (2016) Serum levels of apolipoprotein E correlates with disease progression and poor prognosis in breast cancer. Tumour Biol., **37**, 15959–15966. DOI: 10.1007/s13277-016-5453-8
131. *Tsai I-J., Su E.C.-Y., Tsai I-L., Lin C.-Y.* (2021) Clinical assay for the early detection of colorectal cancer using mass spectrometric wheat germ agglutinin multiple reaction monitoring. Cancers, **13**(9), 2190. DOI: 10.3390/cancers13092190
132. *Wang Y.-B., Zhou B.-X., Ling Y.-B., Xiong Z.-Y., Li R.-X., Zhong Y.-S., Xu M.-X., Lu Y., Liang H., Chen G.-H., Yao Z.-C., Deng M.-H.* (2019) Decreased expression of ApoF associates with poor prognosis in human hepatocellular carcinoma. Gastroenterol. Rep., **7**(5), 354–360. DOI: 10.1093/gastro/goz011
133. *Jing X., Piao Y.-F., Liu Y., Gao P.-J.* (2010) Beta2-GPI: a novel factor in the development of hepatocellular carcinoma. J. Cancer Res. Clin. Oncol., **136**(11), 1671–1680. DOI: 10.1007/s00432-010-0825-8
134. *Mandili G., Notarpietro A., Khadjavi A., Allasia M., Battaglia A., Lucatello B., Frea B., Turrini F., Novelli F., Giribaldi G., Destefanis P.* (2018) Beta-2-glycoprotein-1 and alpha-1-antitrypsin as urinary markers of renal cancer in von Hippel-Lindau patients. Biomarkers, **23**(2), 123–130. DOI: 10.1080/1354750X.2016.1269132
135. *Lee S.-W., Kim I.J., Jeong B.Y., Choi M.-H., Kim J.Y., Kwon K.-H., Lee J.W., Yu A., Shin M.-G.* (2012) Use of MDLC-DIGE and LC-MS/MS to identify serum biomarkers for complete remission in patients with acute myeloid leukemia. Electrophoresis, **33**(12), 1863–1872. DOI: 10.1002/elps.201200047
136. *Cao W.-Q., Jiang B.-Y., Huang J.-M., Zhang L., Liu M.-Q., Yao J., Wu M.-X., Zhang L.-J., Kong S.-Y., Wang Y., Yang P.-Y.* (2019) Straightforward and highly efficient strategy for hepatocellular carcinoma glycoprotein biomarker discovery using a nonglycopeptide-based mass spectrometry pipeline. Anal. Chem., **91**(19), 12435–12443. DOI: 10.1021/acs.analchem.9b03074

137. *Jiang J., Wu C., Luo G., Zheng L., Chen L., Zhang X., Xu N.* (2011) Expression of apolipoprotein M in human hepatocellular carcinoma tissues. Acta Histochem., **113**(1), 53–57. DOI: 10.1016/j.acthis.2009.08.005
138. *Li L., Dong M., Wang X.-G.* (2016) The implication and significance of beta 2 microglobulin: a conservative multifunctional regulator. Chin. Med. J., **129**(4), 448–455. DOI: 10.4103/0366-6999.176084
139. *Sequeira J., Sengupta S., Mhatre B.* (2021) Serum beta-2 microglobulin analysis in patients with oral squamous cell carcinoma. Natl. J. Maxillofac. Surg., **12**(2), 227–232. DOI: 10.4103/njms.NJMS_242_20
140. *Li G., Feng G., Gentil-Perret A., Genin C., Tostain J.* (2008) Serum carbonic anhydrase 9 level is associated with postoperative recurrence of conventional renal cell cancer. J. Urol., **180**(2), 510–514. DOI: 10.1016/j.juro.2008.04.024
141. *Kou W., Li B., Shi Y., Zhao Y., Yu Q., Zhuang J., Xu Y., Peng W.* (2022) High complement protein C1q levels in pulmonary fibrosis and non-small cell lung cancer associated with poor prognosis. BMC Cancer, **22**, 110. DOI: 10.1186/s12885-021-08912-3
142. *Xu B., Lv W., Li X., Zhang L., Lin J.* (2019) Prognostic genes of hepatocellular carcinoma based on gene coexpression network analysis. J. Cell. Biochem., **120**(7), 11616–11623. DOI: 10.1002/jcb.28441
143. *Chinello C., Cazzaniga M., de Sio G, Smith A.J., Grasso A., Rocco B., Signorini S., Grasso M., Bosari S., Zoppis I., Mauri G., Magni F.* (2015) Tumor size, stage and grade alterations of urinary peptidome in RCC. J. Transl. Med., **13**(1), 332. DOI: 10.1186/s12967-015-0693-8
144. *Nedjadi T., Benabdelkamal H., Albarakati N., Masood A., Al-Sayyad A., Alfadda A.A., Alanazi I.O., Al-Ammari A., Al-Maghrabi J.* (2020) Circulating proteomic signature for detection of biomarkers in bladder cancer patients. Sci. Rep., **10**, 10999. DOI: 10.1038/s41598-020-67929-z
145. *Daugan M.V., Revel M., Russick J., Dragon-Durey M.-A., Gaboriaud C., Robe-Rybkine T., Poillerat V., Grunenwald A., Lacroix G., Bougouin A., Meylan M., Verkarre V., Oudard S.M., Mejean A., Vano Y.A., Perkins G., Validire P., Cathelineau X., Sanchez-Salas R., Damotte D., Fremeaux-Bacchi V., Cremer I., Sautès-Fridman C., Fridman W.H., Roumenina L.T.* (2021) Complement C1s and C4d as prognostic biomarkers in renal cancer: emergence of noncanonical functions of C1s. Cancer Immunol. Res., **9**(8), 891–908. DOI: 10.1158/2326-6066.CIR-20-0532
146. *Gürz S., Çelik B., Menteşe A., Us Altay D.* (2018) Diagnostic value of signal peptide-complement C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein 1 on serum and tissue samples in non-small cell lung cancer. Turk Gogus Kalp Damar Cerrahisi Dergisi, **26**(2), 246–253. DOI: 10.5606/tgkdc.dergisi.2018.14600
147. *Tan G, Liu Q., Tang X., Kang T., Li Y., Lu J., Zhao X., Tang F.* (2016) Diagnostic values of serum cathepsin B and D in patients with nasopharyngeal carcinoma. BMC Cancer, **16**, 241. DOI: 10.1186/s12885-016-2283-4
148. *Wei S., Liu W., Xu M., Qin H., Liu C., Zhang R., Zhou S., Li E., Liu Z., Wang Q.* (2022) Cathepsin F and fibulin-1 as novel diagnostic biomarkers for brain metastasis of non-small cell lung cancer. Br. J. Cancer, **126**(12), 1795–1805. DOI: 10.1038/s41416-022-01744-3
149. *Dou X., Lu J., Yu Y., Yi Y., Zhou L.* (2024) Determination of tumor marker screening for lung cancer using ROC curves. Dis. Markers, **2024**, 4782618. DOI: 10.1155/2024/4782618
150. *Chen Z., Liu X., Shang X., Qi K., Zhang S.* (2021) The diagnostic value of the combination of carcinoembryonic antigen, squamous cell carcinoma-related antigen, CYFRA 21-1, neuron-specific enolase, tissue polypeptide antigen, and progastrin-releasing peptide in small cell lung cancer discrimination. Int. J. Biol. Markers, **36**(4), 36–44. DOI: 10.1177/17246008211049446
151. *Zhang J., Yang X., Wei L., Tan H., Chen J., Li W., Chan K., Su Y., Zhao L., Hu S., Zhong S., Xiao Y., Liu H.* (2020) Improved diagnostic value by combining plasma PON1 level with tumor biomarkers in colorectal cancer patients. J. Cancer, **11**(22), 6491–6496. DOI: 10.7150/jca.45204
152. *Chen C., Chen Q., Dong Y., Liu X.* (2020) The clinical significance of sICAM-1 in differentiating benign breast lesions from breast cancer. Ann. Clin. Lab. Sci., **50**(5), 650–656.
153. *Huang Z.-B., Zhou X., Xu J., Du Y.-P., Zhu W., Wang J., Shu Y.-Q., Liu P.* (2014) Prognostic value of preoperative serum tumor markers in gastric cancer. World J. Clin. Oncol., **5**(2), 170–176. DOI: 10.5306/wjco.v5.i2.170
154. *Liu W., Liu B., Xin L., Zhang Y., Chen X., Zhu Z., Lin Y.* (2007) Down-regulated expression of complement factor I: a potential suppressive protein for gastric cancer identified by serum proteome analysis. Clin. Chim. Acta, **377**(1–2), 119–126. DOI: 10.1016/j.cca.2006.09.005
155. *Riihilä P., Nissinen L., Farshchian M., Kallajoki M., Kivisaari A., Meri S., Grénman R., Peltonen S., Peltonen J., Pihlajaniemi T., Heljasvaara R., Kähäri V.-M.* (2017) Complement component C3 and complement factor B promote growth of cutaneous squamous cell carcinoma. Am. J. Pathol., **187**(5), 1186–1197. DOI: 10.1016/j.ajpath.2017.01.006
156. *Wu P., Shi J., Sun W., Zhang H.* (2021) The prognostic value of plasma complement factor B (CFB) in thyroid carcinoma. Bioengineered, **12**(2), 12854–12866. DOI: 10.1080/21655979.2021.2005745
157. *Chambers A.G., Percy A.J., Yang J., Camenzind A.G., Borchers C.H.* (2013) Multiplexed quantitation of endogenous proteins in dried blood spots by multiple reaction monitoring-mass spectrometry. Mol. Cell. Proteomics, **12**(3), 781–791. DOI: 10.1074/mcp.M112.022442
158. *Bouwens T.A.M., Trouw L.A., Veerhuis R., Dirven C.M.F., Lamfers M.L.M., Al-Khawaja H.* (2015) Complement activation in glioblastoma multiforme pathophysiology: evidence from serum levels and presence of complement activation products in tumor tissue. J. Neuroimmunol., **278**, 271–276. DOI: 10.1016/j.jneuroim.2014.11.016
159. *Rajkumar T., Amritha S., Sridevi V., Gopal G., Sabitha K., Shirley S., Swaminathan R.* (2022) Identification and validation of plasma biomarkers for diagnosis of breast cancer in South Asian women. Sci. Rep., **12**, 100. DOI: 10.1038/s41598-021-04176-w
160. *Yang Y., Wan C., Li H., Zhu H., La Y., Xi Z., Chen Y., Jiang L., Feng G., He L.* (2006) Altered levels of acute phase proteins in the plasma of patients with schizophrenia. Anal. Chem., **78**(11), 3571–3576. DOI: 10.1021/ac051916x
161. *Cui T., Chen Y., Knösel T., Yang L., Zöller K., Galler K., Berndt A., Mihlan M., Zipfel P.F., Petersen I.* (2011) Human complement factor H is a novel diagnostic marker for lung adenocarcinoma. Int. J. Oncol., **39**(1), 161–168. DOI: 10.3892/ijo.2011.1010
162. *Cheng Z.-Z., Corey M.J., Pärepalo M., Majno S., Hellwage J., Zipfel P.F., Kinders R.J., Raitanen M., Meri S., Jokiranta T.S.* (2005) Complement factor H as a marker for detection of bladder cancer. Clin. Chem., **51**(5), 856–863. DOI: 10.1373/clinchem.2004.042192

