

Supporting Information

Online Miniaturized Asymmetrical Flow Field-Flow Fractionation and Inductively Coupled Plasma Mass Spectrometry for Metalloprotein Analysis of Plasma from Patients with Lung Cancer

Jin Yong Kim,¹ Heung Bin Lim,^{2,*} Myeong Hee Moon^{1,*}

¹Department of Chemistry, Yonsei University, Seoul 120-749, Korea

²Department of Chemistry, Dankook University, Gyeonggi-do 448-701, Korea

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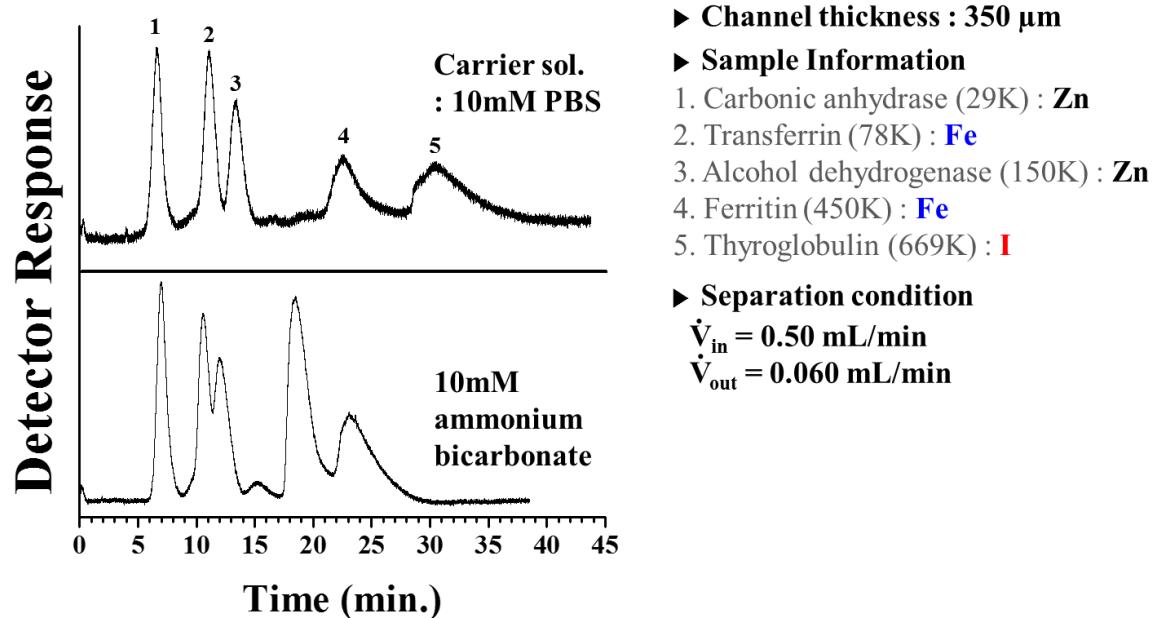


Figure S1. Comparison on protein separation between 10 mM PBS and 10 mM ammonium bicarbonate solutions by mAF4-UV.

