

Supplemental Material

Supplemental Table 1. Protein names and respective Olink® panel sorted in alphabetical order

Protein full name	Entry name	Olink® Panel*	Uniprot ID**
Angiotensin-converting enzyme 2	ACE2	CVD II	Q9BYF1
Adenosine Deaminase	ADA	INF	P00813
Adisintegrin and metalloproteinase with thrombospondin motifs 13	ADAMTS13	CVD II	Q76LX8
ADM	ADM	CVD II	P35318
Agouti-related protein	AGRP	CVD II	O00253
CD166 antigen	ALCAM	CVD III	Q13740
Protein AMBP	AMBP	CVD II	P02760
Angiopoietin-1	ANG1	CVD II	Q15389
Aminopeptidase N	APN	CVD III	P15144
Axin-1	AXIN1	INF	O15169
Tyrosine-protein kinase receptor UFO	AXL	CVD III	P30530
Azurocidin	AZU1	CVD III	P20160
Brain-derived neurotrophic factor	BDNF	INF	P23560
Beta-nerve growth factor	BETANGF	INF	P01138

Bleomycin hydrolase	BLMHYDROL ASE	CVD III	Q13867
Bone morphogenetic protein 6	BMP6	CVD II	P22004
Natriuretic peptides B	BNP	CVD II	P16860
Eukaryotic translation initiation factor 4E- binding protein 1	BP1_4E	INF	Q13541
Carbonic anhydrase 5A, mitochondrial	CA5A	CVD II	P35218
Caspase-3	CASP3	CVD III	P42574
Caspase 8	CASP8	INF	Q14790
Eotaxin-1	CCL11	INF	P51671
C-C motif chemokine 15	CCL15	CVD III	Q16663
C-C motif chemokine 16	CCL16	CVD III	O15467
C-C motif chemokine 17	CCL17	CVD II	Q92583
C-C motif chemokine 19	CCL19	INF	Q99731
C-C motif chemokine 20	CCL20	INF	P78556
C-C motif chemokine 22	CCL22	CVD III	O00626
C-C motif chemokine 23	CCL23	INF	P55773
C-C motif chemokine 24	CCL24	CVD III	O00175

C-C motif chemokine 25	CCL25	INF	O15444
C-C motif chemokine 28	CCL28	INF	Q9NRJ3
C-C motif chemokine 3	CCL3	CVD II	P10147
C-C motif chemokine 4	CCL4	INF	P13236
Scavenger receptor cysteine-rich type 1 protein M130	CD163	CVD III	Q86VB7
Natural killer cell receptor 2B4	CD244	INF	Q9BZW8
T-cell surface glycoprotein CD4	CD4	CVD II	P01730
CD40L receptor	CD40	INF	P25942
CD40 ligand	CD40L	CVD II	P29965
T-cell surface glycoprotein CD5	CD5	INF	P06127
T cell surface glycoprotein CD6	CD6	INF	P30203
SLAM family member 5	CD84	CVD II	Q9UIB8
Complement component C1q receptor	CD93	CVD III	Q9NPY3
CUB domain-containing protein 1	CDCP1	INF	Q9H5V8
Cadherin-5	CDH5	CVD III	P33151
Carcinoembryonic antigenrelated cell adhesion molecule 8	CEACAM8	CVD II	P31997

Chitinase-3-like protein 1	CHI3L1	CVD III	P36222
Chitotriosidase-1	CHIT1	CVD III	Q13231
Contactin-1	CNTN1	CVD III	Q12860
Collagen alpha-1(I) chain	COL1A1	CVD III	P02452
Carboxypeptidase A1	CPA1	CVD III	P15085
Carboxypeptidase B	CPB1	CVD III	P15086
Macrophage colony-stimulating factor 1	CSF1	INF	P09603
Cystatin D	CST5	INF	P28325
Cystatin-B	CSTB	CVD III	P04080
Chymotrypsin C	CTRC	CVD II	Q99895
Cathepsin D	CTSD	CVD III	P07339
Cathepsin L1	CTSL1	CVD II	P07711
Cathepsin Z	CTSZ	CVD III	Q9UBR2
Fractalkine	CX3CL1	INF	P78423
C-X-C motif chemokine 1 (CVD2)	CXCL1	CVD II	P09341
C-X-C motif chemokine 10	CXCL10	INF	P02778
C-X-C motif chemokine 11	CXCL11	INF	O14625
C-X-C motif chemokine 16	CXCL16	CVD III	Q9H2A7

C-X-C motif chemokine 5	CXCL5	INF	P42830
C-X-C motif chemokine 6	CXCL6	INF	P80162
C-X-C motif chemokine 9	CXCL9	INF	Q07325
Decorin	DCN	CVD II	P07585
2,4-dienoyl-CoA reductase, mitochondrial	DECR1	CVD II	Q16698
Dickkopf-related protein 1	DKK1	CVD II	O94907
Azurocidin	DLK1	CVD III	P80370
Delta and Notch-like epidermal growth factor-related receptor	DNER	INF	Q8NFT8
Epidermal growth factor receptor	EGFR	CVD III	P00533
Protein S100-A12	ENRAGE	INF	P80511
Epithelial cell adhesion molecule	EPCAM	CVD III	P16422
Ephrin type-B receptor 4	EPHB4	CVD III	P54760
Fatty acid-binding protein, intestinal	FABP2	CVD II	P12104
Fatty acid-binding protein, adipocyte	FABP4	CVD III	P15090
Tumor necrosis factor receptor superfamily member 6	FAS	CVD III	P25445
Fibroblast growth factor 19	FGF19	INF	O95750

Fibroblast growth factor 21 (CVD2)	FGF21	CVD II	Q9NSA1
Fibroblast growth factor 23 (CVD2)	FGF23	CVD II	Q9GZV9
Fibroblast growth factor 5	FGF5	INF	P12034
Fms-related tyrosine kinase 3 ligand	FLT3L	INF	P49771
Follistatin	FS	CVD II	P19883
Galectin-3	GAL3	CVD III	P17931
Galectin-4	GAL4	CVD III	P56470
Galectin-9	GAL9	CVD II	O00182
Growth/differentiation factor 15	GDF15	CVD III	Q99988
Growth/differentiation factor 2	GDF2	CVD II	Q9UK05
Growth hormone	GH	CVD II	P01241
Gastric intrinsic factor	GIF	CVD II	P27352
Lactoylglutathione lyase	GLO1	CVD II	Q04760
Granulins	GRN	CVD III	P28799
Gastrotropin	GT	CVD II	P51161
Hydroxyacid oxidase 1	HAOX1	CVD II	Q9UJM8
Proheparin-binding EGF-like growth factor	HBEGF	CVD II	Q99075
Glial cell line-derived neurotrophic factor	HGDNF	INF	P39905

Hepatocyte growth factor	HGF	INF	P14210
Heme oxygenase 1	HO1	CVD II	P09601
Osteoclast-associated immunoglobulin-like receptor	HOSCAR	CVD II	Q8IYS5
Heat shock 27 kDa protein	HSP27	CVD II	P04792
Intercellular adhesion molecule 2	ICAM2	CVD III	P13598
Alpha-L-iduronidase	IDUA	CVD II	P35475
Insulin-like growth factor-binding protein 1	IGFBP1	CVD III	P08833
Insulin-like Growth Factor-Binding Protein 2	IGFBP2	CVD III	P18065
Insulin-like growth factor-binding protein 7	IGFBP7	CVD III	Q16270
Low affinity immunoglobulin gamma Fc region receptor II-b	IGGFCRECEPT ORIIIB	CVD II	P31994
Interleukin-10	IL10	INF	P22301
Interleukin-10 receptor subunit alpha	IL10RA	INF	Q13651
Interleukin-10 receptor subunit beta	IL10RB	INF	Q08334
Interleukin-12 subunit beta	IL12B	INF	P29460
Interleukin-13	IL13	INF	P35225
Interleukin-15 receptor subunit alpha	IL15RA	INF	Q13261

Pro-interleukin-16	IL16	CVD II	Q14005
Interleukin-17A	IL17A	INF	Q16552
Interleukin-17C	IL17C	INF	Q9P0M4
Interleukin-17D	IL17D	CVD II	Q8TAD2
Interleukin-17 receptor A	IL17RA	CVD III	Q96F46
Interleukin-18 (CVD2)	IL18	CVD II	Q14116
Interleukin-18-binding protein	IL18BP	CVD III	O95998
Interleukin-18 receptor 1	IL18R1	INF	Q13478
Interleukin-1 receptor antagonist protein	IL1RA	CVD II	P18510
Interleukin-1 receptor-like 2	IL1RL2	CVD II	Q9HB29
Interleukin-1 receptor type 1	IL1RT1	CVD III	P14778
Interleukin-1 receptor type 2	IL1RT2	CVD III	P27930
Interleukin-20 receptor subunit alpha	IL20RA	INF	Q9UHF4
Interleukin-27	IL27	CVD II	Q8NEV9
Interleukin-2 receptor subunit alpha	IL2RA	CVD III	P01589
Interleukin-4 receptor subunit alpha	IL4RA	CVD II	P24394
Interleukin-6 (CVD2)	IL6	CVD II	P05231
Interleukin-6 receptor subunit alpha	IL6RA	CVD III	P08887

