Supplementary Table 4. Functional characterization and association with prostate and other types of malignancy of 20 proteins with differential abundance in PCa identified in this study in more than one group comparison.

Protein name	Gene Name	Protein abundance in PCa in this study	Molecular/biological function(s)	Classification and involvment in disease	Association with PCa (proteomics studies)	Associations with cancer other than PCa (proteomics studies)	Association with cancer (genomics and functional studies)
Monocyte differentiation antigen CD14	CD14	↑	The protein encoded by this gene is a surface antigen that is preferentially expressed on monocytes/ macrophages. It cooperates with other proteins to mediate the innate immune response to bacterial lipopolysaccharide. Alternative splicing results in multiple transcript variants encoding the same protein.		Urinary CD14 bears high potential in differential diagnosis of BPH from the normal as well as from the prostate cancer subjects [1]; Candidate biomarker for PCa in EPS [2]	Serum soluble CD14 is a potential prognostic indicator of recurrence of human breast invasive ductal carcinoma [3]; CD14 is potential serological cancer marker for liver cancer [4]; CD14 were differentially up-regulated in head and neck and breast tumor cells [5]	
Alpha-2-HS-glycoprotein	AHSG	↑	This glycoprotein present in serum is synthesized by hepatocytes. It is involved in several functions, such as endocytosis, brain development and the formation of bone tissue. It has been postulated that it participates in the development of the tissues.		Increased in serum of PCa-non progresing [6]	Increased Complement C3 and AHSG in pancreatic ductal adenocarcinoma [7]; Increased in serum of papillary thyroid cancer [8]; Up-regulated in hypopharyngeal squamous cell carcinoma [9]; Marker for lung carcinoma [10]; Up regulated in plasma of esophageal squamous cell carcinoma patients [11]; Marker for breast and lung cancer [12];	
Alpha-enolase	ENO1	↓	Alpha-enolase is one of three enolase isoenzymes found in mammals. It functions as a glycolytic enzyme and as a structural lens protein (tau-crystallin) in the monomeric form. Alternative splicing of this gene results in a shorter isoform that has been shown to bind to the c-myc promoter and function as a tumor suppressor.	ENO1 overexpression and post-translational modifications could be of diagnostic and prognostic value in many cancer types [13].	Increased in PCa cell lines PC346C and VCap [14]; Stromal ENO1 levels are increased in PCa compared with those in normal tissue [15]; Down-regulated in urine from PCa patients [16];	Upregulated in lung carcinoma [17-19]; Slightly elevated (not significant) in serum and urine of renal cell carcinoma patients [20]; Down-regulation of ENO1 in nasopharyngeal carcinoma [21]; Upregulated in serum in cholangiocarcinoma [22];	ENO1 mRNA and protein levels were upregulated in glioma tissues [23]; ENO1 possesses tumor-suppressing effects in neurocytoma [24] ;
Annexin A1	ANXA1	↑	This gene encodes a membrane-localized protein that binds phospholipids. This protein inhibits phospholipase A2 and has anti-inflammatory activity.	It act as angiogenic factor and can increase the vascular development in the neighbourhood of the tumour [25]	Present in metastasis-derived prostasomes [25];;	Up-regulated in lung carcinoma [26,27]; Tissue marker for lung carcinoma [28].	