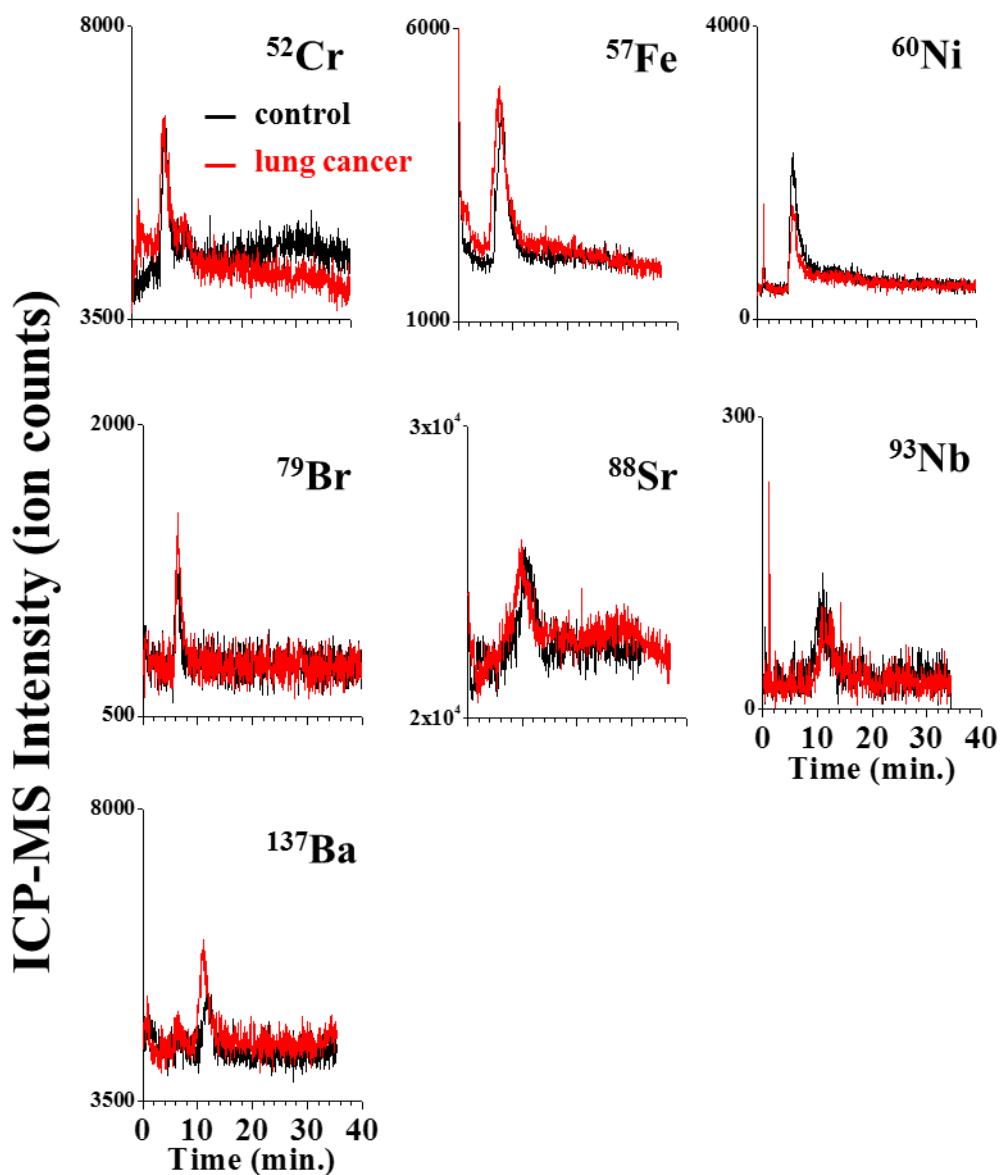


Figure S2. Comparison of elemental distributions of metalloproteins between the pooled healthy normal plasma samples as controls ($n = 10$, black) and the pooled lung cancer plasma samples ($n = 10$, red) (after depletion) by mAF4-ICPMS.

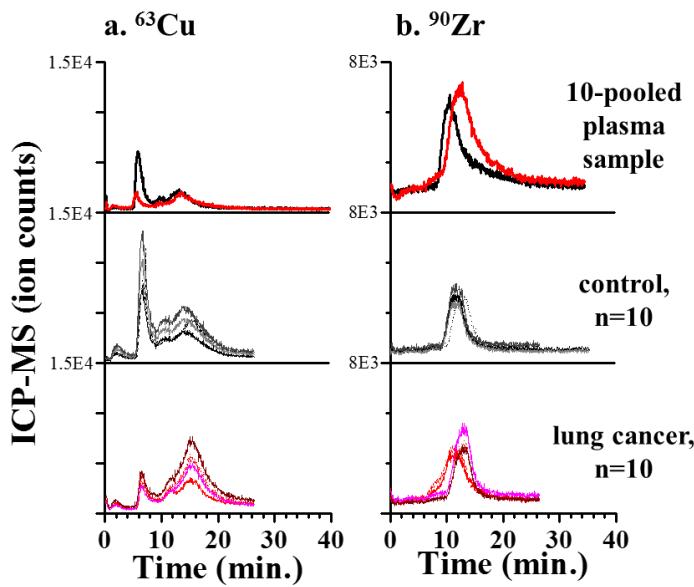


Figure S3. Superimposed elemental fractograms based on the detection of a) ^{63}Cu and b) ^{90}Zr from each 10-sample pool of controls (black) and patients with cancer (red) in the top panels, 10 individual control samples in the middle panels, and 10 individual patients with lung cancer in the bottom panels, as determined by mAF4-ICPMS. Run conditions are the same as in Figure 2.