Interleukin-7	IL7	INF	P13232
Interleukin-8	IL8	INF	P10145
Melusin	ITGB1BP2	CVD II	Q9UKP3
Integrin beta-2	ITGB2	CVD III	P05107
Junctional adhesion molecule A	JAMA	CVD III	Q9Y624
Kidney injury molecule 1	KIM1	CVD II	Q96D42
Kallikrein-6	KLK6	CVD III	Q92876
Latency-associated peptide transforming growth factor beta 1	LAPTGFbeta 1	INF	P01137
Low-density lipoprotein receptor	LDLRECEPTOR	CVD III	P01130
Leptin	LEP	CVD II	P41159
Leukemia inhibitory factor receptor	LIFR	INF	P42702
Lectin-like oxidized LDL receptor 1	LOX1	CVD II	P78380
Lipoprotein lipase	LPL	CVD II	P06858
Lymphotoxin-beta receptor	LTBR	CVD III	P36941
Macrophage receptor MARCO	MARCO	CVD II	Q9UEW3
Myoglobin	MB	CVD III	P02144

Monocyte chemotactic protein 1	MCP1_CVD3	CVD III	P13500
Monocyte chemotactic protein 2	MCP2	INF	P80075
Monocyte chemotactic protein 3	MCP3	INF	P80098
Monocyte chemotactic protein 4	MCP4	INF	Q99616
Matrix extracellular phosphoglycoprotein	MEPE	CVD III	Q9NQ76
Tyrosine-protein kinase Mer	MERTK	CVD II	Q12866
Matrix metalloproteinase-1	MMP1	INF	P03956
Matrix metalloproteinase-10	MMP10	INF	P09238
Matrix metalloproteinase-12	MMP12	CVD II	P39900
Matrix metalloproteinase-2	MMP2	CVD III	P08253
Matrix metalloproteinase-3	MMP3	CVD III	P08254
Matrix metalloproteinase-7	MMP7	CVD II	P09237
Matrix metalloproteinase-9	MMP9	CVD III	P14780
Myeloperoxidase	MPO	CVD III	P05164
NF-kappa-B essential modulator	NEMO	CVD II	Q9Y6K9
Neurogenic locus notch homolog protein 3	NOTCH3	CVD III	Q9UM47
Neurotrophin-3	NT3	INF	P20783
N-terminal prohormone brain natriuretic	NTPROBNP	CVDII	P16860

peptide			
Osteoprotegerin	OPG_CVD3	CVD III	O00300
Osteopontin	OPN	CVD III	P10451
Oncostatin-M	OSM	INF	P13725
Plasminogen activator inhibitor 1	PAI	CVD III	P05121
Pappalysin-1	PAPPA	CVD II	Q13219
Proteinase-activated receptor 1	PAR1	CVD II	P25116
Poly [ADP-ribose] polymerase 1	PARP1	CVD II	P09874
Proprotein convertase subtilisin/kexin type 9	PCSK9	CVD III	Q8NBP7
Platelet-derived growth factor subunit A	PDGFSUBUNI TA	CVD III	P04085
Platelet-derived growth factor subunit B	PDGFSUBUNI TB	CVD II	P01127
Programmed cell death 1 ligand 1	PDL1	INF	Q9NZQ7
Programmed cell death 1 ligand 2	PDL2	CVD II	Q9BQ51
Platelet endothelial cell adhesion molecule	PECAM1	CVD III	P16284
Peptidoglycan recognition protein 1	PGLYRP1	CVD III	O75594
Elafin	PI3	CVD III	P19957

Polymeric immunoglobulin receptor	PIGR	CVD II	P01833
Perlecan	PLC	CVD III	P98160
Placenta growth factor	PLGF	CVD II	P49763
Paraoxonase (PON 3)	PON3	CVD III	Q15166
Prolargin	PRELP	CVD II	P51888
Brother of CDO	PROTEINBOC	CVD II	Q9BWW1
Serine protease 27	PRSS27	CVD II	Q9BQR3
Prostasin	PRSS8	CVD II	Q16651
Myeloblastin	PRTN3	CVD III	P24158
P-selectin glycoprotein ligand 1	PSGL1	CVD II	Q14242
Pulmonary surfactant-associated protein D	PSPD	CVD III	P35247
Pentraxin-related protein PTX3	PTX3	CVD II	P26022
Receptor for advanced glycosylation end products	RAGE	CVD II	Q15109
Retinoic acid receptor responder protein 2	RARRES2	CVD III	Q99969
Renin	REN	CVD II	P00797
Resistin	RETN	CVD III	Q9HD89
Stem cell factor (CVD2)	SCF	CVD II	P21583

Secretoglobin family 3A member 2	SCGB3A2	CVD III	Q96PL1
E-selectin	SELE	CVD III	P16581
P-selectin	SELP	CVD III	P16109
Serpin A12	SERPINA12	CVD II	Q8IW75
Tyrosine-protein phosphatase non-receptor type substrate 1	SHPS1	CVD III	P78324
SIR2-like protein 2	SIRT2	INF	Q8IXJ6
Signaling lymphocytic activation molecule	SLAMF1	INF	Q13291
SLAM family member 7	SLAMF7	CVD II	Q9NQ25
Superoxide dismutase [Mn], mitochondrial	SOD2	CVD II	P04179
Sortilin	SORT1	CVD II	Q99523
Spondin-1	SPON1	CVD III	Q9HCB6
Spondin-2	SPON2	CVD II	Q9BUD6
Proto-oncogene tyrosine-protein kinase Src	SRC	CVD II	P12931
Sulfotransferase 1A1	ST1A1	INF	P50225
ST2 protein	ST2	CVD III	Q01638
STAM-binding protein	STAMPB	INF	O95630
Serine/threonine-protein kinase 4	STK4	CVD II	Q13043

Tissue factor	TF	CVD II	P13726
Trefoil factor 3	TFF3	CVD III	Q07654
Tissue factor pathway inhibitor	TFPI	CVD III	P10646
Transforming growth factor alpha	TGFALPHA	INF	P01135
Protein-glutamine gamma-glutamyltransferase 2	TGM2	CVD II	P21980
Thrombospondin-2	THBS2	CVD II	P35442
Thrombopoietin	THPO	CVD II	P40225
Angiopoietin-1 receptor	TIE2	CVD II	Q02763
Metalloproteinase inhibitor 4	TIMP4	CVD III	Q99727
Trem-like transcript 2 protein	TLT2	CVD III	Q5T2D2
Thrombomodulin	TM	CVD II	P07204
Tumor necrosis factor	TNF	INF	P01375
TNF-beta	TNFB	INF	P01374
Tumor necrosis factor receptor 1	TNFR1	CVD III	P19438
Tumor necrosis factor receptor 2	TNFR2	CVD III	P20333
Tumor necrosis factor receptor superfamily member 10A	TNFRSF10A	CVD II	O00220

Tumor necrosis factor receptor superfamily member 10C	TNFRSF10C	CVD III	O14798
Tumor necrosis factor receptor superfamily member 11A	TNFRSF11A	CVD II	Q9Y6Q6
Tumor necrosis factor receptor superfamily member 13B	TNFRSF13B	CVD II	O14836
Tumor necrosis factor receptor superfamily member 14	TNFRSF14	CVD III	Q92956
Tumor necrosis factor receptor superfamily member 9	TNFRSF9	INF	Q07011
Tumor necrosis factor ligand superfamily member 13B	TNFSF13B	CVD III	Q9Y275
Tumor necrosis factor ligand superfamily member 14	TNFSF14	INF	O43557
Tissue-type plasminogen activator	TPA	CVD III	P00750
Transferrin receptor protein 1	TR	CVD III	P02786
TNF-related apoptosis-inducing ligand	TRAIL	INF	P50591
TNF-related apoptosis-inducing ligand receptor 2	TRAILR2	CVD II	O14763
TNF-related activation-induced cytokine	TRANCE	INF	O14788

Tartrate-resistant acid phosphatase type 5	TRAP	CVD III	P13686
Tumor necrosis factor (Ligand) superfamily, member 12	TWEAK	INF	O43508
Urokinase-type plasminogen activator	UPA_CVD3	CVD III	P00749
Urokinase plasminogen activator surface receptor	UPAR	CVD III	Q03405
Vascular endothelial growth factor A	VEGFA	INF	P15692
Vascular endothelial growth factor D	VEGFD	CVD II	O43915
V-set and immunoglobulin domain-containing protein 2	VSIG2	CVD II	Q96IQ7
von Willebrand factor	VWF	CVD III	P04275
Lymphotactin	XCL1	CVD II	P47992

Supplemental Table 2. Baseline characteristics of the patients by treatment group

	Control		Spirolactone	
	N=262		N=265	
Demographics and Lifestyle				
Age-years	72.9	(68.4, 78.4)	72.9	(68.6, 78.5)
Female-N.(%)	75	(28.6)	60	(22.6)
Caucasian-N.(%)	260	(99.2)	258	(97.4)
Current smoker-N.(%)	20	(7.6)	24	(9.1)
Inclusion risk factors-N.(%)				
CAD	188	(71.8)	189	(71.3)
Diabetes	105	(40.1)	107	(40.4)
Hypertension	198	(75.6)	214	(80.8)
Microalbuminuria	53	(20.2)	55	(20.8)
Abnormal ECG	84	(32.1)	92	(34.7)
NT-pro BNP-pg/ml	209.0	(133.5, 339.5)	218.0	(138.0, 385.0)
BNP-pg/ml	65.0	(47.0, 108.0)	69.5	(48.0, 118.0)
Medical History-N.(%)				
Hypertension	199	(76.0)	214	(80.8)