163. *Suzuki R., Okubo Y., Takagi T., Sugimoto M., Sato Y., Irie H., Nakamura J., Takasumi M., Kato T., Hashimoto M., Kobashi R., Hikichi T., Ohira H.* (2022) The complement C3a-C3a receptor axis regulates epithelial-to-mesenchymal transition by activating the ERK pathway in pancreatic ductal adenocarcinoma. Anticancer Res., **42**(3), 1207–1215. DOI: 10.21873/anticanres.15587
164. *Huang Y., Chen F., Zhang L., Lv Q., Yan J., Cui W.* (2021) MALDI-TOF-MS analysis in the discovery and identification of the serum peptide pattern of pancreatic ductal adenocarcinoma. Lab. Med., **52**(6), 558–566. DOI: 10.1093/labmed/lmab024
165. *Li C.-J., Xia H.-L., Wu Y.-M., Ding G., Xu D.-D.* (2019) [Significance of detecting serum complement C3 and C4 in patients with multiple myeloma]. Zhongguo Shi Yan Xue Ye Xue Za Zhi, **27**(2), 472–476. DOI: 10.19746/j.cnki.issn.1009-2137.2019.02.026
166. *Jiang F., Liu H., Liu Z., Song J., Li L., Ding K., Ren Y., Peng F., Shao Z., Fu R.* (2017) High serum levels of complements C3 and C4 as novel markers for myeloma bone disease. Ann. Hematol., **96**(2), 331–333. DOI: 10.1007/s00277-016-2863-z
167. *Dowling P., Clarke C., Hennessy K., Torralbo-Lopez B., Ballot J., Crown J., Kiernan I., O'Byrne K.J., Kennedy M.J., Lynch V., Clynes M.* (2012) Analysis of acute-phase proteins, AHSG, C3, CLI, HP and SAA, reveals distinctive expression patterns associated with breast, colorectal and lung cancer. Int. J. Cancer, **131**(4), 911–923. DOI: 10.1002/ijc.26462
168. *Ajona D., Pajares M.J., Corrales L., Perez-Gracia J.L., Agorreta J., Lozano M.D., Torre W., Massion P.P., de-Torres J.P., Jantus-Lewintre E., Camps C., Zulueta J.J., Montuenga L.M., Pio R.* (2013) Investigation of complement activation product c4d as a diagnostic and prognostic biomarker for lung cancer. J. Natl. Cancer Inst., **105**(18), 1385–1393. DOI: 10.1093/jnci/djt205
169. *Corrales L., Ajona D., Rafail S., Lasarte J.J., Riezu-Boj J.I., Lambris J.D., Rouzaut A., Pajares M.J., Montuenga L.M., Pio R.* (2012) Anaphylatoxin C5a creates a favorable microenvironment for lung cancer progression. J. Immunol., **189**(9), 4674–4683. DOI: 10.4049/jimmunol.1201654
170. *Hameed B.H., Abdulsatar Al-Rayahi I., Muhsin S.S.* (2022) The preoperative serum levels of the anaphylatoxins C3a and C5a and their association with clinico-pathological factors in breast cancer patients. Arch. Razi Inst., **77**(5), 1873–1879. DOI: 10.22092/ARI.2022.358193.2173
171. *Wang S., Hu W., Xie Y., Wu H., Jia Z., Zhang Z., Zhang X.* (2022) Functional genetic variants in complement component 7 confer susceptibility to gastric cancer. PeerJ, **10**, e12816. DOI: 10.7717/peerj.12816
172. *Fishelson Z., Kirschfink M.* (2019) Complement C5b-9 and cancer: mechanisms of cell damage, cancer counteractions, and approaches for intervention. Front. Immunol., **10**, 752. DOI: 10.3389/fimmu.2019.00752
173. *Joshi V., Shah A., Brown I., Winterford C., Hill M.* (2017) Complement component C9 as a new biomarker for esophageal adenocarcinoma. J. Clin. Oncol., **35**(4_suppl), 19. DOI: 10.1200/jco.2017.35.4_suppl.19
174. *Takakura M., Yokomizo A., Tanaka Y., Kobayashi M., Jung G., Banno M., Sakuma T., Imada K., Oda Y., Kamita M., Honda K., Yamada T., Naito S., Ono M.* (2012) Carbonic anhydrase I as a new plasma biomarker for prostate cancer. ISRN Oncol., **2012**, 768190. DOI: 10.5402/2012/768190
175. *Wang D.-B., Lu X.-K., Zhang X., Li Z.-G., Li C.-X.* (2016) Carbonic anhydrase 1 is a promising biomarker for early detection of non-small cell lung cancer. Tumour Biol., **37**, 553–559. DOI: 10.1007/s13277-015-3834-z
176. *Wang W., Chang J., Jia B., Liu J.* (2020) The blood biomarkers of thyroid cancer. Cancer Manag. Res., **12**, 5431–5438. DOI: 10.2147/CMAR.S261170
177. *Cui R., Wang C., Zhao Q., Wang Y., Li Y.* (2020) Serum carboxypeptidase N1 serves as a potential biomarker complementing CA15-3 for breast cancer. Anticancer Agents Med. Chem., **20**(17), 2053–2065. DOI: 10.2174/1871520620666200703191135
178. *Chang S.T., Zahn J.M., Horecka J., Kunz P.L., Ford J.M., Fisher G.A., Le Q.T., Chang D.T., Ji H., Koong A.C.* (2009) Identification of a biomarker panel using a multiplex proximity ligation assay improves accuracy of pancreatic cancer diagnosis. J. Transl. Med., **7**, 105. DOI: 10.1186/1479-5876-7-105
179. *Pforte A., Schiessler A., Gais P., Beer B., Ehlers M., Schütt C., Ziegler-Heitbrock H.W.* (1994) Expression of CD14 correlates with lung function impairment in pulmonary sarcoidosis. Chest, **105**(2), 349–354. DOI: 10.1378/chest.105.2.349
180. *Seyedmajidi S., Seyedmajidi M., Foroughi R., Zahedpasha A., Zolfaghari Saravi Z., Pourbagher R., Bijani A., Motallebnejad M., Monfared Shabestani A., Mostafazadeh A.* (2018) Comparison of salivary and serum soluble CD44 levels between patients with oral SCC and healthy controls. Asian Pacific J. Cancer Prev., **19**(11), 3059–3063. DOI: 10.31557/APJCP.2018.19.11.3059
181. *Nakagawara A., Ikeda K., Tsuneyoshi M., Daimaru Y., Enjoji M., Watanabe I., Iwafuchi M., Sawada T.* (1985) Hepatoblastoma producing both alpha-fetoprotein and human chorionic gonadotropin. Clinicopathologic analysis of four cases and a review of the literature. Cancer, **56**(7), 1636–1642. DOI: 10.1002/1097-0142(19851001)56:7<1636::aid-cncr2820560729>3.0.co;2-r
182. *Senra Varela A., Lopez Saez J.J., Quintela Senra D.* (1997) Serum ceruloplasmin as a diagnostic marker of cancer. Cancer Lett., **121**(2), 139–145. DOI: 10.1016/s0304-3835(97)00340-6
183. *Yin H., Lin Z., Nie S., Wu J., Tan Z., Zhu J., Dai J., Feng Z., Marrero J., Lubman D.M.* (2014) Mass-selected site-specific core-fucosylation of ceruloplasmin in alcohol-related hepatocellular carcinoma. J. Proteome Res., **13**(6), 2887–2896. DOI: 10.1021/pr500043k
184. *Mampilly M.O., Ravindran N., Parambil M.S., Nilesh K., Jayagopalan P., Dhamali D.* (2021) Assessment of serum selenium and ceruloplasmin in potentially malignant disorders and oral cancer. J. Pharm. Bioall. Sci., **13**(Suppl 2), S989–S992. DOI: 10.4103/jpbs.jpbs_380_21
185. *Sogabe M., Nozaki H., Tanaka N., Kubota T., Kaji H., Kuno A., Togayachi A., Gotoh M., Nakanishi H., Nakanishi T., Mikami M., Suzuki N., Kiguchi K., Ikehara Y., Narimatsu H.* (2014) Novel glycobiomarker for ovarian cancer that detects clear cell carcinoma. J. Proteome Res., **13**(3), 1624–1635. DOI: 10.1021/pr401109n
186. *Harazono A., Kawasaki N., Itoh S., Hashii N., Ishii-Watabe A., Kawanishi T., Hayakawa T.* (2006) Site-specific N-glycosylation analysis of human plasma ceruloplasmin using liquid chromatography with electrospray ionization tandem mass spectrometry. Anal. Biochem., **348**(2), 259–268. DOI: 10.1016/j.ab.2005.10.036
187. *Balmaña M., Sarrats A., Llop E., Barrabés S., Saldova R., Ferri M.J., Figueras J., Fort E., de Llorens R., Rudd P.M., Peracaula R.* (2015) Identification of potential pancreatic

cancer serum markers: increased sialyl-Lewis X on ceruloplasmin. Clin. Chim. Acta, **442**, 56–62. DOI: 10.1016/j.cca.2015.01.007