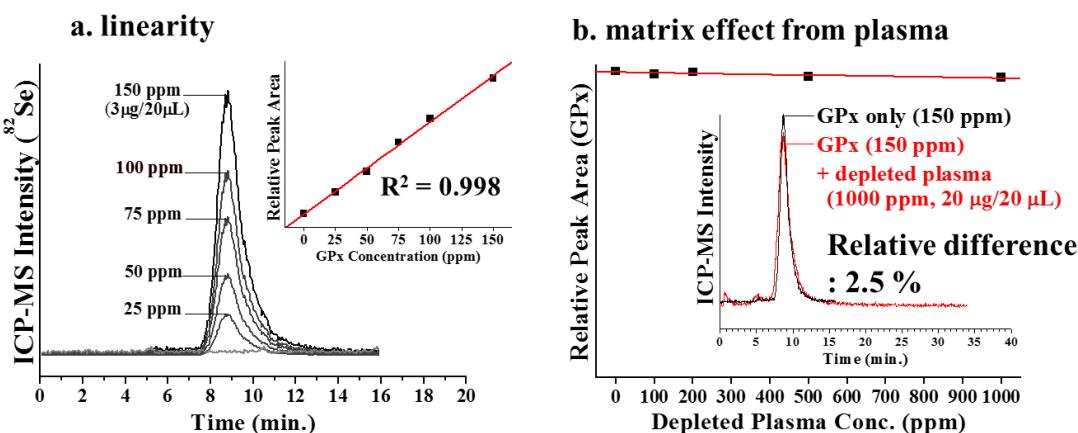


Figure S4. a) Linearity in the peak area of ^{82}Se from the glutathione peroxidase (GPx) standard at different injection amounts by mAF4-ICPMS. b) Variations in the peak areas of 150 ppm GPx spiked with different concentrations of plasma samples (containing proteins at concentrations of 0–20 mg/20 mL), showing that the matrix effect was about ~2.5% for up to 1000 ppm plasma. Run conditions: inflow/outflow rates, 0.5/0.06 mL/min; injection volume, 20 mL; carrier solution, 10 mM NH_4HCO_3 .

Table S1. List of 327 proteins identified by nLC-ESI-MS/MS from mAF4 fractions (^adetected in the control only, ^bdetected in lung cancer samples only).

Fraction 1 (F1)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
Q08EJ9	ABCA2 protein	Q2WGJ6	Kelch-like protein 38	Q9ULI3	Protein HEG homolog 1
Q86TH5	ARFGEF2 protein (Fragment)	Q5W9G4	KIAA0823 splice variant 1 (Fragment)	Q9Y6C5	Protein patched homolog 2
Q86W75	RSK protein (Fragment)	Q5T2D8	KIAA1751 (Fragment)	Q8IY72	RAG1 protein
P35869	Aryl hydrocarbon receptor	Q1HP67	Lipoprotein, Lp(A)	Q9NQW1	Protein transport protein Sec31B
Q8N888	BCoR-like protein 2	Q641Q8	MICAL-L1 protein (Fragment)	Q53ER5	SRY-box 7 variant (Fragment)
A0M8Q9	C1 segment protein	Q05CT8	NEDD1 protein (Fragment)	Q8WWQ8	Stabilin-2
P05160	Coagulation factor XIII B chain	Q95502	Neuronal pentraxin receptor	O15455	Toll-like receptor 3
Q7Z471	CYP19A1 protein (Fragment) ^a	Q6PK21	OGFR protein	B4DHZ6	Transferrin, isoform CRA_c ^b
D3DT08	Dmx-like 1, isoform CRA_a	P47884	Olfactory receptor 1D4	O75396	Vesicle-trafficking protein SEC22b
Q6P3W2	DnaJ homolog subfamily C member 24	POC645	Olfactory receptor 4E1	B3KSA5	Wilms tumor 1, isoform CRA_d
Q12948	Forkhead box protein C1	Q5JYS9	Phospholipase C, beta 4 (Fragment)	O60281	Zinc finger protein 292
B7ZLC9	GEMIN5 protein ^b	Q05BV6	PIK3R2 protein	Q9C0G0	Zinc finger protein 407
Q6IC69	GSTT1 protein	Q86W56	Poly (ADP-ribose) glycohydrolase	B9EGN4	ZNF594 protein
P01834	Ig kappa chain C region	O75530	Polycomb protein EED	Q71RD3	PP11517
Q9HCU4	Cadherin EGF LAG seven-pass G-type receptor 2	Q6P2Q9	Pre-mRNA-processing-splicing factor 8 ^a	Q8N4L2	Type 2 phosphatidylinositol 4,5-bisphosphate 4-phosphatase
Q8IWF9	Coiled-coil domain-containing protein 83	Q53EL0	Protein tyrosine phosphatase, non-receptor type 6 isoform 1 variant (Fragment)	Q4LDE5	Sushi, von Willebrand factor type A, EGF and pentraxin domain-containing protein 1
Q59FF8	CUB and Sushi multiple domains 1 variant (Fragment)	Q5JT02	Protein-O-mannosyltransferase 1 (Fragment)	Q70EL2	Ubiquitin carboxyl-terminal hydrolase 45
P78413	Iroquois-class homeodomain protein IRX-4	Q86WF2	Sarcoma antigen NY-SAR-29 (Fragment)	Q5T5E9	Threonyl-tRNA synthetase 2, mitochondrial
Q86VI8	Kallikrein 13 splicing variant 3				
Fraction 1 (F1) & Fraction 2 (F2)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
Q9H6S1	5-azacytidine-induced protein 2	A0JLR8	EIF5B protein (Fragment)	A6XMV8	Protease serine 2 preproprotein
P10323	Acrosin ^b	B2RTQ9	FANCM protein	Q18PE1	Protein Dok-7 ^b
Q8IW19	Aprataxin and PNK-like factor ^b	A0PJ70	GSG2 protein (Fragment)	Q14DU5	ROCK2 protein ^a
Q9HCU9	Breast cancer metastasis-suppressor 1	Q8IUS9	HCG1992264, isoform CRA_a (Fragment)	A2VEC9	SCO-spondin