Diabetes mellitus	109	(41.6)		110	(41.5)
CAD	190	(72.5)		190	(71.7)
Angina	97	(37.0)		98	(37.0)
Positive coronary angiogram	118	(45.0)		107	(40.4)
Myocardial Infarction	103	(39.3)		113	(42.6)
PCI	138	(52.7)		129	(48.7)
CABG	69	(26.3)		67	(25.3)
Stroke/TIA	13	(5.0)		15	(5.7)
COPD	13	(5.0)		21	(7.9)
Cardiac device	10	(3.8)		12	(4.5)
Medications-N.(%)					
Aspirin	181	(69.1)		195	(73.6)
Beta Blocker	180	(68.7)		186	(70.2)
Thiazides	41	(15.6)		46	(17.4)
ACEi	140	(53.4)		135	(50.9)
ARB	71	(27.1)		74	(27.9)
CCB	51	(19.5)		59	(22.3)
Statin/Lipid lowering drug	217	(82.8)		218	(82.3)

Anticoagulant	12	(4.6)		18	(6.8)
Antiplatelet (excl. aspirin)	51	(19.5)		48	(18.1)
Antiplatelet (incl. aspirin)	205	(78.2)		209	(78.9)
Anthropometrics					
Weight-kg	81.7	(71.0, 91.0)		82.0	(73.0, 92.3)
BMI-kg/msq	27.6	(25.3, 31.4) [1]		28.4	(25.4, 31.7) [1]
Vital Signs					
SBP-mmHg	140.0	(128.0, 155.0) [5]		140.0	(126.0, 155.0) [4]
<120	30	(11.5)		34	(12.8)
120-139	95	(36.3)		90	(34.0)
140-159	87	(33.2)		92	(34.7)
160+	45	(17.2)		45	(17.0)
DBP-mmHg	77.0	(71.0, 84.0) [5]		78.0	(71.0, 85.0) [4]
Heart Rate-bpm	61.0	(54.0, 67.0) [5]		60.0	(55.0, 67.0) [4]
ECHO results					
ECG QRS-msec	92.0	(84.0, 102.0) [0]		92.0	(84.0, 108.0) [2]
LVEF (%)	63.1	(56.5, 66.1) [75]		62.8	(58.5, 66.7) [88]
LVM (g/m ²)	94.7	(80.5, 113.5) [23]		94.5	(81.1, 110.9) [29]

LAV (ml/m ²)	31.4	(26.2, 37.2) [42]		30.4	(25.9, 35.3) [54]
Blood Results					
eGFR-ml/min/1.73msq	71.6	(60.7, 81.0) [1]		73.4	(61.7, 87.5) [0]
<45	13	(5.0)		18	(6.8)
45-60	50	(19.1)		37	(14.0)
>60	199	(76.0)		210	(79.2)
Haemoglobin-g/dl	14.1	(13.2, 14.9) [0]		14.0	(13.1, 14.9) [2]
Creatinine-mg/dl	84.4	(74, 98) [1]		84.0	(71, 100) [0]
Sodium-mmol/l	139.0	(138.0, 141.0) [1]		140.0	(138.0, 141.0) [0]
Potassium-mmol/l	4.3	(4.1, 4.6) [4]		4.3	(4.0, 4.6) [1]
Urea-mmol/l	8.9	(5.8, 13.6)		8.5	(5.9, 14.6)

Supplemental Table 3. Spironolactone effect on all the studied biomarkers at 1 month

Biomarker	Coef.	LCI	UCI	P-value	FDR q
REN	0.48	0.38	0.58	0.00001	0.0009
BNP	-0.46	-0.61	-0.32	0.00001	0.0009
NTPROBNP	-0.3	-0.43	-0.17	0.00001	0.0009
VEGFD	-0.09	-0.14	-0.04	0.0003	0.0207
CCL25	0.1	0.04	0.15	0.0007	0.0311
TNFRSF9	0.11	0.05	0.17	0.0007	0.0311
MMP2	-0.1	-0.16	-0.04	0.0008	0.0311
LEP	0.15	0.06	0.24	0.0009	0.0311
LPL	0.11	0.04	0.18	0.0018	0.0524
CST5	0.09	0.03	0.15	0.0019	0.0524
AMBP	0.05	0.02	0.08	0.0029	0.0701
CTRC	0.12	0.04	0.21	0.0033	0.0701
CSTB	0.13	0.04	0.21	0.0033	0.0701
CXCL9	0.16	0.05	0.27	0.004	0.0789
COL1A1	-0.08	-0.13	-0.02	0.0043	0.0791
CCL20	0.23	0.07	0.38	0.0046	0.0794

IL12B	0.1	0.03	0.17	0.0058	0.0942
CCL19	0.12	0.03	0.21	0.0063	0.0966
NOTCH3	-0.08	-0.13	-0.02	0.0094	0.1365
FABP4	0.12	0.03	0.22	0.01	0.1380
TR	-0.11	-0.2	-0.02	0.0126	0.1656
ST2	-0.08	-0.14	-0.02	0.0136	0.1680
MEPE	0.08	0.02	0.14	0.014	0.1680
CPA1	0.13	0.02	0.23	0.016	0.1840
CPB1	0.11	0.02	0.2	0.0187	0.2064
CD93	-0.06	-0.11	-0.01	0.0212	0.2198
TFF3	0.07	0.01	0.13	0.0215	0.2198
KIM1	-0.09	-0.16	-0.01	0.0244	0.2405
CCL3_INF	0.09	0.01	0.17	0.027	0.2570
BP1_4E	0.16	0.01	0.31	0.033	0.3036
IL18_INF	0.07	0.01	0.14	0.0347	0.3036
GIF	0.1	0.01	0.19	0.0352	0.3036
GAL3	0.06	0	0.12	0.041	0.3429
TRAIL	0.05	0	0.1	0.0424	0.3430

ITGB2	0.08	0	0.15	0.0435	0.3430
ENRAGE	0.11	0	0.21	0.0474	0.3634
CEACAM8	0.1	0	0.19	0.05	0.3730
PSPD	-0.08	-0.16	0	0.0525	0.3813
ARTN	0.02	0	0.05	0.055	0.3857
RARRES2	0.05	0	0.1	0.0559	0.3857
PRSS8	0.05	0	0.1	0.0582	0.3918
GAL9	0.05	0	0.09	0.0633	0.4134
CNTN1	-0.05	-0.1	0	0.0653	0.4134
PAPPA	-0.07	-0.14	0	0.0669	0.4134
SELE	-0.06	-0.12	0	0.0674	0.4134
UPAR	0.06	-0.01	0.13	0.0707	0.4145
TIMP4	0.06	0	0.12	0.0708	0.4145
IL22RA1	0.03	0	0.06	0.0722	0.4145
CCL16	0.06	-0.01	0.13	0.0743	0.4145
THBS2	-0.04	-0.08	0	0.077	0.4145
MB	-0.08	-0.18	0.01	0.0773	0.4145
IL17C	0.1	-0.01	0.21	0.0781	0.4145

SPON1	-0.04	-0.09	0.01	0.0829	0.4182
ACE2	0.06	-0.01	0.13	0.0833	0.4182
RETN	0.07	-0.01	0.14	0.0863	0.4182
AXL	-0.05	-0.1	0.01	0.0863	0.4182
MPO	0.03	0	0.06	0.0881	0.4182
MMP1	0.14	-0.02	0.31	0.0883	0.4182
IL17D	-0.05	-0.1	0.01	0.0894	0.4182
MMP9	0.05	-0.01	0.11	0.0971	0.4467
VEGFA	0.05	-0.01	0.12	0.1057	0.4710
PTX3	-0.05	-0.12	0.01	0.1058	0.4710
TNFSF14	0.08	-0.02	0.18	0.1107	0.4793
TNFSF13B	-0.05	-0.1	0.01	0.1119	0.4793
TGM2	0.11	-0.03	0.25	0.114	0.4793
TPA	0.1	-0.03	0.23	0.1192	0.4793
PGLYRP1	0.06	-0.02	0.13	0.121	0.4793
VSIG2	0.06	-0.02	0.14	0.1222	0.4793
IL2	0	-0.01	0	0.1223	0.4793
CD5	0.05	-0.01	0.12	0.1226	0.4793

IL6RA	0.05	-0.01	0.1	0.1233	0.4793
LOX1	0.07	-0.02	0.16	0.1286	0.4930
IL18R1	0.04	-0.01	0.09	0.1448	0.5442
MCP3	0.05	-0.02	0.12	0.1482	0.5442
CCL17	0.13	-0.05	0.31	0.1508	0.5442
CTSZ	0.04	-0.02	0.1	0.1509	0.5442
TNFRSF14	0.06	-0.02	0.13	0.1528	0.5442
TNFRSF13B	0.04	-0.02	0.1	0.1538	0.5442
IGFBP2	-0.05	-0.12	0.02	0.1743	0.5977
CCL24	0.05	-0.02	0.12	0.1752	0.5977
TNFR2	0.04	-0.02	0.11	0.1754	0.5977
PDL1	0.05	-0.02	0.13	0.1798	0.5989
OPG_INF	0.04	-0.02	0.09	0.1827	0.5989
SERPINA12	-0.04	-0.09	0.02	0.1855	0.5989
IL18	0.05	-0.02	0.11	0.1856	0.5989
HO1	-0.04	-0.1	0.02	0.1866	0.5989
PCSK9	0.04	-0.02	0.1	0.1944	0.6156
IL10RB	0.04	-0.02	0.09	0.1977	0.6156