188. *Gao H., Wan Y., Fan X., Dong Y., Ji X., Song W.* (2021) The role of cholinesterase in differential diagnosis between gastric cancer and benign gastric diseases. Clin. Lab., **67**(2), DOI: 10.7754/Clin.Lab.2020.200525
189. *Shaqi M.A., Rijub-Agha A.K.Y., Hussain R.J.* (2023) Serum pseudocholinesterase as a biomarker in the differentiation between gastric cancer and benign gastric diseases. Al-Kindy College Medical Journal, **19**(2), 190–195. DOI: 10.47723/kcmj.v19i2.959
190. *Lin C.-C., Tsai P., Sun H.-Y., Hsu M.-C., Lee J.-C., Wu I-C., Tsao C.-W., Chang T.-T., Young K.-C.* (2014) Apolipoprotein J, a glucose-upregulated molecular chaperone, stabilizes core and NS5A to promote infectious hepatitis C virus virion production. J. Hepatol., **61**(5), 984–993. DOI: 10.1016/j.jhep.2014.06.026
191. *Koltai T.* (2014) Clusterin: a key player in cancer chemoresistance and its inhibition. OncoTargets Ther., **7**, 447–456. DOI: 10.2147/OTT.S58622
192. *Rasmy H.S., Mohammed H.A., Mohammed E.S., Ahmed A.S.M., Isaac A.* (2022) Serum clusterin as a promising diagnostic and prognostic marker for hepatocellular carcinoma after locoregional treatment. Egypt. J. Immunol., **29**(2), 26–40. DOI: 10.55133/eji.290204
193. *Sansanwal P., Li L., Sarwal M.M.* (2015) Inhibition of intracellular clusterin attenuates cell death in nephropathic cystinosis. J. Am. Soc. Nephrol., **26**(3), 612–625. DOI: 10.1681/ASN.2013060577
194. *Serie D., Myers A.A., Haehn D.A., Parker A.S., Bajalia E., Gonzalez G, Li Q., Wong M.Y., Moser K., Zhou B., Thiel D.D.* (2022) Novel plasma glycoprotein biomarkers predict progression-free survival in surgically resected clear cell renal cell carcinoma. Urol. Oncol., **40**(4), 168.e11–168.e19. DOI: 10.1016/j.urolonc.2021.12.005
195. *Chen Q.-F., Chang L., Su Q., Zhao Y., Kong B.* (2021) Clinical importance of serum secreted clusterin in predicting invasive breast cancer and treatment responses. Bioengineered, **12**(1), 278–285. DOI: 10.1080/21655979.2020.1868732
196. *Bellia F., Vecchio G., Rizzarelli E.* (2014) Carnosinases, their substrates and diseases. Molecules, **19**(2), 2299–2329. DOI: 10.3390/molecules19022299
197. *Arner P., Henjes F., Schwenk J.M., Darmanis S., Dahlman I., Iresjö B.-M., Naredi P., Agustsson T., Lundholm K., Nilsson P., Rydén M.* (2015) Circulating carnosine dipeptidase 1 associates with weight loss and poor prognosis in gastrointestinal cancer. PLOS One, **10**(4), e0123566. DOI: 10.1371/journal.pone.0123566
198. *Schwenk J.M., Igel U., Neiman M., Langen H., Becker C., Bjartell A., Ponten F., Wiklund F., Grųnberg H., Nilsson P., Uhlen M.* (2010) Toward next generation plasma profiling via heat-induced epitope retrieval and array-based assays. Mol. Cell. Proteomics, **9**(11), 2497–2507. DOI: 10.1074/mcp.M110.001560
199. *Hart P.C., Rajab I.M., Alebraheem M., Potempa L.A.* (2020) C-reactive protein and cancer-diagnostic and therapeutic insights. Front. Immunol., **11**, 595835. DOI: 10.3389/fimmu.2020.595835
200. *Bruserud Ø., Aarstad H.H., Tvedt T.H.A.* (2020) Combined C-reactive protein and novel inflammatory parameters as a predictor in cancer-what can we learn from the hematological experience? Cancers, **12**(7), 1966. DOI: 10.3390/cancers12071966
201. *Ma L.-N., Liu X.-Y., Lu Z.-H., Wu L.-G., Tang Y.-Y., Luo X., Hu Y.-C., Yan T.-T., Wang Q., Ding X.-C., Xie Y.* (2017) Assessment of high-sensitivity C-reactive protein tests for the diagnosis of hepatocellular carcinoma in patients with hepatitis B-associated liver cirrhosis. Oncol. Lett., **13**(5), 3457–3464. DOI: 10.3892/ol.2017.5890
202. *Fischer K., Theil G., Hoda R., Fornara P.* (2012) Serum amyloid A: a biomarker for renal cancer. Anticancer Res., **32**(5), 1801–1804.
203. *Lee K.-M., Nam K., Oh S., Lim J., Kim R.K., Shim D., Choi J.-H., Lee S.-J., Yu J.-H., Lee J.W., Ahn S.H., Shin I.* (2015) ECM1 regulates tumor metastasis and CSC-like property through stabilization of β-catenin. Oncogene, **34**(50), 6055–6065. DOI: 10.1038/onc.2015.54
204. *Wang X., Peng Y., Xie M., Gao Z., Yin L., Pu Y., Liu R.* (2017) Identification of extracellular matrix protein 1 as a potential plasma biomarker of ESCC by proteomic analysis using iTRAQ and 2D-LC-MS/MS. Proteomics Clin. Appl., **11**(9–10), 1600163. DOI: 10.1002/prca.201600163
205. *Cheng Y., Liu C., Zhang N., Wang S., Zhang Z.* (2014) Proteomics analysis for finding serum markers of ovarian cancer. Biomed Res. Int., **2014**, 179040. DOI: 10.1155/2014/179040
206. *Isgrò M.A., Bottoni P., Scatena R.* (2015) Neuron-specific enolase as a biomarker: biochemical and clinical aspects. Adv. Exp. Med. Biol., **867**, 125–143. DOI: 10.1007/978-94-017-7215-0_9
207. *Takashi M., Haimoto H., Tanaka J., Murase T., Kato K.* (1989) Evaluation of gamma-enolase as a tumor marker for renal cell carcinoma. J. Urol., **141**(4), 830–834. DOI: 10.1016/s0022-5347(17)41024-x
208. *Gong J., Jie Y., Xiao C., Zhou W., Li X., Chen Y., Wu Y., Cao J., Zhang Q., Gao Z., Hu B., Chong Y.* (2020) Increased expression of fibulin-1 is associated with hepatocellular carcinoma progression by regulating the notch signaling pathway. Front. Cell Dev. Biol., **8**, 478. DOI: 10.3389/fcell.2020.00478
209. *Watany M.M., Elmashad N.M., Badawi R., Hawash N.* (2018) Serum FBLN1 and STK31 as biomarkers of colorectal cancer and their ability to noninvasively differentiate colorectal cancer from benign polyps. Clin. Chim. Acta, **483**, 151–155. DOI: 10.1016/j.cca.2018.04.038
210. *Xia H., Feng L., Lin L., Jiang Z., Chen J., Shi W., Ying S., Yu M., Ju L., Zhu L., Shi L., Zhang X., Lou J.* (2021) Exploration of identifying novel serum biomarkers for malignant mesothelioma using iTRAQ combined with 2D-LC-MS/MS. Environ. Res., **193**, 110467. DOI: 10.1016/j.envres.2020.110467
211. *Zhu J., Chen R., Mo L., Tang H., Kuang Y., Fei W., He C., Hu X.* (2015) Expression of fibulin-1 predicted good prognosis in patients with colorectal cancer. Am. J Transl. Res., **7**(2), 339–347.
212. *Khan R., Gupta N., Kumar R., Sharma M., Kumar L., Sharma A.* (2014) Augmented expression of urokinase plasminogen activator and extracellular matrix proteins associates with multiple myeloma progression. Clin. Exp. Metastasis, **31**(5), 585–593. DOI: 10.1007/s10585-014-9652-7
213. *Świerzko A.S., Michalski M., Sokołowska A., Nowicki M., Szala-Poździej A., Eppa Ł., Mitrus I., Szmigielska-Kapłon A., Sobczyk-Kruszelnicka M., Michalak K., Gołos A., Wierzbowska A., Giebel S., Jamroziak K., Kowalski M.L., Brzezińska O., Thiel S., Matsushita M., Jensenius J.C., Gajek G., Cedzyński M.* (2019) Associations of ficolins with hematological malignancies in patients receiving

high-dose chemotherapy and autologous hematopoietic stem cell transplantations. Front. Immunol., **10**, 3097. DOI: 10.3389/fimmu.2019.03097
214. *Sokołowska A., Świerzko A.S., Gajek G., Gołos A., Michalski M., Nowicki M., Szala-Poździej A., Wolska-Washer A., Brzezińska O., Wierzbowska A., Jamroziak K., Kowalski M.L., Thiel S., Matsushita M., Jensenius J.C., Cedzyński M.* (2020) Associations of ficolins and mannose-binding lectin with acute myeloid leukaemia in adults. Sci. Rep., **10**, 10561. DOI: 10.1038/s41598-020-67516-2
215. *Li Q., Lin Y.* (2019) Evaluation of ficolin-3 as a potential prognostic serum biomarker in Chinese patients with esophageal cancer. Genet. Test. Mol. Biomarkers, **23**(8), 565–572. DOI: 10.1089/gtmb.2019.0045
216. *Okano T., Kondo T., Kakisaka T., Fujii K., Yamada M., Kato H., Nishimura T., Gemma A., Kudoh S., Hirohashi S.* (2006) Plasma proteomics of lung cancer by a linkage of multi-dimensional liquid chromatography and two-dimensional difference gel electrophoresis. Proteomics, **6**(13), 3938–3948. DOI: 10.1002/pmic.200500883
217. *Andersen J.D., Boylan K.L.M., Xue F.S., Anderson L.B., Witthuhn B.A., Markowski T.W., Higgins L., Skubitz A.P.N.* (2010) Identification of candidate biomarkers in ovarian cancer serum by depletion of highly abundant proteins and differential in-gel electrophoresis. Electrophoresis, **31**(4), 599–610. DOI: 10.1002/elps.200900441
218. *Wu A.H., Sell S.* (1990) Markers for hepatocellular carcinoma. Immunol. Series, **53**, 403–422.
219. *Behne T., Copur M.S.* (2012) Biomarkers for hepatocellular carcinoma. Int. J. Hepatol., **2012**, 859076. DOI: 10.1155/2012/859076
220. *Li D., Mallory T., Satomura S.* (2001) AFP-L3: a new generation of tumor marker for hepatocellular carcinoma. Clin. Chim. Acta, **313**(1–2), 15–19. DOI: 10.1016/s0009-8981(01)00644-1
221. *Stone L.* (2015) Fetuin-A — a marker for metastatic disease? Nat. Rev. Urol., **12**(4), 178. DOI: 10.1038/nrurol.2015.34
222. *Ochieng J., Nangami G., Sakwe A., Moye C., Alvarez J., Whalen D., Thomas P., Lammers P.* (2018) Impact of fetuin-A (AHSG) on tumor progression and type 2 diabetes. Int. J. Mol. Sci., **19**(8), 2211. DOI: 10.3390/ijms19082211
223. *Holm M., Joenväärä S., Saraswat M., Mustonen H., Tohmola T., Ristimäki A., Renkonen R., Haglund C.* (2019) Identification of several plasma proteins whose levels in colorectal cancer patients differ depending on outcome. FASEB BioAdvances, **1**(12), 723–730. DOI: 10.1096/fba.2019-00062
224. *Zhang X., Long Q.* (2017) Elevated serum plasma fibrinogen is associated with advanced tumor stage and poor survival in hepatocellular carcinoma patients. Medicine (Baltimore), **96**(17), e6694. DOI: 10.1097/MD.0000000000006694
225. *Bailey M.J., Shield-Artin K.L., Oliva K., Ayhan M., Reisman S., Rice G.E.* (2013) Stage-specific analysis of plasma protein profiles in ovarian cancer: difference in-gel electrophoresis analysis of pooled clinical samples. J. Carcinog., **12**, 10. DOI: 10.4103/1477-3163.114216
226. *Yang W., Shi J., Zhou Y., Liu T., Li J., Hong F., Zhang K., Liu N.* (2019) Co-expression network analysis identified key proteins in association with hepatic metastatic colorectal cancer. Proteomics Clin. Appl., **13**(6), e1900017. DOI: 10.1002/prca.201900017
227. *Zhu W.L., Fan B.L., Liu D.L., Zhu W.X.* (2009) Abnormal expression of fibrinogen gamma (FGG) and plasma level of fibrinogen in patients with hepatocellular carcinoma. Anticancer Res., **29**(7), 2531–2534.
228. *Peng H.H., Wang J.N., Xiao L.F., Yan M., Chen S.P., Wang L., Yang K.* (2021) Elevated serum FGG levels prognosticate and promote the disease progression in prostate cancer. Front. Genet., **12**, 651647. DOI: 10.3389/fgene.2021.651647
229. *Wang Z., Wang C., Huang X., Shen Y., Shen J., Ying K.* (2012) Differential proteome profiling of pleural effusions from lung cancer and benign inflammatory disease patients. Biochim. Biophys. Acta, **1824**(4), 692–700. DOI: 10.1016/j.bbapap.2012.01.016
230. *Gerner C., Steinkellner W., Holzmann K., Gsur A., Grimm R., Ensinger C., Obrist P., Sauermann G.* (2001) Elevated plasma levels of crosslinked fibrinogen gamma-chain dimer indicate cancer-related fibrin deposition and fibrinolysis. Thromb. Haemost., **85**(3), 494–501.
231. *Tas F., Bilgin E., Karabulut S., Tastekin D., Duranyildiz D.* (2016) Levels of serum fibronectin as a biomarker in gastric cancer patients: correlation with clinical diagnosis and outcome. Mol. Clin. Oncol., **4**(4), 655–659. DOI: 10.3892/mco.2016.759
232. *Moon P.-G, Lee J.-E., Cho Y.-E., Lee S.J., Chae Y.S., Jung J.H., Kim I.-S., Park H.Y., Baek M.-C.* (2016) Fibronectin on circulating extracellular vesicles as a liquid biopsy to detect breast cancer. Oncotarget, **7**(26), 40189–40199. DOI: 10.18632/oncotarget.9561
233. *Chai Y.D., Zhang L., Yang Y., Su T., Charugundla P., Ai J., Messadi D., Wong D.T., Hu S.* (2016) Discovery of potential serum protein biomarkers for lymph node metastasis in oral cancer. Head Neck, **38**(1), 118–125. DOI: 10.1002/hed.23870
234. *Kochi N., Tani E., Morimura T., Itagaki T.* (1983) Immunohistochemical study of fibronectin in human glioma and meningioma. Acta Neuropathol., **59**(2), 119–126. DOI: 10.1007/BF00691597
235. *Lin T.-C., Yang C.-H., Cheng L.-H., Chang W.-T., Lin Y.-R., Cheng H.-C.* (2019) Fibronectin in cancer: friend or foe. Cells, **9**(1), 27. DOI: 10.3390/cells9010027
236. *Paizi M., Manaster J., Quitt M., Spira G.* (1991) High plasma fibronectin levels in multiple myeloma patients: possible mechanisms and clinical implications. Scand. J. Immunol., **34**(3), 285–289. DOI: 10.1111/j.1365-3083.1991.tb01548.x
237. *Ivanova T.I., Klabukov I.D., Krikunova L.I., Poluektova M.V., Sychenkova N.I., Khorokhorina V.A., Vorobyev N.V., Gaas M.Y., Baranovskii D.S., Goryainova O.S., Sachko A.M., Shegay P.V., Kaprin A.D., Tillib S.V.* (2022) Prognostic value of serum transferrin analysis in patients with ovarian cancer and cancer-related functional iron deficiency: a retrospective case-control study. J. Clin. Med., **11**(24), 7377. DOI: 10.3390/jcm11247377
238. *Chen Z., Liang Z., Chen K., Zhang S., Huang X., Wu G., Zhu X.* (2024) Serum ferritin predicted prognosis in patients with nasopharyngeal carcinoma. Sci. Rep., **14**, 4311. DOI: 10.1038/s41598-024-54627-3
239. *Essen A., Ozen H., Ayhan A., Ergen A., Tasar C., Remzi F.* (1991) Serum ferritin: a tumor marker for renal cell carcinoma. J. Urol., **145**(6), 1134–1137. DOI: 10.1016/s0022-5347(17)38555-5
240. *Chiu C.-T., Wang P.-W., Asare-Werehene M., Tsang B.K., Shieh D.-B.* (2020) Circulating plasma gelsolin: a predictor of favorable clinical outcomes in head and neck cancer and sensitive biomarker for early disease diagnosis combined with soluble Fas ligand. Cancers, **12**(6), 1569. DOI: 10.3390/cancers12061569

