

Supplemental Table 4. Top networks of genes with significantly different expression in comparisons of HF vs. LF, WR vs. LF, WR vs. HF, and HC vs. HFR as identified by Ingenuity Pathways Analysis.¹

HF vs. LF		
Network	Upregulated	Downregulated
Connective Tissue Disorders, Immunological Disease, Inflammatory Disease	ADAM8, CCL9, CD274, CDC42EP4, CH25H, CLEC4E, COL16A1, CTSZ, CXCL16, GFPT2, HAS1, MYO9B, OASL, PDPN, PLA2G7, PLD3, SLFN2, TNF, TREM2, UBD	BCL7A, CIB2, CIDEC, CTSF, DAB2IP, GSTT1, KIAA1881, OPTN, PHGDH, PXMP2, RASD1, ST3GAL6, TRAFD1, UCK1
Cell-To-Cell Signaling and Interaction, Tissue Development, Cellular Movement	ADAMTS4, CASP1, CASP4, CCL4, CCL5, CCND1, CD9, COL1A1, CORO1A, CTSB, DAB2, FN1, IFITM3, ITGAV, LRG1, MMP19, MTPN, OSTF1, PLAT, PLA2, PLAUR, SPP1, ST6GAL1, TGFBR2, TGM2, TNC	ATF3, CP, H6PD, TF, VHL
Immune Response, Inflammatory Disease, Cell-To-Cell Signaling and Interaction	CCRL2, CD74, CERK, CSF2RA, CSF2RB, CTSS, CYB5R3, EMR1, HLA-DMB, HLA-DQA1, HLA-DQB2, HLA-DRB1, HPR, IL1B, IL3RA, PSCDBP, SEP15, SNAP23, SPI1, STX11, TNFAIP2, UGCG	CD1D, G0S2, GEM, NFKBIZ, PIM3, SLC1A3, SLC25A25, UAP1
Hematological System Development and Function, Immune and Lymphatic System Development and Function, Tissue Morphology	BCL2A1, CAV2, CD14, CD83, DCTN1, EVL, FYB, GDI2, HMGA1, IL15, IRF5, ISG15, MCL1, OAS1, PIM1, PLSCR1, PTP4A2, PVALB, RAB5C, RAB6A, SDC3, SDCBP, SRGN, TGOLN2, TLR2	DST, IRF1, PPP1R9B, PYGL
Connective Tissue Disorders, Genetic Disorder, Renal and Urological Disease	C1QA, CAPRIN1, CD48, CD53, CENPA, DCN, ENO2, FSTL1, GPNMB, IL6, LY86, MMP2, MMP12, MMP13, MMP14, S100A4, STOM, TIMP1, TIMP2	FCGRT, GSTA4, LGALS4, PCSK6, PTGER3, RORC, SFRS5, SLC27A1, TIMP4
Cell Cycle, Cellular Growth and Proliferation, Cancer	CDKN1A, CDT1, CREG1, EIF5A, FGF13, H2AFZ, HIST1H2AB, HNRNPA2B1, IFI16, KLF6, LUM, MCM5, MCM6, NUP62, PCNA, PF4, PLK2, PSAP, STMN1, TPX2, UHRF1, VPS18	CABLES1, GADD45G, MEIS1, SORT1, SSPN, TCN2
Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Immune and Lymphatic System Development and Function	ANPEP, CBFB, CCL3, CKB, CXCL3, ETS, F10, F2R, GRN, GUSB, IGFBP5, LMO2, MAN1C1, MAN2B1, PITPNA, RHOJ, STARD8, THBS1, VCAM1	C6, CYR61, HK2, IGFBP4, LDB1, NDRG1, NTRK2, PRTN3, THBS2, VEGFA