BOC	-0.03	-0.08	0.02	0.1985	0.6156
OSM	0.08	-0.05	0.21	0.2015	0.6179
IL17A	-0.06	-0.16	0.03	0.2061	0.6232
IGFBP1	-0.09	-0.23	0.05	0.208	0.6232
CXCL10	0.06	-0.04	0.16	0.2133	0.6232
ALCAM	-0.03	-0.08	0.02	0.2135	0.6232
CTSL1	-0.03	-0.08	0.02	0.2145	0.6232
STAMBP	0.11	-0.07	0.3	0.2322	0.6573
ICAM2	-0.03	-0.09	0.02	0.2326	0.6573
IDUA	0.04	-0.02	0.1	0.2334	0.6573
RAGE	-0.03	-0.09	0.02	0.2404	0.6702
CXCL11	0.09	-0.06	0.23	0.2447	0.6754
ADA	0.04	-0.03	0.11	0.2509	0.6856
TNFRSF11A	0.04	-0.03	0.1	0.2539	0.6870
CCL15	0.03	-0.03	0.09	0.2666	0.7144
TGFALPHA	0.03	-0.02	0.08	0.2813	0.7429
HGF	0.03	-0.03	0.09	0.2834	0.7429
CD244	0.04	-0.03	0.11	0.2853	0.7429

AZU1	0.04	-0.04	0.12	0.2904	0.7432
ADAMTS13	0.02	-0.02	0.06	0.293	0.7432
CCL4	0.05	-0.04	0.13	0.2935	0.7432
CD4	0.03	-0.03	0.08	0.2994	0.7435
FABP2	0.07	-0.06	0.19	0.3003	0.7435
PGF	0.03	-0.03	0.09	0.3045	0.7435
PRTN3	0.02	-0.02	0.06	0.3058	0.7435
GLO1	0.07	-0.07	0.22	0.3071	0.7435
APN	-0.03	-0.08	0.03	0.3187	0.7649
VWF	0.11	-0.11	0.32	0.3244	0.7718
TNF	-0.01	-0.04	0.01	0.3315	0.7795
IL2RA	0.05	-0.05	0.14	0.3341	0.7795
PRELP	0.02	-0.02	0.06	0.3361	0.7795
TSLP	-0.01	-0.03	0.01	0.3418	0.7861
CXCL6	0.07	-0.07	0.21	0.3513	0.7927
EPCAM	-0.05	-0.14	0.05	0.3574	0.7927
TWEAK	0.02	-0.03	0.08	0.3585	0.7927
CCL11	0.03	-0.03	0.08	0.3591	0.7927

SELP	0.07	-0.08	0.21	0.3632	0.7927
CCL28	0.02	-0.03	0.07	0.3693	0.7927
PDGFSUBUNITA	0.08	-0.1	0.27	0.3705	0.7927
TRAILR2	0.03	-0.03	0.08	0.3727	0.7927
CCL3	0.04	-0.05	0.13	0.3729	0.7927
FGF5	0.01	-0.01	0.04	0.38	0.7927
TRANCE	-0.03	-0.11	0.04	0.3803	0.7927
CD40	0.04	-0.05	0.12	0.3816	0.7927
DECR1	-0.12	-0.39	0.15	0.3859	0.7927
BETANGF	-0.02	-0.05	0.02	0.3879	0.7927
PLC	0.02	-0.03	0.07	0.3896	0.7927
TNFRSF10A	0.02	-0.03	0.08	0.3906	0.7927
DLK1	-0.03	-0.09	0.04	0.3935	0.7927
CA5A	0.05	-0.06	0.15	0.3982	0.7964
BMP6	-0.03	-0.12	0.05	0.403	0.8002
LAPTGBETA1	0.03	-0.05	0.11	0.4113	0.8092
HOSCAR	0.02	-0.02	0.06	0.4134	0.8092
OPG	0.02	-0.03	0.07	0.4185	0.8093

IL13	0.02	-0.02	0.06	0.4193	0.8093
PON3	0.03	-0.04	0.1	0.4287	0.8143
UPA_INF	0.02	-0.03	0.07	0.4288	0.8143
TIE2	-0.02	-0.07	0.03	0.435	0.8143
LIFR	-0.02	-0.07	0.03	0.4365	0.8143
FGF19	0.06	-0.09	0.22	0.4391	0.8143
CD8A	0.03	-0.04	0.09	0.4398	0.8143
DNER	0.02	-0.03	0.06	0.4452	0.8143
NT3	0.03	-0.05	0.12	0.4455	0.8143
MCP2	0.03	-0.05	0.11	0.4608	0.8367
MMP3	-0.03	-0.11	0.05	0.4746	0.8532
HBEGF	0.05	-0.08	0.18	0.478	0.8532
SIRT2	0.09	-0.16	0.33	0.4828	0.8532
IL8	0.03	-0.06	0.13	0.4845	0.8532
MCP4	0.04	-0.07	0.15	0.4856	0.8532
STK4	-0.07	-0.28	0.13	0.4884	0.8532
PSGL1	-0.01	-0.05	0.03	0.4935	0.8566
MMP10	0.03	-0.05	0.1	0.4999	0.8623

SCF_INF	0.01	-0.03	0.06	0.5104	0.8704
UPA	0.02	-0.04	0.08	0.5109	0.8704
BLMHYDROLASE	-0.02	-0.09	0.04	0.5188	0.8785
SORT1	0.02	-0.04	0.08	0.5365	0.8868
PDGFSUBUNITB	0.08	-0.18	0.34	0.5379	0.8868
TFPI	0.02	-0.05	0.09	0.5386	0.8868
KLK6	0.02	-0.05	0.09	0.5393	0.8868
LDLRECEPTOR	-0.02	-0.1	0.05	0.5412	0.8868
PECAM1	0.04	-0.09	0.17	0.5444	0.8868
FGF21	-0.05	-0.21	0.11	0.5469	0.8868
AGRP	0.02	-0.06	0.11	0.5494	0.8868
GP6	0.04	-0.1	0.19	0.5634	0.8999
GAL4	0.02	-0.05	0.09	0.5644	0.8999
ANG1	0.06	-0.16	0.28	0.5727	0.8999
TLT2	0.02	-0.06	0.1	0.576	0.8999
FGF23_INF	0.02	-0.06	0.1	0.5785	0.8999
IL18BP	0.02	-0.04	0.08	0.5839	0.8999
SOD2	-0.01	-0.03	0.02	0.5847	0.8999

FGF21_INF	-0.04	-0.17	0.1	0.5894	0.8999
SCF	0.01	-0.03	0.06	0.593	0.8999
PARP1	0.04	-0.1	0.17	0.5967	0.8999
HAOX1	-0.04	-0.19	0.11	0.5986	0.8999
SLAMF7	-0.02	-0.09	0.05	0.6032	0.8999
IL15RA	0.01	-0.03	0.06	0.6061	0.8999
DKK1	0.03	-0.09	0.16	0.6082	0.8999
FGF23	0.02	-0.06	0.1	0.6091	0.8999
CXCL1_INF	0.06	-0.17	0.29	0.6187	0.8999
GDNF	0.02	-0.05	0.08	0.6192	0.8999
TF	0.01	-0.04	0.06	0.6219	0.8999
CX3CL1	0.02	-0.05	0.08	0.6252	0.8999
MCP1_INF	0.02	-0.05	0.08	0.6261	0.8999
TNFRSF10C	0.01	-0.04	0.07	0.6266	0.8999
EGFR	-0.01	-0.05	0.03	0.6293	0.8999
IL4	0.01	-0.02	0.03	0.6501	0.9178
IFNGAMMA	0	-0.01	0.01	0.6508	0.9178
JAMA	0.04	-0.15	0.24	0.6518	0.9178

SRC	-0.04	-0.22	0.14	0.6577	0.9214
CD163	0.01	-0.05	0.07	0.6616	0.9222
GT	0.02	-0.08	0.12	0.6663	0.9222
IL1RL2	-0.01	-0.07	0.05	0.671	0.9222
SLAMF1	0.01	-0.05	0.08	0.6716	0.9222
IL1RT1	-0.01	-0.06	0.04	0.6775	0.9238
PAI	0.03	-0.12	0.18	0.6886	0.9238
OPN	-0.01	-0.08	0.06	0.6891	0.9238
CD40L	0.05	-0.2	0.3	0.6961	0.9238
XCL1	-0.01	-0.07	0.05	0.6978	0.9238
GDF2	-0.01	-0.07	0.05	0.7002	0.9238
ITGB1BP2	0.05	-0.21	0.31	0.7008	0.9238
GDF15	0.01	-0.06	0.08	0.701	0.9238
CTSD	0.01	-0.05	0.07	0.7029	0.9238
PI3	-0.01	-0.08	0.05	0.7117	0.9308
HSP27	-0.02	-0.1	0.07	0.715	0.9308
NEMO	-0.04	-0.28	0.2	0.726	0.9366
IL4RA	-0.01	-0.06	0.04	0.7262	0.9366