241. *Tsai M.-H., Wu C.-C., Peng P.-H., Liang Y., Hsiao Y.-C., Chien K.-Y., Chen J.-T., Lin S.-J., Tang R.-P., Hsieh L.-L., Yu J.-S.* (2012) Identification of secretory gelsolin as a plasma biomarker associated with distant organ metastasis of colorectal cancer. J. Mol. Med. (Berlin), **90**(2), 187–200. DOI: 10.1007/s00109-011-0817-4
242. *Lee P.-S., Sampath K., Karumanchi S.A., Tamez H., Bhan I., Isakova T., Gutierrez O.M., Wolf M., Chang Y., Stossel T.P., Thadhani R.* (2009) Plasma gelsolin and circulating actin correlate with hemodialysis mortality. J. Am. Soc. Nephrol., **20**(5), 1140–1148. DOI: 10.1681/ASN.2008091008
243. *Agnani D., Camacho-Vanegas O., Camacho C., Lele S., Odunsi K., Cohen S., Dottino P., Martignetti J.A.* (2011) Decreased levels of serum glutathione peroxidase 3 are associated with papillary serous ovarian cancer and disease progression. J. Ovarian Res., **4**(1), 18. DOI: 10.1186/1757-2215-4-18
244. *Psathakis D., Wedemeyer N., Oevermann E., Krug F., Siegers C.P., Bruch H.P.* (1998) Blood selenium and glutathione peroxidase status in patients with colorectal cancer. Dis. Colon Rectum, **41**(3), 328–335. DOI: 10.1007/BF02237487
245. *van Belle S.J.-P.* (2004) What is the value of hemoglobin as a prognostic and predictive factor in cancer? Eur. J. Cancer Suppl., **2**(2), 11–19. DOI: 10.1016/S1359-6349(03)00103-4
246. *Fiorito V., Tolosano E.* (2022) Hemopexin and cancer. Int. J. Mol. Sci., **23**(2), 997. DOI: 10.3390/ijms23020997
247. *Comunale M.A., Lowman M., Long R.E., Krakover J., Philip R., Seeholzer S., Evans A.A., Hann H.-W.L., Block T.M., Mehta A.S.* (2006) Proteomic analysis of serum associated fucosylated glycoproteins in the development of primary hepatocellular carcinoma. J. Proteome Res., **5**(2), 308–315. DOI: 10.1021/pr050328x
248. *Cine N., Baykal Tarik A., Sunnetci D., Canturk Z., Serhatli M., Savli H.* (2014) Identification of ApoA1, HPX and POTEE genes by omic analysis in breast cancer. Oncol. Rep., **32**(3), 1078–1086. DOI: 10.3892/or.2014.3277
249. *Liao W.-Y., Ho C.-C., Hou H.-H., Hsu T.-H., Tsai M.-F., Chen K.-Y., Chen H.-Y., Lee Y.-C., Yu C.-J., Lee C.-H., Yang P.-C.* (2015) Heparin co-factor II enhances cell motility and promotes metastasis in non-small cell lung cancer. J. Pathol., **235**(1), 50–64. DOI: 10.1002/path.4421
250. *Namini N.M., Abdollahi A., Movahedi M., Razavi A.E., Saghiri R.* (2021) Association of *SERPIND1* expression with grade, stage and presence of metastasis in breast cancer. Indian J. Biochem. Biophys., **58**(1), 71–82. DOI: 10.56042/ijbb.v58i1.36308
251. *Beecken W.-D., Bentas W., Engels K., Glienke W., Urbschat A., Jonas D., Binder J., Scharrer I.* (2002) Reduced plasma levels of coagulation factors in relation to prostate cancer. Prostate, **53**(2), 160–167. sDOI: 10.1002/pros.10142
252. *Naryzhny S.N., Legina O.K.* (2021) Haptoglobin as a biomarker. Biomeditsinskaya Khimiya, **67**(2), 105–118. DOI: 10.18097/PBMC20216702105
253. *Zhao C., Annamalai L., Guo C., Kothandaraman N., Koh S.C.L., Zhang H., Biswas A., Choolani M.* (2007) Circulating haptoglobin is an independent prognostic factor in the sera of patients with epithelial ovarian cancer. Neoplasia, **9**(1), 1–7. DOI: 10.1593/neo.06619
254. *Garibay-Cerdenares O.L., Hernández-Ramírez V.I., Osorio-Trujillo J.C., Hernández-Ortíz M., Gallardo-Rincón D., Cantú de León D., Encarnación-Guevara S., Villegas-Pineda J.C., Talamás-Rohana P.* (2014) Proteomic identification of fucosylated haptoglobin alpha isoforms in ascitic fluids and its localization in ovarian carcinoma tissues from Mexican patients. J. Ovarian Res., **7**, 27. DOI: 10.1186/1757-2215-7-27
255. *Ye B., Cramer D.W., Skates S.J., Gygi S.P., Pratomo V., Fu L., Horick N.K., Licklider L.J., Schorge J.O., Berkowitz R.S. Mok S.C.* (2003) Haptoglobin-alpha subunit as potential serum biomarker in ovarian cancer: identification and characterization using proteomic profiling and mass spectrometry. Clin. Cancer Res., **9**(8), 2904–2911.
256. *Zhu J., Lin Z., Wu J., Yin H., Dai J., Feng Z., Marrero J., Lubman D.M.* (2014) Analysis of serum haptoglobin fucosylation in hepatocellular carcinoma and liver cirrhosis of different etiologies. J. Proteome Res., **13**(6), 2986–2997. DOI: 10.1021/pr500128t
257. *Wu J., Zhu J., Yin H., Buckanovich R.J., Lubman D.M.* (2014) Analysis of glycan variation on glycoproteins from serum by the reverse lectin-based ELISA assay. J. Proteome Res., **13**(4), 2197–2204. DOI: 10.1021/pr401061c
258. *Naryzhny S., Ronzhina N., Zorina E., Kabachenko F., Zavialova M., Zgoda V., Klopov N., Legina O., Pantina R.* (2021) Evaluation of haptoglobin and its proteoforms as glioblastoma markers. Int. J. Mol. Sci., **22**(12), 1–12. DOI: 10.3390/ijms22126533
259. *Ronzhina N.L., Zorina E.S., Zavyalova M.G., Legina O.K., Naryzhny S.N.* (2024) Variability of proteoforms of the beta chain of haptoglobin. Biomeditsinskaya Khimiya, **70**(2), 114–124. DOI: 10.18097/PBMC20247002114
260. *Epelbaum R., Shalitin C., Segal R., Valansi C., Arselan I., Faraggi D., Leviov M., Ben-Shahar M., Haim N.* (1998) Haptoglobin-related protein as a serum marker in malignant lymphoma. Pathol. Oncol. Res., **4**(4), 271–276. DOI: 10.1007/BF02905217
261. *Rong Y., Jin D., Hou C., Hu J., Wu W., Ni X., Wang D., Lou W.* (2010) Proteomics analysis of serum protein profiling in pancreatic cancer patients by DIGE: up-regulation of mannose-binding lectin 2 and myosin light chain kinase 2. BMC Gastroenterol., **10**, 68. DOI: 10.1186/1471-230X-10-68
262. *Ahmed M.B., Almogbel E., Khirry I., Hassan S., Salem T., Saeed A.* (2017) Diagnostic and prognostic significance of histidine-rich glycoprotein in acute lymphoblastic leukemia. Open J. Blood Dis., **7**, 16–28. DOI: 10.4236/ojbd.2017.71002
263. *Winiarska A., Zareba L., Krolczyk G., Czyzewicz G., Zabczyk M., Undas A.* (2019) Decreased levels of histidine-rich glycoprotein in advanced lung cancer: association with prothrombotic alterations. Dis. Markers, **2019**, 8170759. DOI: 10.1155/2019/8170759
264. *Göransson J., Jonsson S., Lasson A.* (1996) Pre-operative plasma levels of C-reactive protein, albumin and various plasma protease inhibitors for the pre-operative assessment of operability and recurrence in cancer surgery. Eur. J. Surg. Oncol., **22**(6), 607–617. DOI: 10.1016/S0748-7983(96)92398-7
265. *Lee C.-S., Taib N.A.M., Ashrafzadeh A., Fadzli F., Harun F., Rahmat K., Hoong S.M., Abdul-Rahman P.S., Hashim O.H.* (2016) Unmasking heavily O-glycosylated serum proteins using perchloric acid: identification of serum proteoglycan 4 and protease C1 inhibitor as molecular indicators for screening of breast cancer. PLOS One, **11**(2), e0149551. DOI: 10.1371/journal.pone.0149551