Q15762	CD226 antigen	Q6PIL0	IGHV7-81 protein	P51692	Signal transducer and activator of transcription 5B
Q8TAP6	Centrosomal protein of 76 kDa	Q3KPE8	IL18RAP protein ^b	Q9NRC6	Spectrin beta chain, brain 4
Q3ZCR0	Chromosome 5 open reading frame 5, isoform CRA_c ^b	Q14867	K222 protein (Fragment) ^a	Q5VV42	Threonylcarbamoyladenosine tRNA methylthiotransferase
P17538	Chymotrypsinogen B	O15230	Laminin subunit alpha-5	Q96A61	Tripartite motif-containing protein 52 ^a
Q96T59	CMT1A duplicated region transcript 15 protein ^a	Q8N7C0	Leucine-rich repeat-containing protein 52	Q8IYU4	Ubiquilin-like protein
Q16568	Cocaine- and amphetamine-regulated transcript protein	Q6XYC2	LP3298 ^a	Q8N4T4	Vav-like protein C9orf100
Q14008	Cytoskeleton-associated protein 5	Q9P2M1	LRP2-binding protein ^b	Q8IZ20	Zinc finger protein 683
Q9H2L7	DC33 ^b	B2RTQ5	LRRC16A protein	Q5VV50	Zinc finger protein 691 ^b
P81605	Dermcidin	P02795	Metallothionein	Q19AV6	Zinc finger SWIM domain-containing protein 7
A8KAY3	DNAH9 protein (Fragment)	Q8NH00	Olfactory receptor 2T4	Q9Y6M5	Zinc transporter 1
Q9P225	Dynein heavy chain 2, axonemal	B4DN80	Peptidyl-prolyl cis-trans isomerase ^b	Q9UMY3	3-phosphoglycerate dehydrogenase
Q6ZT12	E3 ubiquitin-protein ligase UBR3	A1L390	Pleckstrin homology domain-containing family G member 3 ^b		

Fraction 2 (F2)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
Q86TH1	ADAMTS-like protein 2	Q9GZZ8	Extracellular glycoprotein lacritin	Q8NGI3	Olfactory receptor 56B1
P40145	Adenylate cyclase type 8	Q59H95	Flightless I homolog variant	P02763	Orosomucoid 1
P02765	Alpha-2-HS-glycoprotein	O95067	G2/mitotic-specific cyclin-B2	Q13041	P67
P0DJI8	Amyloid protein A	Q8WXG9	G-protein coupled receptor 98	A0JP11	Phosphoinositide-3-kinase, regulatory subunit 4
Q59G86	Androgen-regulated short-chain dehydrogenase/reductase 1 variant	P00738	Haptoglobin	P40197	Platelet glycoprotein V
Q5VYY1	Ankyrin repeat domain-containing protein 22	Q8NGD8	HCG1646325	Q9GZV8	PR domain zinc finger protein 14
A6NEL2	Ankyrin repeat domain-containing protein 56	Q8WW2D	HCG2028157	Q9UBL5	Prostate-specific transglutaminase
Q4G1A0	ASCC3 protein ^a	Q8NDA2	Hemicentin-2	Q8NE28	Protein kinase-like protein SgK071
Q68DQ2	Beta/gamma crystallin domain-containing protein 3	Q6MZM0	Hephaestin-like protein 1	Q92837	Proto-oncogene FRAT1
Q13884	Beta-1-syntrophin	Q53AI5	HSD-41	Q6XPR3	Repetin
Q8IXA3	Casein kinase I gamma 1 isoform	B3KSH4	Huntingtin interacting protein 2, isoform CRA_a	A6NJZ7	RIMS-binding protein 3C
Q96KY9	CDH19 protein	Q9Y6R7	IgGFc-binding protein	P02768	Serum albumin