GH	0.05	-0.24	0.34	0.7352	0.9413
IL20	0	-0.02	0.01	0.7367	0.9413
SHPS1	-0.01	-0.06	0.04	0.7404	0.9417
CHIT1	0.01	-0.07	0.09	0.7474	0.9462
IL20RA	-0.01	-0.05	0.03	0.7556	0.9465
IL27	-0.01	-0.06	0.04	0.7583	0.9465
CD84	0.01	-0.08	0.11	0.7643	0.9465
CASP3	0.03	-0.21	0.28	0.7792	0.9465
CXCL16	0.01	-0.04	0.06	0.7814	0.9465
AXIN1	0.04	-0.22	0.29	0.7835	0.9465
IL6	0.02	-0.1	0.14	0.7837	0.9465
IL6_INF	0.02	-0.11	0.14	0.7839	0.9465
CSF1	-0.01	-0.05	0.04	0.7863	0.9465
LIF	0	-0.02	0.02	0.7877	0.9465
TM	0.01	-0.05	0.06	0.7915	0.9465
CASP8	0.01	-0.09	0.12	0.7929	0.9465
MMP7	0.01	-0.06	0.08	0.8068	0.9465
IL10RA	-0.01	-0.06	0.04	0.8071	0.9465

FAS	0.01	-0.05	0.07	0.8082	0.9465
IL1RA	-0.01	-0.08	0.06	0.8135	0.9465
ST1A1	0.02	-0.13	0.17	0.8168	0.9465
PDL2	-0.01	-0.06	0.04	0.8178	0.9465
PAR1	0.01	-0.07	0.09	0.8225	0.9465
IL33	0	-0.01	0.01	0.827	0.9465
MARCO	0	-0.04	0.03	0.8359	0.9465
IL5	0.01	-0.08	0.1	0.8375	0.9465
IL1ALPHA	0	-0.01	0.01	0.8384	0.9465
CXCL1	0.02	-0.22	0.27	0.841	0.9465
DCN	0.01	-0.05	0.06	0.8426	0.9465
THPO	0.01	-0.07	0.08	0.845	0.9465
IL16	-0.01	-0.09	0.07	0.8476	0.9465
FS	0.01	-0.06	0.07	0.8498	0.9465
SCGB3A2	-0.01	-0.1	0.08	0.8511	0.9465
NRTN	0	-0.03	0.02	0.8534	0.9465
IL2RB	0	-0.03	0.04	0.8539	0.9465
PRSS27	-0.01	-0.07	0.05	0.8582	0.9475

TRAP	0	-0.05	0.06	0.8696	0.9562
IL1RT2	0	-0.05	0.06	0.8735	0.9567
IL24	0	-0.04	0.05	0.8829	0.9632
MMP12	0.01	-0.07	0.08	0.8892	0.9654
TNFB	0	-0.05	0.05	0.8957	0.9654
CDH5	0	-0.06	0.06	0.8964	0.9654
CXCL5	-0.02	-0.32	0.28	0.8989	0.9654
FLT3L	0	-0.06	0.06	0.9035	0.9665
ADM	0	-0.06	0.05	0.9132	0.9725
EPHB4	0	-0.05	0.06	0.9161	0.9725
IL17RA	0	-0.08	0.09	0.923	0.9757
CCL23	0	-0.06	0.07	0.9262	0.9757
IL7	0	-0.13	0.14	0.9512	0.9930
SPON2	0	-0.03	0.04	0.9533	0.9930
CHI3L1	0	-0.11	0.11	0.958	0.9930
GRN	0	-0.05	0.05	0.961	0.9930
CDCP1	0	-0.07	0.07	0.9663	0.9930
CD6	0	-0.08	0.07	0.9679	0.9930

MERTK	0	-0.06	0.06	0.9685	0.9930
PIGR	0	-0.03	0.03	0.9786	0.9930
IGGFCRECEPTORIIB	0	-0.07	0.07	0.9813	0.9930
IL10	0	-0.08	0.08	0.9835	0.9930
TNFR1	0	-0.06	0.06	0.9871	0.9930
IGFBP7	0	-0.06	0.06	0.9878	0.9930
LTBR	0	-0.05	0.05	0.9894	0.9930
MCP1	0	-0.06	0.06	0.9943	0.9943

Supplemental Table 4. Spironolactone effect on all the studied biomarkers at month 9

Biomarker	Coef.	LCI	UCI	P-value	FDR q
REN	0.53	0.42	0.63	0.00001	0.0014
COL1A1	-0.14	-0.2	-0.08	0.00001	0.0014
RARRES2	0.09	0.04	0.14	0.0002	0.0184
VWF	0.39	0.18	0.59	0.0003	0.0207
RETN	0.15	0.06	0.24	0.0008	0.0315
MMP2	-0.1	-0.16	-0.04	0.0008	0.0315
CCL16	0.12	0.05	0.19	0.0008	0.0315
BNP	-0.28	-0.44	-0.11	0.0012	0.0414
PAPPA	-0.13	-0.2	-0.05	0.0015	0.0442
IL12B	0.13	0.05	0.22	0.0016	0.0442
PGLYRP1	0.13	0.05	0.22	0.0027	0.0644
VEGFD	-0.08	-0.13	-0.03	0.0028	0.0644
NOTCH3	-0.09	-0.15	-0.03	0.0032	0.0679
IL6RA	0.08	0.03	0.14	0.0043	0.0848
EPCAM	-0.16	-0.27	-0.05	0.0049	0.0902
AMBP	0.05	0.01	0.08	0.0058	0.1001

BOC	-0.06	-0.11	-0.02	0.0068	0.1031
IL4RA	-0.09	-0.15	-0.02	0.0069	0.1031
CCL19	0.15	0.04	0.26	0.0071	0.1031
IL17A	-0.15	-0.27	-0.04	0.0088	0.1214
MMP7	0.1	0.03	0.18	0.0095	0.1224
PLC	0.06	0.02	0.11	0.0101	0.1224
CCL25	0.07	0.02	0.13	0.0102	0.1224
SELE	-0.09	-0.16	-0.02	0.0108	0.1242
TRAIL	0.06	0.01	0.11	0.0114	0.1259
TPA	0.19	0.04	0.34	0.0121	0.1284
GAL9	0.06	0.01	0.11	0.013	0.1301
APN	-0.07	-0.12	-0.01	0.0132	0.1301
NT3	0.11	0.02	0.2	0.0184	0.1683
SRC	0.22	0.04	0.4	0.0186	0.1683
THBS2	-0.04	-0.08	-0.01	0.0189	0.1683
CSTB	0.1	0.02	0.19	0.0208	0.1794
FABP4	0.12	0.02	0.23	0.0235	0.1965
GDF15	0.09	0.01	0.16	0.0244	0.1976

TIE2	-0.05	-0.09	-0.01	0.0267	0.1976
AXL	-0.07	-0.13	-0.01	0.0267	0.1976
TNFRSF9	0.08	0.01	0.15	0.0269	0.1976
ALCAM	-0.06	-0.11	-0.01	0.0272	0.1976
CNTN1	-0.06	-0.12	0	0.0332	0.2289
CST5	0.07	0.01	0.13	0.0334	0.2289
CCL3_INF	0.09	0.01	0.18	0.034	0.2289
CPA1	0.12	0.01	0.22	0.0352	0.2313
IL17D	-0.06	-0.11	0	0.0367	0.2356
MPO	0.04	0	0.07	0.0387	0.2404
TFPI	0.06	0	0.12	0.0392	0.2404
UPAR	0.07	0	0.14	0.0402	0.2412
TFF3	0.07	0	0.13	0.042	0.2466
CXCL9	0.11	0	0.22	0.0433	0.2490
ADM	0.06	0	0.11	0.0459	0.2585
KLK6	0.07	0	0.13	0.0488	0.2690
PRTN3	0.05	0	0.11	0.0497	0.2690
CCL15	0.06	0	0.12	0.0508	0.2696

HO1	-0.06	-0.12	0	0.0548	0.2797
DLK1	-0.07	-0.14	0	0.056	0.2797
CPB1	0.09	0	0.19	0.0579	0.2797
NTPROBNP	-0.13	-0.27	0	0.058	0.2797
GAL3	0.06	0	0.13	0.0586	0.2797
HSP27	0.08	0	0.16	0.0591	0.2797
PRSS27	-0.06	-0.11	0	0.0598	0.2797
CD93	-0.05	-0.11	0	0.0612	0.2815
ST2	-0.08	-0.16	0.01	0.0669	0.2983
LIFR	-0.05	-0.09	0	0.067	0.2983
PSPD	-0.08	-0.17	0.01	0.0718	0.3144
HAOX1	-0.16	-0.33	0.01	0.0729	0.3144
PI3	-0.07	-0.15	0.01	0.0809	0.3341
TIMP4	0.06	-0.01	0.13	0.0811	0.3341
CD40	0.06	-0.01	0.14	0.0811	0.3341
CCL23	0.06	-0.01	0.12	0.0853	0.3462
VEGFA	0.05	-0.01	0.11	0.0946	0.3784
VSIG2	0.07	-0.01	0.14	0.0971	0.3784

XCL1	-0.05	-0.12	0.01	0.0979	0.3784
PSGL1	-0.03	-0.07	0.01	0.0987	0.3784
JAMA	0.16	-0.03	0.34	0.103	0.3875
DCN	-0.04	-0.09	0.01	0.1047	0.3875
IL16	-0.07	-0.16	0.02	0.1065	0.3875
CTRC	0.07	-0.02	0.17	0.1067	0.3875
MEPE	0.05	-0.01	0.12	0.1124	0.4029
FGF23_INF	0.07	-0.02	0.16	0.1142	0.4041
PTX3	-0.06	-0.13	0.02	0.1194	0.4116
LPL	0.05	-0.01	0.12	0.1195	0.4116
CHI3L1	-0.1	-0.23	0.03	0.1208	0.4116
FGF19	0.12	-0.04	0.29	0.1284	0.4322
MMP9	0.05	-0.02	0.12	0.1333	0.4433
LEP	0.07	-0.02	0.17	0.135	0.4436
TM	-0.04	-0.09	0.01	0.1392	0.4482
TNFRSF14	0.06	-0.02	0.13	0.1397	0.4482
PDL2	-0.04	-0.09	0.01	0.1425	0.4482
TSLP	-0.02	-0.04	0.01	0.1429	0.4482