Clusterin	CLU	↓	The protein encoded by this gene is a secreted chaperone. It has been suggested to be involved in several basic biological events such as cell death, tumor progression, and neurodegenerative disorders.		Decresed in G7 vs G5, decreased with PCa progression [29]; Decreased with PCa progression [30]; Decreased in PCa [31]	Urine biomarker for lung adenocarcinoma [32]	
Collagen alpha-1(VI) chain	COL6A1	↓	The collagens are a superfamily of proteins that play a role in maintaining the integrity of various tissues. Collagen VI is a major structural component of microfibrils.		Decreased in PCa tissue [33]; Decreased in PCa [31]	Up-regulated in lung cancer [34]; Up regulated in bone metastasis [35]; Down regulated in colorectal cancer [36];	Down-regulated in ovarian cancer [37];
Complement C3	C3	↑	Complement component C3 plays a central role in the activation of complement system. Its activation is required for both classical and alternative complement activation pathways.	Mutations in this gene are associated with atypical hemolytic uremic syndrome and age-related macular degeneration in human patients.	Increased in serum of PCa [38]; Increased in G7 vs G5, increased with PCa progression [29];	Up-regulated in pancreatic ductal adenocarcinoma [7]; Increased in serum of lung cancer [39]; Up-regulated in plasma of patients with squamous cell carcinoma of the uterine cervix [40]; Marker for breast and lung cancer [12]; Up regulated in lung cancer [27]; Increased in serum of patients with lung cancer [41]; Increased in serum of patient with neuroblastoma [42,43]; Increased in serum of 200 different cancer patients (colon, pancreas, esophagus, lung, prostate,bladder, ovary, cervix, breast) [44];	Up-regulated in ovarian cancer cells [45];
Fibrinogen alpha chain	FGA	↓	The protein encoded by this gene is the alpha component of fibrinogen. Following vascular injury, fibrinogen is cleaved by thrombin to form fibrin which is the most abundant component of blood clots. In addition, various cleavage products of fibrinogen and fibrin regulate cell adhesion and spreading, display vasoconstrictor and chemotactic activities, and are mitogens for several cell types.	Mutations in this gene lead to several disorders, including dysfibrinogenemia, hypofibrinogenemia, afibrinogenemia and renal amyloidosis.	Up-regulated in urine of PCa patients [46]	Degradation products in urine - markers for bladder cancer [47]; Up-regulated in urine of bladder cancer patients [48]; Down regulated in liver cancer [49]; Up-regulated in the plasma of ovarian cancer patients [50]; Up-regulated in serum of ovarian cancer patients [51]; Up-regulated in plasma of patients with squamous cell carcinoma of the uterine cervix [40]	
Fibrinogen gamma chain	FGG	↓	The protein encoded by this gene is the gama component of fibrinogen.	Mutations in this gene lead to several disorders, including dysfibrinogenemia, hypofibrinogenemia and thrombophilia.	Differentially expressed in PCa tissue [52]; Down-regulated in urine of PCa patients [46]	Degradation products in urine - markers for bladder cancer [47]; Up-regulated in urine of bladder cancer patients [48]; down-regulated in hypopharyngeal squamous cell carcinoma [9]; up-regulated in the hepatocellular carcinoma serum samples [53]; Down regulated in plasma of esophageal squamous cell carcinoma patients [11]	

Hemopexin	HPX	↓	This gene encodes a plasma glycoprotein that binds heme with high affinity. The encoded protein is an acute phase protein that transports heme from the plasma to the liver and may be involved in protecting cells from oxidative stress.	Decreased in serum of PCa patients [38]; Increased in serum of PCa patients [30]	Up-regulated in non-small-cell lung cancer [54]; Down-regulated in plasma of breast cancer patients [55];	Up-regulated in testicular germ cell tumors [56]; Differentially expressed in breast cancer tissues [57];
Prostaglandin-H2 D-isomerase	PTGDS	↑	This protein catalyzes the conversion of prostaglandin H2 (PGH2) to postaglandin D2 (PGD2).	Up-regulated in urine of PCa patients [46,58];	Down-regulated in human cerebrospinal fluid from meningioma [59];	