P56748	Claudin-8	O14498	Immunoglobulin superfamily containing leucine-rich repeat protein	Q9BSK2	Solute carrier family 25 member 33
Q5JVE8	Coagulation factor X	B4DE09	Inosine-5'-monophosphate dehydrogenase	Q9NWM0	Spermine oxidase
Q96IX0	DCBLD2 protein	P23677	Inositol-triphosphate 3-kinase A	Q5TGI4	Sterile alpha motif domain-containing protein 5
Q8NFP7	Diphosphoinositol polyphosphate phosphohydrolase 3-alpha	Q13797	Integrin alpha-9	Q5I0X7	Tetratricopeptide repeat protein 32
Q92796	Disks large homolog 3	Q9HCG4	KIAA1608 protein	Q6ZMP0	Thrombospondin type-1 domain-containing protein 4
Q86UC6	DLC1 protein	P19397	Leukocyte surface antigen CD53	Q7Z4N2	Transient receptor potential cation channel subfamily M member 1
B0I1R7	DNAH5 variant protein	Q6LAM0	Light chain of factor I	A6XMH1	Transthyretin ^a
Q8WXX0	Dynein heavy chain 7, axonemal	B7ZMN0	LINGO2 protein	Q6PIF1	TTC7B protein
Q5VTR2	E3 ubiquitin-protein ligase BRE1A	Q6GPG7	LPAR1 protein	A6NNM8	Tubulin polyglutamylase TTLL13
Q5T4S7	E3 ubiquitin-protein ligase UBR4	Q59H95	Metabotropic glutamate receptor 7 variant	C6ZGQ9	WDR79
A8MYE2	EF-hand domain-containing protein	B6EC89	MUC1 isoform J1	O43345	Zinc finger protein 208
Q96AC5	ETS1 protein	Q5JRM6	Nuclear RNA export factor 2	Q96AP4	Zinc finger with UFM1-specific peptidase domain protein

Fraction 2 (F2) & Fraction 3 (F3)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
Q9H1A4	Anaphase-promoting complex subunit 1 ^a	Q6NXG8	HIP1R protein ^a	Q9Y4R7	Tubulin monoglycylase TTLL3
Q6UB98	Ankyrin repeat domain-containing protein 12	Q6LE88	Manganese superoxide dismutase (Fragment) ^a	O95226	Voltage-gated L-type calcium channel alpha-1 subunit
P02647	Apolipoprotein A-I	Q8NCL9	Protein APCDD1-like	Q8N2Y6	ZFHX3 protein
Q15057	Arf-GAP with coiled-coil, ANK repeat and PH domain-containing protein 2	P02787	Serotransferrin	Q9UEG4	Zinc finger protein 629
Q5JRU8	Caspase 9	A6NKL6	Transmembrane protein 200C	P25311	Zinc-alpha-2-glycoprotein
P02790	Hemopexin				
Fraction 3 (F3)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
Q8N433	ADRBK2 protein	Q96KN9	Gap junction delta-4 protein	Q6P2Q9	Pre-mRNA-processing-splicing factor 8
P04217	Alpha-1B-glycoprotein	Q6PEJ8	HP protein	Q9NTK1	Protein DEPP
P02765	Alpha-2-HS-glycoprotein	P05556	Integrin beta-1	Q5SZM4	Protein eyes shut homolog ^b
A0MZ5	AMP-activated alpha 2 subunit	Q59GP7	Interleukin enhancer binding factor 3 isoform c variant	O60320	Protein FAM189A1

Q13784	APOA4 protein	Q05CF8	KNG1 protein	Q8TCP9	Protein FAM200A
P02652	Apolipoprotein A-II	Q96RQ9	L-amino-acid oxidase	Q86WI3	Protein NLRC5
P05090	Apolipoprotein D	P51884	Lumican	Q9NQW1	Protein transport protein Sec31B
AIL3U4	Cadherin-related family member 2 ^a	Q6ZNC8	Lysophospholipid acyltransferase 1	P11498	Pyruvate carboxylase ^a
Q53G30	Carcinoembryonic antigen-related cell adhesion molecule 5 variant	O43451	Maltase-glucoamylase, intestinal	P10745	Retinol-binding protein 3
A2RRR7	CCDC46 protein	A2A368	Melanoma-associated antigen B16	Q9C0B0	RING finger protein unkempt homolog ^a
A0PJB2	CDT1 protein	P10620	Microsomal glutathione S-transferase 1	Q86WF2	Sarcoma antigen NY-SAR-29
Q1L857	Ceruloplasmin	Q96QA9	Multidrug resistance associated protein	B4DMH7	Serine incorporator 5
Q02388	Collagen alpha-1(VII) chain	B2RWP3	MYO18B protein	Q5TBR0	Sialic acid synthase
Q6VCV8	Complement C4B	Q9UHE5	N-acetyltransferase 8	Q75691	Small subunit processome component 20 homolog
Q96NU0	Contactin-associated protein-like 3B	B7ZKS9	NACHT, LRR and PYD domains-containing protein 3	Q9C093	Sperm flagellar protein 2
Q8N1N0	C-type lectin domain family 4 member F	C7B3J8	NADH-ubiquinone oxidoreductase chain 2	P60508	Syncytin-2
Q8IWT3	Cullin-9	P16860	Natriuretic peptides B	Q96DH7	TBC1 domain family member 16
Q9H2H0	CXXC-type zinc finger protein 4	Q59FP8	Neogenin	B9A6M5	TBC1 domain family member 23
Q96S65	Cysteine-serine-rich nuclear protein 1	Q8NGN2	Olfactory receptor 10S1	Q59EF3	TEA domain family member 1 variant
A6YWY5	Cytochrome b	P0C645	Olfactory receptor 4E1	Q59FH1	Transformation/transcription domain-associated protein variant
Q86SJ6	Desmoglein-4	Q7RTY7	Ovochymase-1	Q96AQ2	Transmembrane protein 125
Q9Y2H0	Disks large-associated protein 4	Q5JVF3	PCI domain-containing protein 2	A6XMH1	Transthyretin
Q69G20	E3 ISG15--protein ligase HERC5	C7AZ55	Phosphatase 1 binding protein	P52333	Tyrosine-protein kinase JAK3
Q5TI74	E-selectin	Q5JYS9	Phospholipase C, beta 4	Q9GZZ9	Ubiquitin-like modifier-activating enzyme 5 ^a
Q5T376	FERM domain containing 4A, isoform CRA_c	Q96DM1	PiggyBac transposable element-derived protein 4	P04004	Vitronectin
Q8TES4	FLJ00119 protein	O60486	Plexin-C1	Q9ULM2	Zinc finger protein 490
Q6FIG5	FN3KRP protein	Q9BZT3	PNAS-31	Q9H040	Zinc finger RAD18 domain-containing protein C1orf124 ^a
Q9NY99	Gamma-2-syntrophin	P01833	Polymeric immunoglobulin receptor	Q6NTE1	Zinc finger, imprinted 3