IL1ALPHA	-0.02	-0.05	0.01	0.1484	0.4591
MARCO	-0.02	-0.06	0.01	0.1497	0.4591
NRTN	-0.02	-0.06	0.01	0.1608	0.4875
AGRP	0.06	-0.02	0.14	0.1625	0.4875
IL20	-0.02	-0.05	0.01	0.1647	0.4886
OPN	-0.06	-0.13	0.02	0.1664	0.4886
BP1_4E	-0.1	-0.24	0.04	0.1684	0.4892
TR	-0.07	-0.17	0.03	0.1751	0.5034
TNFRSF13B	0.04	-0.02	0.1	0.18	0.5078
TF	-0.03	-0.08	0.02	0.1803	0.5078
AZU1	0.06	-0.03	0.15	0.1828	0.5089
TNFSF14	0.07	-0.03	0.17	0.1844	0.5089
SELP	0.09	-0.05	0.23	0.1925	0.5260
TRAP	0.04	-0.02	0.1	0.2017	0.5458
ENRAGE	0.08	-0.04	0.2	0.2057	0.5512
BLMHYDROLASE	-0.04	-0.1	0.02	0.211	0.5600
IFNGAMMA	-0.01	-0.01	0	0.2176	0.5720
PDGFSUBUNITA	0.11	-0.07	0.28	0.2276	0.5769

IL15RA	-0.03	-0.07	0.02	0.2285	0.5769
UPA	0.04	-0.02	0.1	0.2311	0.5769
HGF	0.04	-0.02	0.09	0.2317	0.5769
CASP3	0.15	-0.09	0.39	0.2321	0.5769
CDCP1	-0.04	-0.11	0.03	0.2329	0.5769
CD6	-0.04	-0.12	0.03	0.2341	0.5769
PECAM1	0.08	-0.05	0.2	0.2409	0.5884
IL1RT1	-0.03	-0.08	0.02	0.2497	0.5974
CXCL1	0.13	-0.1	0.36	0.253	0.5974
GP6	0.08	-0.06	0.22	0.2537	0.5974
CEACAM8	0.06	-0.04	0.16	0.2548	0.5974
IL4	0.02	-0.01	0.04	0.2554	0.5974
CXCL16	0.03	-0.02	0.08	0.2621	0.6035
TNFR2	0.04	-0.03	0.12	0.2633	0.6035
FGF5	0.02	-0.01	0.04	0.2646	0.6035
PDGFSUBUNITB	0.14	-0.11	0.38	0.2721	0.6035
GIF	0.06	-0.05	0.16	0.2737	0.6035
MCP3	-0.04	-0.12	0.03	0.2738	0.6035

CXCL1_INF	0.12	-0.1	0.33	0.2765	0.6035
CTSL1	-0.03	-0.09	0.03	0.2795	0.6035
GLO1	-0.07	-0.2	0.06	0.2796	0.6035
LDLRECEPTOR	0.04	-0.04	0.13	0.2799	0.6035
OSM	0.08	-0.06	0.21	0.2854	0.6064
EGFR	-0.02	-0.06	0.02	0.2865	0.6064
TGFALPHA	0.04	-0.03	0.1	0.2878	0.6064
CCL3	0.05	-0.04	0.15	0.2909	0.6082
SLAMF7	-0.04	-0.12	0.04	0.2967	0.6094
CASP8	-0.06	-0.17	0.05	0.298	0.6094
PAI	0.08	-0.07	0.23	0.2981	0.6094
SCGB3A2	0.05	-0.04	0.14	0.3008	0.6104
IL6	-0.07	-0.22	0.07	0.3115	0.6249
IL5	0.06	-0.05	0.16	0.3167	0.6249
IL2	0	0	0	0.317	0.6249
CSF1	-0.02	-0.06	0.02	0.317	0.6249
IL22RA1	-0.02	-0.05	0.02	0.3204	0.6272
CD40L	0.11	-0.11	0.34	0.3295	0.6404

TWEAK	0.03	-0.03	0.08	0.3356	0.6477
CD5	0.03	-0.03	0.1	0.3529	0.6764
IL1RL2	-0.03	-0.09	0.03	0.3673	0.6968
SPON1	-0.02	-0.08	0.03	0.3708	0.6968
CTSD	-0.03	-0.09	0.03	0.3754	0.6968
GH	0.13	-0.15	0.41	0.3761	0.6968
IGGFCRECEPTORIIB	-0.03	-0.11	0.04	0.3769	0.6968
PON3	0.03	-0.04	0.1	0.3806	0.6968
IL10RA	-0.03	-0.09	0.03	0.3812	0.6968
AXIN1	0.1	-0.13	0.33	0.3873	0.7033
NEMO	0.1	-0.13	0.32	0.393	0.7085
IGFBP1	-0.07	-0.22	0.09	0.3953	0.7085
RAGE	-0.02	-0.08	0.03	0.4047	0.7106
SLAMF1	-0.03	-0.1	0.04	0.4055	0.7106
TRAILR2	0.03	-0.04	0.09	0.4067	0.7106
MMP1	0.07	-0.09	0.22	0.4068	0.7106
PRELP	0.02	-0.02	0.05	0.41	0.7111
IL2RB	0.01	-0.02	0.05	0.4133	0.7111

CCL17	0.07	-0.1	0.23	0.4148	0.7111
FGF23	0.04	-0.05	0.12	0.4176	0.7115
KIM1	-0.04	-0.12	0.05	0.4286	0.7191
CTSZ	0.02	-0.04	0.08	0.4362	0.7191
IL6_INF	-0.06	-0.2	0.09	0.438	0.7191
FS	0.03	-0.04	0.1	0.4382	0.7191
GAL4	0.03	-0.04	0.1	0.443	0.7191
ACE2	-0.03	-0.11	0.05	0.4434	0.7191
CD4	0.02	-0.03	0.07	0.4438	0.7191
IL10	-0.03	-0.12	0.05	0.445	0.7191
IL18BP	-0.02	-0.08	0.04	0.4455	0.7191
CHIT1	-0.03	-0.12	0.06	0.4731	0.7592
FLT3L	-0.02	-0.08	0.04	0.4765	0.7602
CCL24	0.03	-0.05	0.11	0.4826	0.7655
CDH5	0.02	-0.04	0.08	0.4885	0.7704
IL1RA	-0.03	-0.12	0.06	0.5042	0.7806
TNF	0.02	-0.03	0.06	0.5046	0.7806
ANG1	0.07	-0.13	0.27	0.5056	0.7806

SHPS1	-0.02	-0.07	0.04	0.509	0.7806
CXCL5	0.1	-0.19	0.38	0.5091	0.7806
CD244	0.02	-0.04	0.09	0.5194	0.7920
CD8A	0.02	-0.05	0.1	0.5227	0.7927
CCL11	-0.02	-0.08	0.04	0.543	0.8075
OPG_INF	-0.02	-0.07	0.04	0.5438	0.8075
DECR1	0.08	-0.18	0.33	0.5447	0.8075
PRSS8	0.02	-0.03	0.06	0.5464	0.8075
TLT2	0.02	-0.05	0.1	0.5471	0.8075
SOD2	-0.01	-0.03	0.02	0.5509	0.8088
BMP6	-0.02	-0.09	0.05	0.5714	0.8286
TNFR1	0.02	-0.05	0.09	0.5728	0.8286
IL27	-0.02	-0.07	0.04	0.5734	0.8286
CD163	-0.02	-0.08	0.05	0.5835	0.8372
CCL4	0.02	-0.06	0.11	0.5854	0.8372
TNFB	-0.02	-0.07	0.04	0.5963	0.8474
CXCL6	0.04	-0.1	0.17	0.5987	0.8474
STK4	0.05	-0.15	0.26	0.6126	0.8626

MMP10	0.02	-0.06	0.11	0.6207	0.8674
UPA_INF	0.01	-0.04	0.06	0.6311	0.8674
ITGB1BP2	0.06	-0.18	0.29	0.6315	0.8674
MERTK	-0.02	-0.08	0.05	0.6321	0.8674
CXCL11	-0.03	-0.16	0.1	0.6341	0.8674
TRANCE	-0.02	-0.1	0.06	0.6348	0.8674
MMP3	-0.02	-0.12	0.07	0.6383	0.8678
IL17C	0.03	-0.09	0.15	0.6467	0.8749
IDUA	0.01	-0.05	0.08	0.6579	0.8854
HOSCAR	0.01	-0.03	0.05	0.6619	0.8854
TNFRSF10C	0.01	-0.05	0.08	0.6682	0.8854
GDNF	0.01	-0.05	0.08	0.6718	0.8854
TNFRSF11A	0.02	-0.06	0.09	0.6721	0.8854
CD84	-0.02	-0.1	0.06	0.6767	0.8854
TNFRSF10A	-0.01	-0.07	0.05	0.6769	0.8854
ARTN	0.01	-0.03	0.04	0.6913	0.8967
DNER	-0.01	-0.05	0.03	0.696	0.8967
HBEGF	0.02	-0.09	0.13	0.6979	0.8967