Protein S100-A9	S100A9	↓	S100A9 is a calcium- and zinc-binding protein which plays a prominent role in the regulation of inflammatory processes and immune response. The extracellular functions involve proinfammatory, antimicrobial, oxidant-scavenging and apoptosis-inducing activities. Its proinflammatory activity includes recruitment of leukocytes, promotion of cytokine and chemokine production, and regulation of leukocyte adhesion and migration.	S100A9 serum levels were significantly elevated in PCa patients compared with BPH or healthy individuals [60]; Overexxpressed in urine from subset of PCa patients but absent in urine from BPH [16]	Up-regulated in human hypopharyngeal cancer cell [61]; Up-regulated in both serum and tissue samples of clear-cell renal cell carcinoma [62]; Up-regulated in hepatocellular carcinoma [63,64]; Up-regulated in serum of colorectal cancer [65]; Up-regulated in serum of bladder cancer [66]; Down-regulated in non-small lung cancer [67]	TSPAN13-to-S100A9 ratio showed a strong potential as a diagnostic marker for PCa [68]; S100A8/A9 mRNA, protein and urinary nucleic acid levels are lower in PCa than in BPH [69];
Vesicular integral-membrane protein VIP36	LMAN2	↑	The encoded protein shuttles between the endoplasmic reticulum, the Golgi apparatus and the plasma membrane. It binds high mannose type glycoproteins and may facilitate their sorting and trafficking.	Up-regulated in urine of PCa patients [46]	Up-regulated in gastric cancer cells [70];	
Inter-alpha-trypsin inhibitor heavy chain H4	ITIH4	↑	The protein encoded by this gene is secreted into the blood, where it is cleaved by plasma kallikrein into two smaller forms. Expression of this gene has been detected only in liver, and it seems to be up-regulated during surgical trauma.	Up-regulated in urine of PCa patients [71]; Down-regulated in serum of PCa patients [72]; Up-regulated in urine of PCa patients [46]; Up-regulated in serum of progresing PCa [6]	Up-regulated in serum peptide biomarkers for breast cancer [73]; up-regulated in serum of gastric cancer patients [74]; Up-regulated in serum of colonic adenomas [75]; Up-regulated in serum of breast cancer patients [76,77]; Up-regulated in liver cancer [49]	
Actin, aortic smooth muscle	ACTA2	↓	The protein encoded by this gene belongs to the actin family of proteins, which are highly conserved proteins that play a role in cell motility, structure and integrity. Alpha, beta and gamma actin isoforms have been identified, with alpha actins being a major constituent of the contractile apparatus, while beta and gamma actins are involved in the regulation of cell motility.	increased ACTA2 observed in extraprostatic extension components of locally advanced PCa [78,79]; decreased in cancer-associated stroma when compared to BPH stroma [80];	A proteomic study identified α-smooth muscle actin (ACTA2) as a PGAM1-associated protein. PGAM1 modulated actin filaments assembly, cell motility and cancer cell migration via directly interacting with ACTA2 [81]; Candidate biomarker for blader cancer [82]; ACTA2 regulates c-MET and FAK expression in lung adenocarcinoma cells, which	mRNA and protein expression levels down-regulated in bladder cancer [84]; aberrant ACTA2 expression accelerated the invasiveness and metastasis of breast cancer cells[85];

						positively and selectively influence metastatic potential [83];	
Granulins	GRN	↓	The 88 kDa precursor protein, progranulin, is also called proepithelin and PC cell-derived growth factor. Cleavage of the signal peptide produces mature granulin which can be further cleaved into a variety of active, 6 kDa peptides. These smaller cleavage products are named granulin A, granulin B, granulin C, etc. Both the peptides and intact granulin protein regulate cell growth. Granulin family members are important in normal development, wound healing, and tumorigenesis.		GRN-A can serve as a prostate cancer serum and tumor marker [86]	Up-regulated in urine of hepatocarcinoma patients [63]; Progranulin is overexpressed in ovarian cancer [87];	Proepithelin is stimulating the migration, invasion, proliferation, and anchorage-independent growth of prostate cancer cells [88];