Fraction 3 (F3) & Fraction 4 (F4)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
P43652	Afamin	P01024	Complement C3	Q9Y666	Solute carrier family 12 member 7
P01011	Alpha-1-antichymotrypsin	P78492	Inter-alpha-trypsin inhibitor	Q5TAX3	Terminal uridylyltransferase 4 ^a
P01009	Alpha-1-antitrypsin	Q59HA6	Laminin alpha 3b chain variant (Fragment)	P02774	Vitamin D-binding protein

Q02224	Centromere-associated protein E	Q16322	Potassium voltage-gated channel subfamily A member 10	O60281	Zinc finger protein 292
Q96FZ7	Charged multivesicular body protein 6	Q96S08	Protein CTF18 homolog		
Fraction 4 (F4)					
Accession	Identified proteins	Accession	Identified proteins	Accession	Identified proteins
A2A2Z9	Ankyrin repeat domain-containing protein 18B ^b	Q0VAC5	HP protein	Q8NGL4	Olfactory receptor 5D13
Q59F96	ATP-binding cassette, sub-family F, member 1 variant	P01876	Ig alpha-1 chain C region	B4DTR3	Oxysterol-binding protein ^b
A0M8Q9	C1 segment protein	Q8NI35	InaD-like protein	O76105	PDE4C-791 ^a
Q8NA31	Coiled-coil domain-containing protein 79	D3DT96	Integrator complex subunit 7, isoform CRA_a ^b	B7ZML4	PLA2R1 protein
P02748	Complement component C9	Q5T985	Inter-alpha (Globulin) inhibitor H2	Q7Z443	Polycystic kidney disease protein 1-like 3
Q05C85	CUL9 protein	Q14867	K222 protein	Q9H6L5	Protein FAM134B
B0I1R7	DNAH5 variant protein	Q92876	Kallikrein-6	P02768	Serum albumin
Q3MS94	Dominant-negative kinase-deficient Brutons tyrosine kinase isoform 4 ^b	Q5CZ91	Methionine aminopeptidase ^a	P40225	Thrombopoietin ^a
O60216	Double-strand-break repair protein rad21 homolog ^b	P98088	Mucin-5AC	Q15645	Thyroid receptor-interacting protein 13
P13804	Electron transfer flavoprotein subunit alpha ^a	B2ZZ87	Nedd4 binding protein 2 ^b	Q8N442	Translation factor GUF1
O94905	Erlin-2	Q8IZJ1	Netrin receptor UNC5B	Q96F25	UDP-N-acetylglucosamine transferase subunit ALG14 homolog
Q92913	Fibroblast growth factor 13	P17787	Neuronal acetylcholine receptor subunit beta-2	Q969S3	Zinc finger protein 622 ^a
B7ZLC9	GEMIN5 protein	Q59GJ8	Notchless gene homolog variant	Q6PK66	ZNF711 protein ^a

Table S2. List of 58 metalloproteins identified from the Uniprot Knowledgebase (UniprotKB, <http://www.uniprot.org/>) and classified according to metals (including transition metals only). F# represents the fraction number.