IL1RT2	-0.01	-0.06	0.04	0.6985	0.8967
MB	0.02	-0.08	0.12	0.706	0.8983
MMP12	-0.02	-0.1	0.07	0.7084	0.8983
SERPINA12	0.01	-0.05	0.07	0.7095	0.8983
LTBR	0.01	-0.05	0.07	0.713	0.8986
PDL1	0.01	-0.06	0.08	0.7203	0.9036
SPON2	0.01	-0.03	0.04	0.7309	0.9128
IL17RA	-0.01	-0.1	0.07	0.7398	0.9160
FAS	0.01	-0.05	0.07	0.7401	0.9160
PARP1	0.02	-0.12	0.16	0.7468	0.9202
CCL28	-0.01	-0.06	0.04	0.7567	0.9259
ST1A1	0.02	-0.12	0.17	0.7604	0.9259
IL10RB	0.01	-0.04	0.06	0.7615	0.9259
IL8	-0.02	-0.13	0.09	0.7748	0.9294
CCL20	-0.02	-0.19	0.14	0.7748	0.9294
MCP2	0.01	-0.07	0.09	0.7791	0.9294
IL18	-0.01	-0.09	0.07	0.7886	0.9294
LIF	0	-0.02	0.02	0.7896	0.9294

GDF2	-0.01	-0.07	0.05	0.7916	0.9294
DKK1	0.02	-0.1	0.13	0.7953	0.9294
SIRT2	-0.03	-0.25	0.19	0.7961	0.9294
MCP1	-0.01	-0.08	0.06	0.8049	0.9294
FABP2	0.02	-0.11	0.14	0.8058	0.9294
OPG	-0.01	-0.06	0.05	0.8062	0.9294
SCF	0.01	-0.05	0.06	0.8099	0.9294
PCSK9	-0.01	-0.07	0.05	0.8109	0.9294
PIGR	0	-0.02	0.03	0.813	0.9294
EPHB4	-0.01	-0.06	0.05	0.8149	0.9294
BETANGF	0	-0.04	0.03	0.8223	0.9340
IL24	0	-0.05	0.04	0.848	0.9561
ICAM2	-0.01	-0.07	0.05	0.8509	0.9561
LOX1	-0.01	-0.1	0.08	0.8571	0.9561
SCF_INF	0	-0.05	0.06	0.8573	0.9561
LAPTGBETA1	0.01	-0.07	0.08	0.8674	0.9561
IL18R1	0	-0.05	0.06	0.8685	0.9561
PAR1	0.01	-0.07	0.08	0.8719	0.9561

IL13	0	-0.06	0.07	0.8787	0.9561
TGM2	0.01	-0.13	0.14	0.8861	0.9561
ADAMTS13	0	-0.04	0.04	0.8887	0.9561
ITGB2	0.01	-0.07	0.08	0.8896	0.9561
GRN	0	-0.05	0.05	0.8896	0.9561
SORT1	0	-0.05	0.06	0.8921	0.9561
THPO	0	-0.06	0.05	0.8962	0.9561
IL2RA	-0.01	-0.1	0.09	0.9064	0.9561
IL33	0	-0.01	0.01	0.9065	0.9561
CA5A	-0.01	-0.12	0.11	0.9077	0.9561
IL18_INF	0	-0.07	0.08	0.9079	0.9561
IGFBP7	0	-0.07	0.07	0.9108	0.9561
CXCL10	-0.01	-0.11	0.1	0.9111	0.9561
IL7	-0.01	-0.13	0.11	0.9182	0.9585
FGF21	-0.01	-0.18	0.16	0.9219	0.9585
FGF21_INF	0.01	-0.14	0.16	0.9238	0.9585
PGF	0	-0.06	0.06	0.9288	0.9601
MCP4	0	-0.11	0.1	0.9398	0.9656

GT	0	-0.11	0.11	0.9429	0.9656
CX3CL1	0	-0.06	0.07	0.9446	0.9656
ADA	0	-0.07	0.07	0.9529	0.9681
MCP1_INF	0	-0.07	0.06	0.9561	0.9681
IGFBP2	0	-0.08	0.08	0.9576	0.9681
IL20RA	0	-0.04	0.04	0.9637	0.9707
STAMBP	0	-0.17	0.16	0.9779	0.9815
TNFSF13B	0	-0.06	0.06	0.9958	0.9958

Supplemental Table 5. Biomarker-biomarker correlations with Spearman Rho>0.5

Protein	Protein	Spearman
MMP2	NOTCH3	0.69
ALCAM	CNTN1	0.68
CSTB	UPAR	0.67
IL12B	TNFRSF9	0.66
PLC	TFF3	0.66
GDF15	TFF3	0.65
RETN	PGLYRP1	0.65
PLC	UPAR	0.64
UPAR	TFF3	0.64
ALCAM	UPAR	0.62
PLC	CSTB	0.62
GAL9	CSTB	0.61
RARRES2	CSTB	0.61
RETN	UPAR	0.61
TPA	VWF	0.61
NOTCH3	CNTN1	0.6

TFF3	CSTB	0.6
ALCAM	AXL	0.59
AMBP	ADM	0.59
NOTCH3	ALCAM	0.59
PLC	ADM	0.59
TFF3	ADM	0.59
GAL9	UPAR	0.58
RARRES2	PLC	0.58
TNFRSF9	UPAR	0.58
MMP2	CNTN1	0.57
NOTCH3	UPAR	0.57
PLC	RETN	0.57
TNFRSF9	CXCL9	0.57
APN	CNTN1	0.56
CSTB	FABP4	0.56
ALCAM	APN	0.55
GAL9	ADM	0.55
GAL9	TNFRSF9	0.55

PLC	TNFRSF9	0.55
RARRES2	TFF3	0.55
RARRES2	TFPI	0.55
ADM	FABP4	0.54
ALCAM	MMP2	0.54
AXL	UPAR	0.54
BOC	TIE2	0.54
AMBP	GAL9	0.53
APN	MMP2	0.53
CCL16	RARRES2	0.53
GDF15	PLC	0.53
RARRES2	UPAR	0.53
TFF3	TNFRSF9	0.53
UPAR	PGLYRP1	0.53
AXL	NOTCH3	0.52
CCL3	TNFRSF9	0.52
FABP4	PLC	0.52
GDF15	UPAR	0.52

ADM	UPAR	0.51
FABP4	RARRES2	0.51
GDF15	RARRES2	0.51
NOTCH3	PLC	0.51
ADM	CSTB	0.5

Supplemental Table 6. Change from baseline to month 9 biomarker-clinical statistically significant correlations

Clinical parameter	Biomarker	Rho	P
BMI	REN	-0.15	0.001
BMI	COL1A1	0.11	0.017
BMI	MMP2	0.12	0.01
BMI	BNP	0.15	0.001
BMI	SELE	0.12	0.01
BMI	MPO	-0.1	0.027
SBP	REN	-0.36	0
SBP	COL1A1	0.14	0.002
SBP	MMP2	0.14	0.003
SBP	CCL16	-0.11	0.019
SBP	BNP	0.11	0.014
SBP	PAPPA	0.09	0.041
SBP	VEGFD	0.16	0
SBP	NOTCH3	0.1	0.028
SBP	EPCAM	0.09	0.042

SBP	MMP7	-0.11	0.014
SBP	CCL25	-0.1	0.03
SBP	SELE	0.11	0.015
SBP	GAL9	-0.1	0.029
SBP	THBS2	0.12	0.01
SBP	FABP4	-0.12	0.011
SBP	GDF15	-0.16	0
SBP	TNFRSF9	-0.09	0.041
SBP	CNTN1	0.09	0.047
SBP	CST5	-0.14	0.002
SBP	CCL3_INF	-0.12	0.008
SBP	TFF3	-0.12	0.009
SBP	CXCL9	-0.14	0.003
SBP	ADM	-0.1	0.036
DBP	REN	-0.23	0
DBP	IL12B	-0.1	0.038
DBP	PGLYRP1	-0.14	0.002
DBP	GDF15	-0.14	0.002

DBP	TNFRSF9	-0.1	0.034
DBP	TFF3	-0.12	0.013
DBP	ADM	-0.1	0.027
DBP	KLK6	-0.11	0.023
eGFR	REN	-0.22	0
eGFR	COL1A1	0.1	0.035
eGFR	RARRES2	-0.12	0.007
eGFR	RETN	-0.09	0.047
eGFR	MMP2	0.12	0.011
eGFR	PAPPA	0.09	0.042
eGFR	IL12B	-0.1	0.029
eGFR	VEGFD	0.09	0.042
eGFR	EPCAM	0.09	0.037
eGFR	CCL19	-0.14	0.003
eGFR	MMP7	-0.25	0
eGFR	PLC	-0.15	0.001
eGFR	GAL9	-0.15	0.001
eGFR	SRC	-0.1	0.03

eGFR	CSTB	-0.2	0
eGFR	FABP4	-0.21	0
eGFR	GDF15	-0.19	0
eGFR	TNFRSF9	-0.1	0.024
eGFR	CST5	-0.19	0
eGFR	CCL3_INF	-0.13	0.003
eGFR	CPA1	-0.12	0.01
eGFR	TFF3	-0.22	0
eGFR	CXCL9	-0.17	0
eGFR	ADM	-0.14	0.002
Creatinine	REN	0.21	0
Creatinine	COL1A1	-0.09	0.038
Creatinine	RARRES2	0.12	0.009
Creatinine	MMP2	-0.12	0.01
Creatinine	BNP	-0.1	0.023
Creatinine	PAPPA	-0.11	0.017
Creatinine	IL12B	0.11	0.015
Creatinine	CCL19	0.15	0.001