Hemoglobin subunit beta	HBB	↓	The alpha (HBA) and beta (HBB) loci determine the structure of the 2 types of polypeptide chains in adult hemoglobin. The normal adult hemoglobin tetramer consists of two alpha chains and two beta chains.	Mutant beta globin causes sickle cell anemia. Absence of beta chain causes beta-zero-thalassemia. Reduced amounts of detectable beta globin causes beta-plus-thalassemia.	HBB is selectively deregulated in prostate, breast and lung cancer cells [89];	Down-regulated in colorectal carcinoma [90]; Down-regulated in lung cancer [91]; HBB suppresses lung neuroblastoma cells growth and metastasis [92];	Decreased expression of HBB in anaplastic thyroid cancer [93];
Phosphatidyl ethanolamin e-binding protein 1	PEBP1	↓	This gene encodes a member of the phosphatidylethanolamine-binding family of proteins and has been shown to modulate multiple signaling pathways, including the MAP kinase (MAPK), NF-kappa B, and glycogen synthase kinase-3 (GSK-3) signaling pathways. The encoded protein can be further processed to form a smaller cleavage product, hippocampal cholinergic neurostimulating peptide (HCNP), which may be involved in neural development.	This gene has been implicated in numerous human cancers and may act as a metastasis suppressor gene.	PEBP1 inhibits the migration and invasion of human prostate cancer PC-3M cells [94]; Down-regulated in prostate cancer tissues [95];	Down-regulated in glioblastoma [96]; Loss of PEBP1 expression is observed in many cancers as they progress [97]; Up-regulated in nasopharyngeal carcinoma [98]; PEBP1 is a metastasis suppressor gene of human epithelial ovarian cancer [99];	Up-regulated in nasopharyngeal carcinoma [100]; Up-regulated in breast cancer [101]; mRNA expression was found to be significantly down-regulated in non-small cell lung cancer [102]; reduced PEBP1 mRNA in transitional cell carcinoma of the urinary bladder [103];

Cathepsin B	CTSB	↓	This enzyme is a lysosomal cysteine protease with both endopeptidase and exopeptidase activity that may play a role in protein turnover. It is also known as amyloid precursor protein secretase and is involved in the proteolytic processing of amyloid precursor protein (APP). Multiple pseudogenes of this gene have been identified.	Incomplete proteolytic processing of APP has been suggested to be a causative factor in Alzheimer's disease. Overexpression of CTSB has been associated invasive and metastatic phenotypes in cancers [104].	Up-regulated in prostate cancer biopsy specimens [105];	Up-regulated in cholangiocarcinoma [106]; Up-regulated in Inflammatory breast cancer (IBC) as compared to non-IBC tissues [107]; Up-regulated in late stage colorectal cancer patients with lymph node metastases when compared to early stage patients [108];	Up-regulated in ovarian cancer cell lines [37];
Osteopontin	SPP1	↑	This protein is involved in the attachment of osteoclasts to the mineralized bone matrix. It is secreted and binds hydroxyapatite with high affinity. The osteoclast vitronectin receptor is found in the cell membrane and may be involved in the binding to this protein. This protein is also a cytokine that upregulates expression of interferon-gamma and interleukin-12.		Increased in human prostate cancer specimens and human prostate cancer cell lines LNCaP and C4-2 [109]; Increased gradient of osteopontin expression throughout the stages of murine prostate cancer, beginning from the preneoplastic lesions to distant metastases [110];	Increased in ovarial, endometrium, esophagus, stomach, pancreas, bile duct, liver, colon, kidney, bladder, prostate, head and neck, lung and brain cancers [111]; Increased in advance stage oesophageal squamous cell carcinoma [112]; The osteopontin levels in non-small cell lung cancer were significantly higher compared to those of the controls [113]; Elevated serum levels in patients with pancreatic cancer [114];	Identified as lead marker of colon cancer progression [115]; Significantly higher levels of osteopontin mRNA in PCa tissue [116]; Up regulated gene expression in metastatic PCa [117]; Down-regulation of SPP1 expression by RNAi led to a decline in the malignant phenotype in PCa cells [118,119];

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