Hematological System Development and Function, Immune and Lymphatic System Development and Function, Tissue Morphology	CD72, CD93, CSF1, CXCR4, CYBA, FCER1G, FCGR2A, FCGR3A, IL10, IL7R, INPP5D, ITGB2, LAT2, LILRB4, NCF2, NCF4, PLAGL2, PPAN, PTPN6, RAP1B, RASA1, SH3BP2	CHKA, HOXA7, ID3, RBP4
Genetic Disorder, Neurological Disease, Amino Acid Metabolism	ACADM, EEF2, NPY, PMP22, PRKCD, PTPRC, PTPRE, RTN4, SLC6A6, UCP2	ACADSB, ADIPOR2, ADM, AKT2, CCNL1, CDO1, EGR2, HSD3B7, IVD, NPR2, PALM, PCCB, PFKFB3, PTPRM, S100A1, SLC2A3
Hematological System Development and Function, Immune Response, Tissue Development	ACTN4, ATP6V1B2, CAPG, GSN, ICAM1, IQGAP1, MARCKS, MSN, PFN1, PLEC1, PRKX, RAB8B, RCAN1, S100A6, SELP, SELPLG, TES, TPM1, TPM3, VIL2	ACTA1, ADRB3, ALDH2, ENC1, MKNK2
WR vs. LF		
Network	Upregulated	Downregulated
Immunological Disease, Connective Tissue Disorders, Inflammatory Disease	CCL6, CCL9, CD274, CDC42EP4, COL15A1, COL16A1, CTSZ, CXCL16, EXT1, GFPT2, MAFF, MFGE8, NNMT, PDPN, PLA2G7, PLD3, PPAP2A, SLFN2, TNF, TREM2, UBD	ARF4, BAG4, BCL7A, DAB2IP, G0S2, HMGN2, KIAA1881, NFKBIZ, PPP1R3C, RASA3, RASD1, ST3GAL6, ZFP36L1
Cellular Development, Skeletal and Muscular System Development and Function, Cancer	ATF4, ATP6V0D1, CDKN1A, CDT1, CTSK, EIF5A, FGF13, GDF15, IFI16, KLF4, LGALS3, MCM6, MTHFD2, PCBP1, PLK2, PPAN, PSAT1, RAB5C, SDC3, SDCBP, STMN1, SYP, TNFRSF12A	ASNS, DDI4, ID3, MEIS1, TCF7L2, TSPAN7, ZBTB5
Cardiovascular System Development and Function, Organismal Development, Cancer	CASP4, COL1A1, CTSB, IFI30, IGFBP5, LMNA, MMP2, MMP12, MMP14, MMP23B, PLAU, PLAUR, RANGAP1, SEMA3F, SLC25A1, SLC2A1, SPHK1, THBS1, TIMP1, TIMP2	ABTB1, ANP32A, LDB1, PTEN, RORC, TFPI, VEGFA
RNA Post-Transcriptional Modification, Gene Expression, RNA Trafficking	ALDOA, BCAR1, CD83, Ck2, CREG1, DNASE1L1, DOT1L, E2f, EIF4A1, FBL, GRB2, HSP90AB1, MDM2, NEDD4L, PIP4K2A, SGK, STIP1, WDR1	BIRC2, CDC37L1, DNAJC7, EIF4A2, EIF4G2, HTATSF1, PGRMC1, SFRS5, TACC2, USP3
Cellular Movement, Cell Death, Hematological System Development and Function	ALOX5AP, CASP1, CCL4, CCL5, CSF1, DUSP10, FAS, FCER1G, FEM1B, HIPK2, HMGA1, IL10, IRF8, JAK2, LAT2, LY6E, NEDD9, NFKB2, PLEC1, PTK2B, TNFSF13, TXNRD1	IER2, IRF1, RPL30

Cellular Development, Lipid Metabolism, Small Molecule Biochemistry	ACADL, ACADM, BCL3, BLVRA, CSK, GUSB, IFITM1, LYZ, NFKB1, PCMT1, PEPD, PITPNA, RTN4	ACADSB, CES1, EGR1, EGR2, EGR4, FABP4, HOXA7, IRF4, MLYCD, PPARG, SATB1, TNFAIP3
Cell-To-Cell Signaling and Interaction, Cardiovascular System Development and Function, Tissue Development	C1QA, C1QB, C1QC, CCL3, CCRL2, CERK, ICAM1, IGFALS, IL1B, ITGAX, MARCKSL1, PHLDA1, PSCDBP, PTX3, RCAN1, S100A6, VCAM1	C2, C6, DBP, GEM, PIM3, PTP4A1, SLC1A3
Behavior, Nervous System Development and Function, Hematological System Development and Function	ARNTL, ATP6V0A1, ATP6V1A, ATP6V1B2, CAPG, FGF1, FOSL1, LIPA, P2RY2, PFN1, SCN1B, TCAG7.1260, TCIRG1, THBD	ABCG1, ACTA1, ATP5I, DUSP4, HMGB1, NDRG1, PCK1, PER1, PPP1R10, PPP1R1A
Hematological System Development and Function, Immune Response, Immune and Lymphatic System Development and Function	BCL2A1, BOK, CD14, CDC42EP2, CORO1A, HNRPK, IQGAP1, IRS3, ITGB2, MGP, PLTP, PRKCD, PRKCDBP, SELP, SELPLG, SERPING1, TYROBP, UCP2, VCL	ADIPOR2, AGT, GSTA3, HSD11B1, MYO1B
Cellular Assembly and Organization, Cellular Movement, Gene Expression	ARPC4, ARPC5, ARPC1A, ARPC1B, CTSH, FSTL1, GCLM, MSN, MYH9, MYLK, RAB8B, RNH1, S100A4, TNC, TPM1, TPM3	ARHGEF18, CUGBP2, FOS, GHR, KLHL2, MST1R, TEF