Creatinine	MMP7	0.23	0
Creatinine	PLC	0.15	0.001
Creatinine	GAL9	0.17	0
Creatinine	SRC	0.1	0.023
Creatinine	CSTB	0.21	0
Creatinine	FABP4	0.21	0
Creatinine	GDF15	0.18	0
Creatinine	TNFRSF9	0.12	0.008
Creatinine	CST5	0.17	0
Creatinine	CCL3_INF	0.15	0.001
Creatinine	CPA1	0.09	0.039
Creatinine	TFF3	0.22	0
Creatinine	CXCL9	0.18	0
Creatinine	ADM	0.16	0
Sodium	REN	-0.25	0
Sodium	COL1A1	0.15	0.001
Sodium	RETN	-0.12	0.008
Sodium	MMP2	0.2	0

Sodium	BNP	0.23	0
Sodium	PAPPA	0.14	0.001
Sodium	PGLYRP1	-0.15	0.001
Sodium	NOTCH3	0.13	0.004
Sodium	BOC	0.14	0.002
Sodium	IL17A	0.13	0.006
Sodium	SELE	0.11	0.014
Sodium	THBS2	0.18	0
Sodium	CSTB	-0.12	0.009
Sodium	IL17D	0.1	0.026
Sodium	UPAR	-0.14	0.002
Sodium	TFF3	-0.1	0.032
Sodium	KLK6	-0.1	0.031
Sodium	PRTN3	-0.09	0.043
Potassium	REN	0.27	0
Potassium	COL1A1	-0.1	0.031
Potassium	RARRES2	0.11	0.019
Potassium	RETN	0.09	0.038

Potassium	CCL16	0.11	0.017
Potassium	BNP	-0.1	0.025
Potassium	IL6RA	0.12	0.006
Potassium	AMBP	0.1	0.024
Potassium	MMP7	0.1	0.024
Potassium	CCL25	0.11	0.017
Potassium	CST5	0.11	0.018
Potassium	CCL3_INF	0.09	0.048
Potassium	KLK6	0.1	0.023
Urea	REN	0.28	0
Urea	COL1A1	-0.14	0.002
Urea	MMP2	-0.14	0.002
Urea	BNP	-0.13	0.005
Urea	PAPPA	-0.12	0.007
Urea	VEGFD	-0.12	0.011
Urea	NOTCH3	-0.12	0.009
Urea	AMBP	0.13	0.004
Urea	BOC	-0.1	0.021

Urea	IL4RA	-0.11	0.021
Urea	MMP7	0.15	0.001
Urea	CCL25	0.17	0
Urea	SELE	-0.11	0.015
Urea	THBS2	-0.11	0.014
Urea	FABP4	0.16	0.001
Urea	GDF15	0.11	0.015
Urea	AXL	-0.11	0.012
Urea	ALCAM	-0.1	0.029
Urea	CNTN1	-0.1	0.027
Urea	CST5	0.18	0
Urea	CPA1	0.14	0.003
Urea	TFF3	0.15	0.001
Urea	ADM	0.1	0.032

Supplemental Table 7. Intermediates of the extended network (Figure 2)

Intermediate Label	Uniprot ID	Description
AGT	P01019	Angiotensinogen
AGTR1	P30556	Angiotensin II receptor type 1
Aldosterone	—	Aldosterone
Angiotensin I	—	Angiotensin I
Angiotensin II	—	Angiotensin II
CCR7	P32248	C-C chemokine receptor type 7
CTRC	Q99895	Chymotrypsin-C (Caldecrin)
CTSD	P07339	Cathepsin D
CTSG	P08311	Cathepsin G (CG)
Fra1/FOS-JUN	—	Transcription factor Activator protein 1 (AP-1) with subunits of FOS or Fos-Related Antigen 1 and Jun Proto-Oncogene
IκB(α):NF-κB complex	—	NF-kappaB transcription factor inhibited by IκBα (NF-κB inhibitor, alpha)
IL6	P05231	Interleukin-6 (IL-6)
IRF5	Q13568	Interferon regulatory factor 5 (IRF-5)
KLKB1	P03952	Plasma kallikrein
LPA/LPA1	—	Lysophosphatidic acid and its receptor LPA1
LRP1	Q07954	Prolow-density lipoprotein receptor-related protein 1 (LRP-1)

Mineralocorticoid receptor	P08235	Mineralocorticoid receptor
MYB	P10242	Transcriptional activator Myb (Proto-oncogene c-Myb)
NFkB.complex	—	Nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB)
PLG	P00747	Plasminogen
p-STAT6 dimer	—	phosphorylated Signal Transducer And Activator Of Transcription 6, Interleukin-4 Induced
RUNX1	Q01196	Runt-related transcription factor 1 (Acute myeloid leukemia 1 protein)
SP1	P08047	Transcription factor Sp1
Spirolactone	—	Spirolactone
STAT1	P42224	Signal transducer and activator of transcription 1-alpha/beta
STAT5B	P51692	Signal transducer and activator of transcription 5B
TGFB1	P01137	Transforming growth factor beta-1 proprotein
TYK2:JAK2 IL12:IL12R	—	Non-receptor tyrosine-protein kinase TYK2 and Tyrosine-protein kinase JAK2 activated by IL12 binding to IL12 receptor

Supplemental Table 8. Interaction analysis between the baseline proteomic biomarker level (below vs. above median) and the spironolactone effect on PIIINP and PICP

PIIINP						
Level (< vs. >median)	Biomarker	Coef.	LCI	UCI	P-value	Interaction P
Low	CCL28	-0.74	-1.26	-0.22	0.0054	0.0031
High	CCL28	0.37	-0.15	0.9	0.1603	
Low	ST1A1	-0.71	-1.22	-0.19	0.0071	0.0041
High	ST1A1	0.37	-0.15	0.9	0.164	
Low	IL5	-0.5	-0.93	-0.08	0.0207	0.0063
High	IL5	0.68	-0.05	1.4	0.0691	
Low	LAPTGBETA1	-0.7	-1.23	-0.18	0.0084	0.007
High	LAPTGBETA1	0.31	-0.21	0.84	0.2385	
Low	PAI	-0.63	-1.15	-0.11	0.0184	0.0214
High	PAI	0.24	-0.28	0.77	0.3652	
Low	DLK1	-0.63	-1.15	-0.11	0.0181	0.0234
High	DLK1	0.22	-0.3	0.75	0.4005	
Low	PRTN3	-0.33	-0.71	0.06	0.0978	0.0336
High	PRTN3	1.11	-0.16	2.38	0.0857	

Low	CXCL1	-0.59	-1.1	-0.07	0.0269	0.034
High	CXCL1	0.22	-0.31	0.74	0.4235	
Low	TGM2	0.2	-0.32	0.72	0.4495	0.0351
High	TGM2	-0.6	-1.12	-0.07	0.0262	
Low	CD244	-0.58	-1.1	-0.06	0.0292	0.0354
High	CD244	0.22	-0.31	0.74	0.4219	
Low	ITGB1BP2	-0.55	-1.07	-0.04	0.0352	0.0376
High	ITGB1BP2	0.23	-0.3	0.76	0.3917	
Low	SPON1	-0.58	-1.1	-0.07	0.0273	0.041
High	SPON1	0.19	-0.34	0.72	0.4811	
PICP						
Low	AXL	-1.33	-7.13	4.48	0.6532	0.0048
High	AXL	-13.17	-18.98	-7.35	<0.0001	
Low	CHIT1	-1.8	-7.56	3.96	0.5393	0.0095
High	CHIT1	-12.66	-18.48	-6.84	<0.0001	
Low	IL22RA1	-9.25	-13.66	-4.84	<0.0001	0.0112
High	IL22RA1	6.29	-4.86	17.44	0.2685	
Low	LIF	-8.62	-12.85	-4.39	0.0001	0.0173

High	LIF	12.23	-4.38	28.85	0.1487	
Low	PDL2	-12.16	-17.93	-6.38	<0.0001	0.018
High	PDL2	-2.27	-8.06	3.52	0.4408	
Low	VEGFD	-2.37	-8.14	3.4	0.4203	0.0198
High	VEGFD	-12.11	-17.91	-6.3	<0.0001	
Low	FGF21	-2.44	-8.23	3.35	0.4081	0.0225
High	FGF21	-12.01	-17.83	-6.18	0.0001	
Low	GDNF	-2.65	-8.42	3.12	0.367	0.028
High	GDNF	-11.87	-17.72	-6.01	0.0001	
Low	CTSL1	-2.72	-8.5	3.06	0.3553	0.0326
High	CTSL1	-11.68	-17.51	-5.84	0.0001	
Low	CXCL6	-11.6	-17.36	-5.85	0.0001	0.0343
High	CXCL6	-2.74	-8.58	3.1	0.3564	
Low	MMP9	-10.08	-15.01	-5.16	0.0001	0.0363
High	MMP9	-0.56	-7.99	6.86	0.8815	
Low	PRTN3	-8.44	-12.75	-4.13	0.0001	0.0418
High	PRTN3	6.78	-7.22	20.78	0.342	
Low	UPA	-2.96	-8.79	2.88	0.32	0.0458

High	UPA	-11.34	-17.14	-5.54	0.0001	
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