266. *Yakut M., Özkan H., Karakaya M.F., Erdal H.* (2018) Diagnostic and prognostic role of serum interleukin-6 in malignant transformation of liver cirrhosis. Euroasian J. Hepatogastroenterol., **8**(1), 23–30. DOI: 10.5005/jp-journals-10018-1253
267. *Tanouti I.-A., Fellah H., Haddaji A., Zerrad C., Tahiri M., Badre W., Nfaoui K., Pineau P., Benjelloun S., Ezzikouri S.* (2024) High plasma interleukin-6 level, but not IL-6 gene variants, as a predictive marker for the development of hepatocellular carcinoma in a Moroccan population. Int. J. Immunogenet., **51**(4), 206–216. DOI: 10.1111/iji.12669
268. *Łukaszewicz-Zając M., Mroczko B., Kozłowski M., Nikliński J., Laudański J., Szmitkowski M.* (2012) Higher importance of interleukin 6 than classic tumor markers (carcinoembryonic antigen and squamous cell cancer antigen) in the diagnosis of esophageal cancer patients. Dis. Esophagus, **25**(3), 242–249. DOI: 10.1111/j.1442-2050.2011.01242.x
269. *Hamm A., Veeck J., Bektas N., Wild P.J., Hartmann A., Heindrichs U., Kristiansen G., Werbowetski-Ogilvie T., del Maestro R., Knuechel R., Dahl E.* (2008) Frequent expression loss of inter-alpha-trypsin inhibitor heavy chain (ITIH) genes in multiple human solid tumors: a systematic expression analysis. BMC Cancer, **8**, 25. DOI: 10.1186/1471-2407-8-25
270. *Jiang X., Bai X.-Y., Li B., Li Y., Xia K., Wang M., Li S., Wu H.* (2019) Plasma inter-alpha-trypsin inhibitor heavy chains H3 and H4 serve as novel diagnostic biomarkers in human colorectal cancer. Dis. Markers, **2019**, 5069614. DOI: 10.1155/2019/5069614
271. *Chang Q.-H., Mao T., Tao Y., Dong T., Tang X.-X., Ge G.-H., Xu Z.-J.* (2021) Pan-cancer analysis identifies ITIH1 as a novel prognostic indicator for hepatocellular carcinoma. Aging (Albany NY), **13**(8), 11096–11119. DOI: 10.18632/aging.202765
272. *Chong P.K., Lee H., ZhouJ., Liu S.-C., Loh M.C.S., Wang T.T., Chan S.P., Smoot D.T., Ashktorab H., So J.B.Y., Lim K.H., Yeoh K.G., Lim Y.P.* (2010) ITIH3 is a potential biomarker for early detection of gastric cancer. J. Proteome Res., **9**(7), 3671–3679. DOI: 10.1021/pr100192h
273. *Sun Y., Jin J., Jing H., Lu Y., Zhu Q., Shu C., Zhang Q., Jing D.* (2021) ITIH4 is a novel serum biomarker for early gastric cancer diagnosis. Clin. Chim. Acta, **523**, 365–373. DOI: 10.1016/j.cca.2021.10.022
274. *Ura B., Biffi S., Monasta L., Arrigoni G., Battisti I., di Lorenzo G., Romano F., Aloisio M., Celsi F., Addobbati R., Valle F., Rampazzo E., Brucale M., Ridolfi A., Licastro D., Ricci G.* (2021) Two dimensional-difference in gel electrophoresis (2D-DIGE) proteomic approach for the identification of biomarkers in endometrial cancer serum. Cancers, **13**(14), 3639. DOI: 10.3390/cancers13143639
275. *Chapman M.H., Sandanayake N.S., Andreola F., Dhar D.K., Webster G.J., Dooley J.S., Pereira S.P.* (2011) Circulating CYFRA 21-1 is a specific diagnostic and prognostic biomarker in biliary tract cancer. J. Clin. Exp. Hepatol., **1**(1), 6–12. DOI: 10.1016/S0973-6883(11)60110-2
276. *Brockmann J.G., St Nottberg H., Glodny B., Heinecke A., Senninger N.J.* (2000) CYFRA 21-1 serum analysis in patients with esophageal cancer. Clin. Cancer Res., **6**(11), 4249–4252.
277. *Pavićević R., Milicić J., Bubanović G., Supe S.* (1998) Serum tumor marker CYFRA 21-1 in the diagnostics of NSCLC lung cancer. Collegium Antropologicum, **22**(2), 629–635.
278. *Jeong S., Park Y., Cho Y., Kim Y.R., Kim H.-S.* (2012) Diagnostic values of urine CYFRA21-1, NMP22, UBC, and FDP for the detection of bladder cancer. Clin. Chim. Acta, **414**, 93–100. DOI: 10.1016/j.cca.2012.08.018
279. *Cheng Z., Lv Y., Pang S., Bai R., Wang M., Lin S., Xu T., Spalding D., Habib N., Xu R.* (2015) Kallistatin, a new and reliable biomarker for the diagnosis of liver cirrhosis. Acta Pharm. Sin. B, **5**(3), 194–200. DOI: 10.1016/j.apsb.2015.02.003
280. *Ma C., Luo C., Yin H., Zhang Y., Xiong W., Zhang T., Gao T., Wang X., Che D., Fang Z., Li L., Xie J., Huang M., Zhu L., Jiang P., Qi W., Zhou T., Yang Z., Wang W., Ma J., Gao G., Yang X.* (2018) Kallistatin inhibits lymphangiogenesis and lymphatic metastasis of gastric cancer by downregulating VEGF-C expression and secretion. Gastric Cancer, **21**(4), 617–631. DOI: 10.1007/s10120-017-0787-5
281. *Luo L.-Y., Katsaros D., Scorilas A., Fracchioli S., Bellino R., van Gramberen M., de Bruijn H., Henrik A., Stenman U.-H., Massobrio M., van der Zee A.G.J., Vergote I., Diamandis E.P.* (2003) The serum concentration of human kallikrein 10 represents a novel biomarker for ovarian cancer diagnosis and prognosis. Cancer Res., **63**(4), 807–811.
282. *David M.K., Leslie S.W.* (2024) Prostate-Specific Antigen. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557495/
283. *Wang J., Wang X., Lin S., Chen C., Wang C., Ma Q., Jiang B.* (2013) Identification of kininogen-1 as a serum biomarker for the early detection of advanced colorectal adenoma and colorectal cancer. PLOS One, **8**(7), e70519. DOI: 10.1371/journal.pone.0070519
284. *Yu J., Huang Y., Lin C., Li X., Fang X., Zhong C., Yuan Y., Zheng S.* (2018) Identification of kininogen 1 as a serum protein marker of colorectal adenoma in patients with a family history of colorectal cancer. J. Cancer, **9**(3), 540–547. DOI: 10.7150/jca.22405
285. *Amoev Z.V., Alyasova A.V., Gorshkova T.N., Samsonova E.I., Strokina E.V., Kontorshchikova K.N.* (2020) Tumor M2-pyruvate kinase, matrix carbonic anhydrase IX, and metalloproteinase 9 — novel prognostic markers of renal cell carcinoma. Sovremennye Tehnologii v Medicine, **12**(2), 43–47. DOI: 10.17691/stm2020.12.2.05
286. *Lüftner D., Mesterharm J., Akrivakis C., Geppert R., Petrides P.E., Wernecke K.D., Possinger K.* (2000) Tumor type M2 pyruvate kinase expression in advanced breast cancer. Anticancer Res., **20**(6D), 5077–5082.
287. *Giatagana E.-M., Berdiaki A., Tsatsakis A., Tzanakakis G.N., Nikitovic D.* (2021) Lumican in carcinogenesis — revisited. Biomolecules, **11**(9), 1319. DOI: 10.3390/biom11091319
288. *Pan S., Chen R., Brand R.E., Hawley S., Tamura Y., Gafken P.R., Milless B.P., Goodlett D.R., Rush J., Brentnall T.A.* (2012) Multiplex targeted proteomic assay for biomarker detection in plasma: a pancreatic cancer biomarker case study. J. Proteome Res., **11**(3), 1937–1948. DOI: 10.1021/pr201117w
289. *Appunni S., Anand V., Khandelwal M., Seth A., Mathur S., Sharma A.* (2017) Altered expression of small leucine-rich proteoglycans (Decorin, Biglycan and Lumican): plausible diagnostic marker in urothelial carcinoma of bladder. Tumour Biol., **39**(5), 1010428317699112. DOI: 10.1177/1010428317699112
290. *Su C., Lin Y., Cai L., Mao Q., Niu J.* (2016) Association between mannose-binding lectin variants, haplotypes and risk of hepatocellular carcinoma: a case-control study. Sci. Rep., **6**, 32147. DOI: 10.1038/srep32147

