**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 | BLMHYDROLASE | 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 chemikine 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 | IGGFCRECEPTORIIB | 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 | LAPTGFBETA1 | 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 peptide | NTPROBNP | CVDII | P16860 |
| 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 | PDGFSUBUNITA | CVD III | P04085 |
| Platelet-derived growth factor subunit B | PDGFSUBUNITB | 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 | Q9BWV1 |
| 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** | |  | **Spironolactone** | |
|  | **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/m2) | 94.7 | (80.5, 113.5) [23] |  | 94.5 | (81.1, 110.9) [29] |
| LAV (ml/m2) | 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 |
| LAPTGFBETA1 | 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 |
| LAPTGFBETA1 | 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 |
| IkB(alpha):NF-kB complex | — | NF-kappaB transcription factor inhibited by IκBα (NF-kB 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 |
| Spironolactone | — | Spironolactone |
| 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 actived 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 | LAPTGFBETA1 | -0.7 | -1.23 | -0.18 | 0.0084 | 0.007 |
| High | LAPTGFBETA1 | 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 |