Metal	Identified proteins	F#	Metal	Identified proteins	F#	Metal	Identified proteins	F#
Mn	RAG1 protein	1	Mn, Fe	Manganese superoxide dismutase (Fragment) ^a	2,3		E3 ubiquitin-protein ligase UBR4	2
	Dermcidin	1,2	Cr, Fe	Serotransferrin	2,3		PR domain zinc finger protein 14	2
	Adenylate cyclase type 8	2	Mn, Zn	PDE4C-791 ^a	4		Zinc finger protein 208	2
	Diphosphoinositol polyphosphate phosphohydrolase 3-alpha	2		DnaJ homolog subfamily C member 24	1		Zinc finger with UFM1-specific peptidase domain protein	2
	Phosphatase 1 binding protein	3		Ubiquitin carboxyl-terminal hydrolase 45	1		Arf-GAP with coiled-coil, ANK repeat and PH domain-containing protein 2	2,3
	Pyruvate carboxylase ^a	3		Wilms tumor 1, isoform CRA_d	1		ZFHX3 protein	2,3
	Terminal uridylyltransferase 4 ^a	3,4		Zinc finger protein 292	1		Zinc finger protein 629	2,3
	CYP19A1 protein (Fragment) ^a	1		Zinc finger protein 407	1		Zinc-alpha-2-glycoprotein	2,3
	Threonylcarbamoyladenosine tRNA methylthiotransferase	1,2		ZNF594 protein	1	Zn	Ubiquitin-like modifier-activating enzyme 5 ^a	3
	Haptoglobin	2		Acrosin ^b	1,2		CXXC-type zinc finger protein 4	3
Fe	Hemopexin	2,3	Zn	Aprataxin and PNK-like factor ^b	1,2		RING finger protein unkempt homolog ^a	3
	Complement C3	3,4		E3 ubiquitin-protein ligase UBR3	1,2		Cullin-9	3
	Complement component C9	4		ROCK2 protein ^a	1,2		Zinc finger protein 490	3
	Methionine aminopeptidase ^a	4		Zinc finger SWIM domain-containing protein 7	1,2		Zinc finger RAD18 domain-containing protein C1orf124 ^a	3
Ni	Poly (ADP-ribose) glycohydrolase	1		Zinc finger protein 683	1,2		Zinc finger, imprinted 3	3
	3-phosphoglycerate dehydrogenase	1,2		Zinc finger protein 691 ^b	1,2		Zinc finger protein 292	3,4
Cu	Hephaestin-like protein 1	2		Tripartite motif-containing protein 52 ^a	1,2		Zinc finger protein 622 ^a	3,4
	Ceruloplasmin	2		Zinc transporter 1	1,2		ZNF711 protein ^a	4
Cu, Zn	Metallothionein	1,2		ADAMTS-like protein 2	2			
	Serum albumin	2,4		E3 ubiquitin-protein ligase BRE1A	2			

Table S3. Quantification results of metalloproteins represented as the peak area ratio (P/C) of lung cancer (P) to control (C) plasma for each peptide quantified by nLC-ESI-MS/MS using iCCM. Data for albumin and IgG were excluded since plasma sample were initially treated to deplete these two proteins.

Accession	Description	Metal	MW (kDa)	Fraction	Peptide sequence	Identified peptides		
						CM (control)	m/z (charge) iCCM (cancer)	Peak area ratio (P/C)
Q0MQR4	Poly (ADP-ribose) glycohydrolase	Ni	17.0	F1	VPPSSPAcVPGRAGQHR	887.08 (+2)	889.09 (+2)	1.37 ± 0.35
B9EGN4	ZNF594 protein	Zn	93.9	F1	EcKEcGKTQSEL	735.09 (+2)	739.10 (+2)	2.14 ± 0.29
Q9C0G0	Zinc finger protein 407	Zn	247.2	F1	FQNENSGSSALNcETAK	929.08 (+2)	931.09 (+2)	4.02 ± 0.43
O60281	Zinc finger protein 292	Zn	304.6	F1 F3	DALEMICnNLESEGDEK	926.51 (+2)	928.52 (+2)	1.69 ± 0.11 1.03 ± 0.28
P02795	Metallothionein	Cu, Zn	4.3	F1 F2	MDPNcSCAAGVScTcASSCK	1055.02 (+2)	1061.04 (+2)	0.92 ± 0.08 2.44 ± 0.53
Q19AV6	Zinc finger SWIM domain-containing protein 7	Zn	15.4	F1 F2	TcQQLSVSDK	582.88 (+2)	584.89 (+2)	1.86 ± 0.29 0.95 ± 0.16
Q5VV50	Zinc finger protein 691	Zn	34.6	F1 F2 F1 F2	IccEcGKSFSNSSF MAQISSGGGGQSRcL	885.59 (+2) 755.05 (+2)	891.61 (+2) 757.06 (+2)	N.D. from control 1.25 ± 0.18 N.D. from control 0.90 ± 0.25
P10323	Acrosin	Zn	45.8	F1 F2	HTcGGSLLNSRW	694.24 (+2)	696.25 (+2)	N.D. from control 1.32 ± 0.09
Q5VV42	Threonylcarbamoyladenosine tRNA methylthiotransferase	Fe	49.8	F1 F2	cTTDQLEAEIQScLDF	965.52 (+2)	969.54 (+2)	1.25 ± 0.15 1.05 ± 0.08
Q9Y6M5	Zinc transporter 1	Zn	55.3	F1 F2	LDPTLcVVMVcIL	774.63 (+2)	778.64 (+2)	1.58 ± 0.36 0.98 ± 0.12
P00738	Haptoglobin	Fe	45.2	F2	LPEcEAVcGKPK	694.84 (+2)	698.86 (+2)	1.10 ± 0.22
Q96AP4	Zinc finger with UFM1-specific peptidase domain protein	Zn	65.9	F2	QNDAYNDcLKGM	771.62 (+2)	773.63 (+2)	0.71 ± 0.08
Q6MZM0	Hephaestin-like protein 1	Cu	131.6	F2	QTDYQQVQScALPTDAL	969.95 (+2)	971.96 (+2)	0.49 ± 0.13
Q5VTR2	E3 ubiquitin-protein ligase BRE1A	Zn	113.6	F2	cFHVFcFEcVKTR	895.63 (+2)	901.65 (+2)	0.88 ± 0.20
Q9UMY3	3-phosphoglycerate	Ni	24.2	F2	NAGNcLSPAVIVGLLK	813.95 (+2)	815.96 (+2)	0.39 ± 0.05