291. *Nikkola J., Vihinen P., Vuoristo M.-S., Kellokumpu-Lehtinen P., Kähäri V.-M., Pyrhönen S.* (2005) High serum levels of matrix metalloproteinase-9 and matrix metalloproteinase-1 are associated with rapid progression in patients with metastatic melanoma. Clin. Cancer Res., **11**(14), 5158–5166. DOI: 10.1158/1078-0432.CCR-04-2478
292. *Dyachenko E.I., Bel'skaya L.V.* (2024) Salivary transmembrane mucins of the MUC1 family (CA 15-3, CA 27.29, MCA) in breast cancer: the effect of human epidermal growth factor receptor 2 (HER2). Cancers, **16**(20), 3461. DOI: 10.3390/cancers16203461
293. *Lawicki S., Bкdkowska G.E., Gacuta-Szumarska E., Szmitkowski M.* (2013) The plasma concentration of VEGF, HE4 and CA125 as a new biomarkers panel in different stages and sub-types of epithelial ovarian tumors. J. Ovarian Res., **6**(1), 45. DOI: 10.1186/1757-2215-6-45
294. *Duk J.M., Aalders J.G., Fleuren G.J., de Bruijn H.W.* (1986) CA 125: a useful marker in endometrial carcinoma. Am. J. Obstet. Gynecol., **155**(5), 1097–1102. DOI: 10.1016/0002-9378(86)90358-3
295. *Shimada Y., Watanabe G., Kawamura J., Soma T., Okabe M., Ito T., Inoue H., Kondo M., Mori Y., Tanaka E., Imamura M.* (2005) Clinical significance of osteopontin in esophageal squamous cell carcinoma: comparison with common tumor markers. Oncology, **68**(2–3), 285–292. DOI: 10.1159/000086961
296. *Maier T., Laubender R.P., Sturm R.A., Klingenstein A., Korting H.C., Ruzicka T., Berking C.* (2012) Osteopontin expression in plasma of melanoma patients and in melanocytic tumours. J. Eur. Acad. Dermatol. Venereol., **26**(9), 1084–1091. DOI: 10.1111/j.1468-3083.2011.04210.x
297. *Cho H., Hong S.W., Oh Y.J., Kim M.A., Kang E.S., Lee J.M., Kim S.W., Kim S.H., Kim J.H., Kim Y.T., Lee K.* (2008) Clinical significance of osteopontin expression in cervical cancer. J. Cancer Res. Clin. Oncol., **134**(8), 909–917. DOI: 10.1007/s00432-007-0351-5
298. *Nedjadi T., Albarakati N., Benabdelkamel H., Masood A., Alfadda A.A., Al-Maghrabi J.* (2021) Proteomic profiling of plasma-derived biomarkers in patients with bladder cancer: a step towards clinical translation. Life (Basel), **11**(12), 1294. DOI: 10.3390/life11121294
299. *Jackson D., Craven R.A., Hutson R.C., Graze I., Lueth P., Tonge R.P., Hartley J.L., Nickson J.A., Rayner S.J., Johnston C., Dieplinger B., Hubalek M., Wilkinson N., Perren T.J., Kehoe S., Hall G.D., Daxenbichler G., Dieplinger H., Selby P.J,. Banks R.E.* (2007) Proteomic profiling identifies afamin as a potential biomarker for ovarian cancer. Clin. Cancer Res., **13**(24), 7370–7379. DOI: 10.1158/1078-0432.CCR-07-0747
300. *Ide H., Yamagishi S.-I., Lu Y., Sakamaki K., Nakajima A., Horiuchi A., Kitamura K., Hisasue S.-I., Muto S., Yamaguchi R., Horie S.* (2015) Circulating pigment epithelium-derived factor (PEDF) is associated with pathological grade of prostate cancer. Anticancer Res., **35**(3), 1703–1708.
301. *Yang Z., Feng J., Xiao L., Chen X., Yao Y., Li Y., Tang Y., Zhang S., Lu M., Qian Y., Wu H., Shi M.* (2020) Tumor-derived peptidoglycan recognition protein 2 predicts survival and antitumor immune responses in hepatocellular carcinoma. Hepatology, **71**(5), 1626–1642. DOI: 10.1002/hep.30924
302. *Yang L., Cui R., Li Y., Liang K., Ni M., Gu Y.* (2020) Hypoxia-induced TGFBI as a serum biomarker for laboratory diagnosis and prognosis in patients with pancreatic ductal adenocarcinoma. Lab. Med., **51**(4), 352–361. DOI: 10.1093/labmed/lmz063
303. *Kang D.W., Choi K.-Y., Min D.S.* (2014) Functional regulation of phospholipase D expression in cancer and inflammation. J. Biol. Chem., **289**(33), 22575–22582. DOI: 10.1074/jbc.R114.569822
304. *Tang J.-H., He W.-J., Huang H., Tan C.-C., Duan Q., Wang K.-J., Yuan X.-Y., Zhu X.-J.* (2009) Important roles of glycosylphosphatidylinositol (GPI)-specific phospholipase D and some GPI-anchored proteins in the pathogenesis of hepatocellular carcinoma. Clin. Biochem., **42**(4–5), 400–407. DOI: 10.1016/j.clinbiochem.2008.11.019
305. *Kwaan H.C., McMahon B.* (2009) The role of plasminogen-plasmin system in cancer. Cancer Treat. Res., **148**, 43–66. DOI: 10.1007/978-0-387-79962-9_4
306. *Bharadwaj A.G., Holloway R.W., Miller V.A., Waisman D.M.* (2021) Plasmin and plasminogen system in the tumor microenvironment: implications for cancer diagnosis, prognosis, and therapy. Cancers, **13**(8), 1838. DOI: 10.3390/cancers13081838
307. *Vecka M., Jáchymová M., Vávrová L., Kodydková J., Macášek J., Urbánek M., Krechler T., Slabý A., Dušková J., Muravská A., Zák A.* (2012) Paraoxonase-1 (PON1) status in pancreatic cancer: relation to clinical parameters. Folia Biologica, **58**(6), 231–237.
308. *Aldonza M.B.D., Son Y.S., Sung H.-J., Ahn J.M., Choi Y.-J., Kim Y.-I., Cho S., Cho J.-Y.* (2017) Paraoxonase-1 (PON1) induces metastatic potential and apoptosis escape via its antioxidative function in lung cancer cells. Oncotarget, **8**(26), 42817–42835. DOI: 10.18632/oncotarget.17069
309. *Ahn S.B., Sharma S., Mohamedali A., Mahboob S., Redmond W.J., Pascovici D., Wu J.X., Zaw T., Adhikari S., Vaibhav V., Nice E.C., Baker M.S.* (2019) Potential early clinical stage colorectal cancer diagnosis using a proteomics blood test panel. Clin. Proteomics, **16**, 34. DOI: 10.1186/s12014-019-9255-z
310. *Afsar C.U., Gunaldı M., Okuturlar Y., Gedikbası A., Tiken E.E., Kahraman S., Karaca F., Ercolak V., Karabulut M.* (2015) Paraoxonase-1 and arylesterase activities in patients with colorectal cancer. Int. J. Clin. Exp. Med., **8**(11), 21599–21604.
311. *Akçay M.N., Yilmaz I., Polat M.F., Akçay G.* (2003) Serum paraoxonase levels in gastric cancer. Hepato-gastroenterology, **50 Suppl 2**, cclxxiii–cclxxv.
312. *Hung M.J., Oremek G.M.* (2011) Value of TRAcP 5b as a diagnostic marker for detection of bone metastases in patients with breast cancer. Eur. J. Gynaecol. Oncol., **32**(6), 615–618.
313. *Schlesinger M., Broman I., Lugassy G.* (1996) The complement system is defective in chronic lymphatic leukemia patients and in their healthy relatives. Leukemia, **10**(9), 1509–1513.
314. *Uehara S., Fukuzawa Y., Matuyama T., Gotoh K.* (2017) Role of Tyro 3, Axl, and Mer receptors and their ligands (Gas 6, and Protein S) in patients with hepatocellular carcinoma. J. Cancer Ther., **8**(2), 112–130. DOI: 10.4236/jct.2017.82010
315. *Bushue N., Wan Y.-J.Y.* (2010) Retinoid pathway and cancer therapeutics. Adv. Drug Deliv. Rev., **62**(13), 1285–1298. DOI: 10.1016/j.addr.2010.07.003
316. *Hu X., Huang W., Wang F., Dai Y., Hu X., Yue D., Wang S.* (2020) Serum levels of retinol-binding protein 4 and the risk of non-small cell lung cancer: a case-control study. Medicine (Baltimore), **99**(31), e21254. DOI: 10.1097/MD.0000000000021254