WR vs. HF

Network	Upregulated	Downregulated
Cellular Growth and Proliferation, Embryonic Development, Cellular Development	CHKA, CRIP2, FCGRT, GART, LAMB2, LIMS2, MAFF, MGST3, MYC, RPS19, SFXN1, SQRDL, SRXN1	ANXA4, ATPIF1, CCL6, CD9, CD48, CD151, CPD, CSTB, ECM1, GCS1, GDI2, H2AFZ, LIMS1, LY6A, MRC1, PFKP, PLA1A, PMP22, PRDX1, SLC11A1, TAGLN2, TPD52
Connective Tissue Disorders, Immunological Disease, Inflammatory Disease	ACADS, ALAD, AQP7, CIB2, CTSF, DGCR6, GSTT1, NFS1, OPTN, PDRG1, PHGDH, PXMP2, TRAFD1, UCK1	ADAM8, ALCAM, CCL9, CD274, CH25H, CLEC4E, CTSZ, CXCL16, DEK, HAS1, MYO9B, OASL, PDPN, PLA2G7, PLD3, SLFN2, TNF, TNFAIP8, TREM2, UBD
Molecular Transport, Drug Metabolism, Cell Death	CFD, GATA6, IRF1, PACSIN3, PTPRD, PTPRM, SH3GLB1, SH3GLB2, TF	ATP6AP1, ATP6V0A1, ATP6V0B, ATP6V1A, ATP6V1B2, ATP6V1C1, CASP1, CEBPA, CTSB, DIAPH1, DNASE1L1, EIF4G2, GLIPR1, IFIH1, ISG15, LMNA, MUP1, PFN1, PLP2, PTPRE, TBXAS1, TCIRG1,

Online Supporting Material

Cellular Growth and Proliferation, Cellular Movement, Connective Tissue Development and Function	CDKN2C, FGF10, FGFR1, NPDC1, PER1, PTOV1, RASSF1, S100A13, SCN1B, SERTAD1, TENC1, UBTF	BHLHB2, CCND1, CSNK1D, CTSH, DAB2, GJA1, GRN, IL10RB, LGALS3, LRG1, MARCKSL1, OSTF1, PF4, TGFB1, TGFB1R, TGFB2, TMOD3
Lipid Metabolism, Small Molecule Biochemistry, Molecular Transport	ACO1, ACO2, CYP2E1, IRAK2, LONP1, NR1D1, ORM2, PIM3, PLA2G6, PTX3, SF1, SLC1A3, SLC25A25, UAP1	CCRL2, CD83, CERK, CYB5R3, HPR, IL1A, IL1B, IL3RA, MAP3K7IP2, PDGFB, PSCDBP, SAA2, UGCG
Cancer, Cellular Movement, Endocrine System Disorders	CP, CSDA, FOSB, GAS6, H6PD, JUN, RRAD, SLC27A1, TGIF1, TIMP4	AXL, BTG1, CD68, DARS, EHD4, FOLR2, ITGAX, JDP2, MTPN, PLAT, S100A4, S100A6, TIMP1, TIMP2, TPM2, TPM3, UHRF1
Cell Signaling, Nucleic Acid Metabolism, Small Molecule Biochemistry	ADCY6, AKT2, CXCL9, GNA11, HOXA7, HSPB8, IER3, MCAM, NTRK2, PALM, RGS3, TSHR	CSF2RA, EDNRB, GNA13, GNAI1, GNAS, GNG2, GPI, IL7R, LAT2, LPXN, LY86, PLEK, SCAMP2, SNAP23, STX11,
Immune Response, Cell-To-Cell Signaling and Interaction, Connective Tissue Disorders	C4A, CARD10, CLPP, DDR1, IL15RA	C1QA, C1QB, C1QC, C3AR1, CD74, CD93, CTSS, DCN, EDG5, EMR1, HLA-DMA, HLA-DMB, HLA-DQA1, HLA-DQB2, HLA-DRB1, LGMN, MALT1, NUP62, PIP5K1A, SLC2A6, TNFSF9
Cell Cycle, DNA Replication, Recombination, and Repair, Gene Expression	BMP4, CABLES1, FHIT, GADD45G, HIST4H4, ID3, KLF4, TCN2	ALOX5AP, CDKN1A, CDT1, FEN1, HIST1H2AB, HNRNPA2B1, ID2, IFI16, KLF6, LUM, MCM5, MCM6, PCNA, PLK2, SIPA1L1, TPX2, VGLL4
Cell-To-Cell Signaling and Interaction, Immunological Disease, Hematological System Development and Function	ANKS1A, DUSP10, GPX3, NFIX, PCSK6, RHOU, SOD1	BCL2A1, CCL3, CCL4, CD14, CD40, CD86, CD200, CLEC7A, CTGF, F10, IL10, MMP2, MMP13, MMP14, SPI1, SPP1, TANK, TFEC, TRAF5