dehydrogenase									
Q9H2H0	CXXC-type Zn finger protein 4	Zn	21.0	F2	cGAAEAEIMNLPER	780.55 (+2)	782.56 (+2)	0.61 ± 0.14	
Q9ULM2	Zinc finger protein 490	Zn	61.3	F2	QCRQcGKAFSYSKSL	588.46 (+3)	589.79 (+3)	1.03 ± 0.31	
Q86TH1	ADAMTS-like protein 2	Zn	104.6	F2	ScGGGVTSQERHcLQQR	980.37 (+2)	984.39 (+2)	0.54 ± 0.02	
Q8N2Y6	ZFHX3 protein	Zn	98.5	F2 F3	QcAVcNKFTTDNLDM	973.62 (+2)	977.64 (+2)	1.12 ± 0.18 0.96 ± 0.07	
P02790	Hemopexin	Fe	51.7	F2 F3	ALPQPQNVTSSLGcTH	868.94 (+2)	870.95 (+2)	1.31 ± 0.21 1.09 ± 0.17	
P02787	Serotransferrin	Fe, Cr	77.1	F2	SDNcEDTPEAGYFAIAVVK	1043.97 (+2)	1045.98 (+2)	1.14 ± 0.05	
				F3	EGTcPEAPTDEcKPVK	909.90 (+2)	913.92 (+2)	1.26 ± 0.10 1.11 ± 0.15	
				F2	LcIAMIDTGK	561.04 (+2)	563.05 (+2)	0.93 ± 0.18 0.85 ± 0.08	
				F3	AYLEEEcPATLR	726.23 (+2)	728.24 (+2)	0.76 ± 0.09 1.45 ± 0.23	
P25311	Zinc-alpha-2-glycoprotein	Zn	34.2	F2 F3	DEATGLcPEGDEcPF	848.74 (+2)	852.76 (+2)	0.90 ± 0.06 0.63 ± 0.17	
Q9C0B0	RING finger protein unkempt homolog	Zn	88.0	F3	ccKScWNEYL	709.66 (+2)	715.68 (+2)	0.84 ± 0.07	
Q8IWT3	Cullin-9	Zn	281.0	F3 F3	ADcLSTGMELLRR	761.30 (+2)	763.30 (+2)	1.08 ± 0.16	
P00450	Ceruloplasmin	Cu	115.4	F3	EVGPTNADPVcLAK	735.76 (+2)	737.77 (+2)	1.13 ± 0.15	
P01024	Complement C3	Co	187.0	F3 F4	DIcEEQVNSLPGSITK	895.85 (+2)	897.86 (+2)	2.02 ± 0.45 1.87 ± 0.64	
Q5TAX3	Terminal uridylyltransferase 4	Mn	185.0	F3	INAEREQPVQcDEMDCTSQR	823.01 (+3)	-	N.D. from cancer	
				F3 F4	VSAGNDMAcLTTDLLTALGK	1026.21 (+2)	-	N.D. from cancer	
				F4	IITEYMANcLL	698.91 (+2)	700.92 (+2)	N.D. from cancer 0.33 ± 0.08	
Q3MS94	Dominant-negative kinase-deficient Brutons tyrosine kinase isoform 4	Mn	22.8	F4	cHTcQNGGTVILMDGK	896.22 (+2)	900.23 (+2)	0.87 ± 0.12	
P02748	Complement component C9	Co	63.1	F4					