317. *Jiao C., Cui L., Ma A., Li N., Si H.* (2016) Elevated serum levels of retinol-binding protein 4 are associated with breast cancer risk: a case-control study. PLOS One, **11**(12), e0167498. DOI: 10.1371/journal.pone.0167498
318. *Biaoxue R., Hua L., Wenlong G., Shuanying Y.* (2016) Increased serum amyloid A as potential diagnostic marker for lung cancer: a meta-analysis based on nine studies. BMC Cancer, **16**, 836. DOI: 10.1186/s12885-016-2882-0
319. *Malle E., Sodin-Semrl S., Kovacevic A.* (2009) Serum amyloid A: an acute-phase protein involved in tumour pathogenesis. Cell. Mol. Life Sci., **66**(1), 9–26. DOI: 10.1007/s00018-008-8321-x
320. *Wang J.-Y., Zheng Y.-Z., Yang J., Lin Y.-H., Dai S.-Q., Zhang G., Liu W.-L.* (2012) Elevated levels of serum amyloid A indicate poor prognosis in patients with esophageal squamous cell carcinoma. BMC Cancer, **12**, 365. DOI: 10.1186/1471-2407-12-365
321. *Kaneti J., Winikoff Y., Zimlichman S., Shainkin-Kestenbaum R.* (1984) Importance of serum amyloid A (SAA) level in monitoring disease activity and response to therapy in patients with prostate cancer. Urol. Res., **12**(5), 239–241. DOI: 10.1007/BF00256147
322. *Zhang G., Sun X., Lv H., Yang X., Kang X.* (2012) Serum amyloid A: a new potential serum marker correlated with the stage of breast cancer. Oncol. Lett., **3**(4), 940–944. DOI: 10.3892/ol.2012.584
323. *Yokoi K., Raber M.N., Shih L.-C.N., Li D., Hamilton S.R., Fidler I.J., Abbruzzese J.L.* (2004) Serum amyloid A (SAA) in patients with pancreatic carcinoma. J. Clin. Oncol., **22**(14_suppl), 9649. DOI: 10.1200/jco.2004.22.90140.9649
324. *Lin H.-Y., Tan G.-Q., Liu Y., Lin S.-Q.* (2019) The prognostic value of serum amyloid A in solid tumors: a meta-analysis. Cancer Cell Int., **19**(1), 62. DOI: 10.1186/s12935-019-0783-4
325. *Levo Y., Wollner S., Treves A.J.* (1986) Serum amyloid P-component levels in patients with malignancy. Scand. J. Immunol., **24**(2), 147–151. DOI: 10.1111/j.1365-3083.1986.tb02080.x
326. *de Nunzio C., Lombardo R., Albisinni S., Gacci M., Tubaro A.* (2013) Serum levels of sex hormone binding globulin (SHBG) are not predictive of prostate cancer diagnosis and aggressiveness: results from an Italian biopsy cohort. Int. Braz. J. Urol, **39**(6), 793–799. DOI: 10.1590/S1677-5538.IBJU.2013.06.04
327. *Cheng C.-W., Chang C.-C., Patria Y.N., Chang R.-T., Liu Y.-R., Li F.-A., Shih H.-M., Lin C.-Y.* (2018) Sex hormone-binding globulin (SHBG) is a potential early diagnostic biomarker for gastric cancer. Cancer Med., **7**(1), 64–74. DOI: 10.1002/cam4.1254
328. *Gebhardt C., Németh J., Angel P., Hess J.* (2006) S100A8 and S100A9 in inflammation and cancer. Biochem. Pharmacol., **72**(11), 1622–1631. DOI: 10.1016/j.bcp.2006.05.017
329. *Petsa A., Pergialiotis V., Konstantopoulos P., Katsichti A., Petrou K., Giannopoulos A., Botsis D., Perrea D.* (2017) Serum calprotectin and prealbumin levels among ovarian cancer patients aged 30-45 years. Open J. Obstet. Gynecol., **7**, 303–311. DOI: 10.4236/ojog.2017.73032
330. *Ni Bhriain H., Trovik J., Wik E., Stefansson I.M., Akslen L.A., Salvesen H.B., Staff A.C.* (2009) Plasma calprotectin concentrations in women with endometrial carcinoma. Gynecol. Oncol., **114**(3), 491–495. DOI: 10.1016/j.ygyno.2009.06.008
331. *Kim H.J., Kang H.J., Lee H., Lee S.T., Yu M.H., Kim H., Lee C.* (2009) Identification of S100A8 and S100A9 as serological markers for colorectal cancer. J. Proteome Res., **8**(3), 1368–1379. DOI: 10.1021/pr8007573
332. *Wang L., Chang E.W.Y., Wong S.C., Ong S.-M., Chong D.Q.Y., Ling K.L.* (2013) Increased myeloid-derived suppressor cells in gastric cancer correlate with cancer stage and plasma S100A8/A9 proinflammatory proteins. J. Immunol., **190**(2), 794–804. DOI: 10.4049/jimmunol.1202088
333. *Markowitz J., Carson W.E. 3rd* (2013) Review of S100A9 biology and its role in cancer. Biochim. Biophys. Acta, **1835**(1), 100–109. DOI: 10.1016/j.bbcan.2012.10.003
334. *Jury C.S., Mcallister E.J., Mackie R.M.* (2000) Rising levels of serum S100 protein precede other evidence of disease progression in patients with malignant melanoma. Br. J. Dermatol., **143**(2), 269–274. DOI: 10.1046/j.1365-2133.2000.03650.x
335. *Polivka J., Gouda M.A., Sharif M., Pesta M., Huang H., Treskova I., Woznica V., Windrichova J., Houfkova K., Kucera R., Fikrle T., Ricar J., Pivovarcikova K., Topolcan O., Janku F.* (2024) Predictive significance of combined plasmatic detection of BRAF mutations and S100B tumor marker in early-stage malignant melanoma. Cancer Med., **13**(19), e70313. DOI: 10.1002/cam4.70313
336. *Sehitogulları A., Aslan M., Sayır F., Kahraman A., Demir H.* (2014) Serum paraoxonase-1 enzyme activities and oxidative stress levels in patients with esophageal squamous cell carcinoma. Redox Rep., **19**(5), 199–205. DOI: 10.1179/1351000214Y.0000000091
337. *Zhu H.* (2022) Squamous cell carcinoma antigen: clinical application and research status. Diagnostics, **12**(5), 1065. DOI: 10.3390/diagnostics12051065
338. *Kagohashi K., Satoh H., Kurishima K., Kadono K., Ishikawa H., Ohtsuka M., Sekizawa K.* (2008) Squamous cell carcinoma antigen in lung cancer and nonmalignant respiratory diseases. Lung, **186**(5), 323–326. DOI: 10.1007/s00408-008-9108-4
339. *Begum F.D., Høgdall C.K., Kjaer S.K., Christensen L., Blaakaer J., Bock J.E., Glud E., Høyer-Hansen G., Ring-Larsen H., Høgdall E.V.S.* (2004) The prognostic value of plasma soluble urokinase plasminogen activator receptor (suPAR) levels in stage III ovarian cancer patients. Anticancer Res., **24**(3b), 1981–1985.
340. *Arellano-Garcia M.E., Li R., Liu X., Xie Y., Yan X., Loo J.A., Hu S.* (2010) Identification of tetranectin as a potential biomarker for metastatic oral cancer. Int. J. Mol. Sci., **11**(9), 3106–3121. DOI: 10.3390/ijms11093106
341. *Lemos-González Y., Rodríguez-Berrocal F.J., Cordero O.J., Gómez C., Páez de la Cadena M.* (2007) Alteration of the serum levels of the epidermal growth factor receptor and its ligands in patients with non-small cell lung cancer and head and neck carcinoma. Br. J. Cancer, **96**(10), 1569–1578. DOI: 10.1038/sj.bjc.6603770
342. *Agrusa J.E., Scull B.P., Abhyankar H.A., Lin H., Ozuah N.W., Chakraborty R., Eckstein O.S., Gulati N., Fattah E.A., El-Mallawany N.K., Rouce R.H., Dreyer Z.E., Brackett J., Margolin J.F., Lubega J., Horton T.M., Bollard C.M., Gramatges M.M., Kamdar K.Y., McClain K.L., Man T.K., Allen C.E.* (2020) Defining the inflammatory plasma proteome in pediatric Hodgkin lymphoma. Cancers, **12**(12), 3603. DOI: 10.3390/cancers12123603
343. *Terui S., Moriya Y., Yamamoto H., Koyama Y.* (1987) Thyroxine-binding globulin as a marker of liver tumors. Cancer Detect. Prev., **10**(5–6), 371–378.

344. *Sieg A., Schönpflug A., Seitz H.K., Kommerell B.* (1991) [Thyroxine-binding globulin — not a tumor marker of hepatocellular cancer]. Zeitschrift fur Gastroenterologie, **29**(3), 101–104.
345. *Cui S.-X., Yu X.-F., Qu X.-J.* (2016) Roles and signaling pathways of des-γ-carboxyprothrombin in the progression of hepatocellular carcinoma. Cancer Invest., **34**(9), 459–464. DOI: 10.1080/07357907.2016.1227445
346. *Yang Y., Li G., Lu Z., Liu Y., Kong J., Liu J.* (2021) Progression of prothrombin induced by vitamin K absence-II in hepatocellular carcinoma. Front. Oncol., **11**, 726213. DOI: 10.3389/fonc.2021.726213
347. *Feng X., Song P., Bie P., Jiang P., Ma K., Li X., Wang S., Wang Z., Tang W., Zheng S.* (2016) Des-γ-carboxyprothrombin plasma level in diagnosis of hepatocellular carcinoma in a Chinese population undergoing surgery. Med. Sci. Monit., **22**, 1663–1672. DOI: 10.12659/msm.895483
348. *Jain S., Gautam V., Naseem S.* (2011) Acute-phase proteins: as diagnostic tool. J. Pharm. Bioallied Sci., **3**(1), 118–127. DOI: 10.4103/0975-7406.76489
349. *Lee C.-C., Ding X., Zhao T., Wu L., Perkins S., Du H., Yan C.* (2019) Transthyretin stimulates tumor growth through regulation of tumor, immune, and endothelial cells. J. Immunol., **202**(3), 991–1002. DOI: 10.4049/jimmunol.1800736
350. *Shimura T., Shibata M., Gonda K., Okayama H., Saito M., Momma T., Ohki S., Kono K.* (2018) Serum transthyretin level is associated with prognosis of patients with gastric cancer. J. Surg. Res., **227**, 145–150. DOI: 10.1016/j.jss.2018.02.035
351. *Gericke B., Raila J., Sehouli J., Haebel S., Könsgen D., Mustea A., Schweigert F.J.* (2005) Microheterogeneity of transthyretin in serum and ascitic fluid of ovarian cancer patients. BMC Cancer, **5**, 133. DOI: 10.1186/1471-2407-5-133
352. *Liu L., Wang J., Liu B., Dai S., Wang X., Chen J., Huang L., Xiao X., He D.* (2008) Serum levels of variants of transthyretin down-regulation in cholangiocarcinoma. J. Cell. Biochem., **104**(3), 745–755. DOI: 10.1002/jcb.21661
353. *Shimura T., Shibata M., Inoue T., Owada-Ozaki Y., Yamaura T., Muto S., Hasegawa T., Shio Y., Suzuki H.* (2019) Prognostic impact of serum transthyretin in patients with non-small cell lung cancer. Mol. Clin. Oncol., **10**(6), 597–604. DOI: 10.3892/mco.2019.1837
354. *Grenache D.G., Heichman K.A., Werner T.L., Vucetic Z.* (2015) Clinical performance of two multi-marker blood tests for predicting malignancy in women with an adnexal mass. Clin. Chim. Acta, **438**, 358–363. DOI: 10.1016/j.cca.2014.09.028
355. *Hertlein L., Stieber P., Kirschenhofer A., Krocker K., Nagel D., Lenhard M., Burges A.* (2012) Human epididymis protein 4 (HE4) in benign and malignant diseases. Clin. Chem. Lab. Med., **50**(12), 2181–2188. DOI: 10.1515/cclm-2012-0097
356. *Malik S., Fu L., Juras D.J., Karmali M., Wong B.Y.L., Gozdzik A., Cole D.E.C.* (2013) Common variants of the vitamin D binding protein gene and adverse health outcomes. Crit. Rev. Clin. Lab. Sci., **50**(1), 1–22. DOI: 10.3109/10408363.2012.750262
357. *Speeckaert M., Huang G., Delanghe J.R., Taes Y.E.C.* (2006) Biological and clinical aspects of the vitamin D binding protein (Gc-globulin) and its polymorphism. Clin. Chim. Acta, **372**(1-2), 33–42. DOI: 10.1016/j.cca.2006.03.011
358. *Bera A., Subramanian M., Karaian J., Eklund M., Radhakrishnan S., Gana N., Rothwell S., Pollard H., Hu H., Shriver C.D., Srivastava M.* (2020) Functional role of vitronectin in breast cancer. PLOS One, **15**(11), e0242141. DOI: 10.1371/journal.pone.0242141
359. *Hassan M.I., Waheed A., Yadav S., Singh T.P., Ahmad F.* (2008) Zinc alpha 2-glycoprotein: a multidisciplinary protein. Mol. Cancer Res., **6**(6), 892–906. DOI: 10.1158/1541-7786.MCR-07-2195
360. *Hale L.P., Price D.T., Sanchez L.M., Demark-Wahnefried W., Madden J.F.* (2001) Zinc alpha-2-glycoprotein is expressed by malignant prostatic epithelium and may serve as a potential serum marker for prostate cancer. Clin. Cancer Res., **7**(4), 846–853.
361. *Bundred N.J., Scott W.N., Davies S.J., Miller W.R., Mansel R.E.* (1991) Zinc alpha-2 glycoprotein levels in serum and breast fluids: a potential marker of apocrine activity. Eur. J. Cancer, **27**(5), 549–552. DOI: 10.1016/0277-5379(91)90213-w
362. *Xue Y., Yu F., Yan D., Cui F., Tang H., Wang X., Chen J., Lu H., Zhao S., Peng Z.* (2014) Zinc-α-2-glycoprotein: a candidate biomarker for colon cancer diagnosis in Chinese population. Int. J. Mol. Sci., **16**(1), 691–703. DOI: 10.3390/ijms16010691
363. *Filella X., Molina R., Jo J., Bedini J.L., Joseph J., Ballesta A.M.* (1992) Tumor associated glycoprotein-72 (TAG-72) levels in patients with non-malignant and malignant disease. Bulletin du Cancer, **79**(3), 271–277.
364. *Hu P.-J., Chen M.-Y., Wu M.-S., Lin Y.-C., Shih P.-H., Lai C.-H., Lin H.-J.* (2019) Clinical evaluation of CA72-4 for screening gastric cancer in a healthy population: a multicenter retrospective study. Cancers, **11**(5), 733. DOI: 10.3390/cancers11050733
365. *Bray K.R., Koda J.E., Gaur P.K.* (1987) Serum levels and biochemical characteristics of cancer-associated antigen CA-549, a circulating breast cancer marker. Cancer Res., **47**(22), 5853–5860.
366. *Zamagni C., Martoni A., Cacciari N., Bellanova B., Vecchi F., Pannuti F.* (1992) CA-549 serum levels in breast cancer monitoring. Int. J. Biol. Markers, **7**(4), 217–221. DOI: 10.1177/172460089200700402
367. *le Large T.Y.S., Meijer L.L., Paleckyte R., Boyd L.N.C., Kok B., Wurdinger T., Schelfhorst T., Piersma S.R., Pham T.V., van Grieken N.C.T., Zonderhuis B.M., Daams F., van Laarhoven H.W.M., Bijlsma M.F., Jimenez C.R., Giovannetti E., Kazemier G.* (2020) Combined expression of plasma thrombospondin-2 and CA19-9 for diagnosis of pancreatic cancer and distal cholangiocarcinoma: a proteome approach. Oncologist, **25**(4), e634–e643. DOI: 10.1634/theoncologist.2019-0680
368. (2024) Clinical guidelines // Ministry of Health of the Russian Federation. Retrieved January 17, 2025, from: https://oncology-association.ru/clinical-guidelines-update#nav-main
369. *Arnold M., Soerjomataram I., Ferlay J., Forman D.* (2015) Global incidence of oesophageal cancer by histological subtype in 2012. Gut, **64**(3), 381–387. DOI: 10.1136/gutjnl-2014-308124
370. *d'Journo X.B., Thomas P.A.* (2014) Current management of esophageal cancer. J. Thorac. Dis., **6**(S2), S253-S264. DOI: 10.3978/j.issn.2072-1439.2014.04.16
371. *Lessi F., Franceschi S., Morelli M., Menicagli M., Pasqualetti F., Santonocito O., Gambacciani C., Pieri F., Aquila F., Aretini P., Mazzanti C.M.* (2022) Single-cell

molecular characterization to partition the human glioblastoma tumor microenvironment genetic background. Cells, **11**(7), 1127. DOI: 10.3390/cells11071127

372. *Kopylov A.M., Antipova O.A., Pavlova G.V.* (2022) Molecular markers of neuro-oncogenesis in patients with glioblastoma. Burdenko's Journal of Neurosurgery, **86**(6), 99–105. DOI: 10.17116/neiro20228606199
373. *Tan A.C., Ashley D.M., López G.Y., Malinzak M., Friedman H.S., Khasraw M.* (2020) Management of glioblastoma: state of the art and future directions. CA Cancer J. Clin., **70**(4), 299–312. DOI: 10.3322/caac.21613
374. *Patel A.P., Tirosh I., Trombetta J.J., Shalek A.K., Gillespie S.M., Wakimoto H., Cahill D.P., Nahed B.V., Curry W.T., Martuza R.L., Louis D.N., Rozenblatt-Rosen O., Suvà M.L., Regev A., Bernstein B.E.* (2014) Single-cell RNA-seq highlights intratumoral heterogeneity in primary glioblastoma. Science, **344**(6190), 1396–1401. DOI: 10.1126/science.1254257
375. Tumor markers: primary liver cancer. Retrived January 23, 2025, from: https://oncology.ru/specialist/diagnostic/tumor_marker/liver/
376. *Kashihara T., Ohki A., Kobayashi T., Sato T., Nishizawa H., Ogawa K., Tako H., Kawakami F., Tsuji M., Tamaoka K.* (1998) Intrahepatic cholangiocarcinoma with increased serum CYFRA 21-1 level. J. Gastroenterol., **33**(3), 447–453. DOI: 10.1007/s005350050112
377. *Hiyama E.* (2014) Pediatric hepatoblastoma: diagnosis and treatment. Transl. Pediatr., **3**(4), 293–299. DOI: 10.3978/j.issn.2224-4336.2014.09.01
378. *Meisl C.J., Karakiewicz P.I., Einarsson R., Koch S., Hallmann S., Weiß S., Hemdan T., Malmström P.-U., Styrke J., Sherif A., Hasan M.N., Pichler R., Tulchiner G., Palou J., Rodríguez Faba Ó., Hennenlotter J., Stenzl A., Ritter R., Niegisch G., Grunewald C.M., Schlomm T., Friedersdorff F., Barski D., Otto T., Gössl A., Arndt C., Esuvaranathan K., Kesavan N.R., Zhijiang Z., Kramer M.W., Hennig M.J.P., Ecke T.H.* (2022) Nomograms including the UBC® Rapid test to detect primary bladder cancer based on a multicentre dataset. BJU International, **130**(6), 754–763. DOI: 10.1111/bju.15677
379. *Li M., Men X., Zhang X.* (2020) Diagnostic value of carbohydrate antigen 72-4 combined with carbohydrate antigen 15.3 in ovarian cancer, cervical cancer and endometrial cancer. J. BUON, **25**(4), 1918–1927.
380. *Fung E.T.* (2010) A recipe for proteomics diagnostic test development: the OVA1 test, from biomarker discovery to FDA clearance. Clin. Chem., **56**(2), 327–329. DOI: 10.1373/clinchem.2009.140855
381. *Reilly G.P., Gregory D.A., Scotti D.J., Lederman S., Neiman W.A., Sussman S., Bean L.M., Ekono M.M.* (2023) A real-world comparison of the clinical and economic utility of OVA1 and CA125 in assessing ovarian tumor malignancy risk. J. Comp. Eff. Res., **12**(6), e230025. DOI: 10.57264/cer-2023-0025
382. *Toledo S.P.A., Lourenço D.M.J., Santos M.A., Tavares M.R., Toledo R.A., Correia-Deur J.E.* (2009) Hypercalcitoninemia is not pathognomonic of medullary thyroid carcinoma. Clinics (Sao Paulo), **64**(7), 699–706. DOI: 10.1590/S1807-59322009000700015
383. *Kim H., Kim Y.N., Kim H.I., Park S.Y., Choe J.-H., Kim J.-H., Kim J.S., Chung J.H., Kim T.H., Kim S.W.* (2017) Preoperative serum thyroglobulin predicts initial distant metastasis in patients with differentiated thyroid cancer. Sci. Rep., **7**, 16955. DOI: 10.1038/s41598-017-17176-6
384. *Sergeeva N.S., Marshutina N.V., Solokhina M.P., Alentov I.I., Parilova N.K., Zenkina E.V., Skachkova T.E.* (2014) Modern concepts of serological tumor-associated markers and their place in oncology. Advances in Molecular Oncology, **1**(1), 69–80.
385. *Kyle R.A., Gertz M.A., Witzig T.E., Lust J.A., Lacy M.Q., Dispenzieri A., Fonseca R., Rajkumar S.V., Offord J.R., Larson D.R., Plevak M.E., Therneau T.M., Greipp P.R.* (2003) Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin. Proc., **78**(1), 21–33. DOI: 10.4065/78.1.21
386. *Basheeth N., Patil N.* (2019) Biomarkers in head and neck cancer an update. Indian J. Otolaryngol. Head Neck Surg., **71**(Suppl 1), 1002–1011. DOI: 10.1007/s12070-019-01683-1
387. *Vigneswaran N., Williams M.D.* (2014) Epidemiologic trends in head and neck cancer and aids in diagnosis. Oral Maxillofac. Surg. Clin. North Am., **26**(2), 123–141. DOI: 10.1016/j.coms.2014.01.001
388. *Singh P., Barpande S.R., Bhavthankar J.D., Mandale M.S., Bhagwat A.U.* (2017) Serum Cyfra 21-1 levels in oral squamous cell carcinoma patients and its clinicopathologic correlation. Indian J. Dent. Res., **28**(2), 162–168. DOI: 10.4103/0970-9290.207789
389. *Kochurova E.V., Kudasova E.O., Nikolenko V.N., Panferova O.I.* (2022) The role of the saliva biomarkers in the diagnostics of the oral mucosal cancer. Voprosy Onkologii, **68**(5), 565–570. DOI: 10.37469/0507-3758-2022-68-5-565-570
390. *Topuz M.F., Binnetoglu A., Yumusakhuylu A.C., Sarı M., Baglam T., Gerin F.* (2017) Circulating calprotectin as a biomarker of laryngeal carcinoma. Eur. Arch. Otorhinolaryngol., **274**(6), 2499–2504. DOI: 10.1007/s00405-017-4480-4
391. *Schapher M., Wendler O., Gröschl M., Schäfer R., Iro H., Zenk J.* (2009) Salivary leptin as a candidate diagnostic marker in salivary gland tumors. Clin. Chem., **55**(5), 914–922. DOI: 10.1373/clinchem.2008.116939
392. *Zhang H., Ren D., Jin X., Wu H.* (2020) The prognostic value of modified Glasgow Prognostic Score in pancreatic cancer: a meta-analysis. Cancer Cell Int., **20**, 462. DOI: 10.1186/s12935-020-01558-4
393. *Yang M., Lin S.-Q., Liu X.-Y., Tang M., Hu C.-L., Wang Z.-W., Zhang Q., Zhang X., Song M.-M., Ruan G.-T., Zhang X.-W., Liu T., Xie H.-L., Zhang H.-Y., Liu C.-A., Zhang K.-P., Li Q.-Q., Li X.-R., Ge Y.-Z., Liu Y.-Y., Chen Y., Zheng X., Shi H.-P.* (2023) Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer: From the investigation on nutrition status and clinical outcome of common cancers study. Front. Immunol., **14**, 1131496. DOI: 10.3389/fimmu.2023.1131496
394. *Chen Y.-R., Chen Y.-L., Ouyang S.-S., Xu H.-W., Li P., He L.-J., Zhu S.-L.* (2020) Prognostic efficacy of preoperative mGPS, SIS and LCS in patients with gastric cancer. Clin. Chim. Acta, **511**, 81–89. DOI: 10.1016/j.cca.2020.09.027
395. *Kumari S.* (2018) Serum biomarker based algorithms in diagnosis of ovarian cancer: a review. Indian J. Clin. Biochem., **33**(4), 382–386. DOI: 10.1007/s12291-018-0786-2

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ВЫБОР ОПТИМАЛЬНЫХ НАБОРОВ БЕЛКОВ В КАЧЕСТВЕ СЕРОЛОГИЧЕСКИХ ОНКОМАРКЕРНЫХ СИГНАТУР

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На сегодняшний день описано достаточно много онкомаркеров, как потенциальных, так и применяемых в клинике. Хотя некоторые из них успешно используются в диагностике и лечении, ни один из них в полной мере не удовлетворяет потребностям онкологии. Поэтому поиск новых маркеров продолжается. Здесь мультиомные технологии, такие как геномика, транскриптомика и метаболомика, очень важны, но протеомика играет центральную роль, поскольку биомаркеры опухолей в основном представляют собой белки. Особое внимание уделяется белкам плазмы/сыворотки крови, так как кровь является самым популярным источником получения информации о здоровье пациента. Чтобы повысить чувствительность и специфичность анализа, весьма перспективным подходом выглядит оценка уровней не просто отдельных белков, а их определённых наборов. Этому и посвящён данный обзор.

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Ключевые слова: онкомаркер; сигнатура; плазма; сыворотка; кровь

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