HC vs. HFR

Network	Upregulated	Downregulated
Protein Synthesis, Cancer, Cell Cycle	BRD2, CDR2, FBL, IMPACT, LAMB2, MYO1B, NARS, NOP5/NOP58, PCBP1, PTGES, RBMS1, RIOK1, SRM, TSPAN7	AK2, ANXA2, ATP1F1, HNRPH1, MYC, PABPC1, PFKP, PTMA, RPL17, RPL19, RPL23, RPL32, RPL41, RPL27A, RPS5, RPS14, RPS18, RPS20, RPS25, SLC11A1, TAGLN2
Cell Morphology, Cellular Development, Cell Signaling	BAIAP2, BCAR1, CLIP1, DDEF1, EGFR, FUT8, LRIG1, NCK2, NXF1, PACSIN3, PTK2B, SFRS1, SFRS2, SFRS2IP, SNX9, SPG20, WASL, XPO6	ACTB, BCAR3, CLK1, CNN3, DEGS1, GNB2L1, GSN, HPR, LIMS1, LIMS2, SFRS5, TAPBP

Online Supporting Material

Immune Response, Inflammatory Disease, Gene Expression	ARIH1, CYLD, DDR1, HDGF, IFIT2, IRF2, IRF8, MAP3K8, MAP3K7IP2, PIP5K1A, TNFAIP8, TNIP1, UBE2E2, UBE2G1	ACADL, CFB, CFP, CTSS, CXCL3, EMR1, HLA-G, HMGB1, IRF1, PIM3, PNPT1, SLPI, TRIM25, TRPC4AP, UBE2V1
Gene Expression, Organ Development, Cell Death	ATN1, CSNK1E,CUTL1, DOT1L, ECE1, EHMT2, GATA6, PBEF1, PURB, RELB, SATB1, SIRT1, SRRM2, TANK, TGFB1	BCL3, BCL2A1, C4B, CBX3, CSNK1G2, FABP4, H3F3A, HBA2, HBB, NPC2, RBBP4, SCARB1, SMAD6, UBB
Cellular Compromise, Cellular Function and Maintenance, Drug Metabolism	AKT1S1, C6, CDC37L1, CSR1P1, CTPS,DAPK1, NDEL1, NEDD4L, PAPOLA, PSME3, ZHX2	ATP5A1, ATP5G3, ATP5I, ATP6V0A1, CTSB, DNAJB1, DNAJB4, DNAJC15, DNASE1L1, HSP90AA1, HSP90AB1, MTCH1, RPS3, YWHAE, YWHAZ
Cancer, Cell Morphology, Connective Tissue Disorders	AMD1, ATXN2, BMP1, CLU, GCLM, GGA2, LOX, MERTK, NFX1, PON1, PRKD1, RPS6KA3, RRAS2, SLC19A1, SORT1	ALAS1, FOS, FSTL1, JUN, PSAP, RPS6, RPS7, SNCG, SNX3, SPTBN1, UBA52
Cardiovascular System Development and Function, Cell-To-Cell Signaling and Interaction, Hematological System Development and Function	AGT, BOK, CDKN2B, COL4A1, EIF5, EIF1AY, EIF2B1, HSD11B1, MEST, OGT, SLC2A1, THBS1, THBS2, VLDLR	CCT5, CD36, CPT2, CYBA, EPHX2, IGFBP4, LRG1, LTA4H, NCF2, PLAU, SPARC, VHL
Cell Death, Connective Tissue Disorders, Dermatological Diseases and Conditions	ABCC3, CP, HTATSF1, ITGA6,RDBP, SNAPC4, TWIST1, UBTF	CAT, CYR61, EGR1, EGR2, FTL1, FXYD5, GEM, GSTM1, ID1, LTC4S, LYZ, MCL1, PDLM1, SNURF, UBD, UCK1, ZFP36L1
Cellular Assembly and Organization, Cellular Compromise, Nervous System Development and Function	ACTA1, CAMK2D, DVL1, LETMD1, MARCKS, MYH9, PABPN1, PHGDH, PKD2, PPP1R12A, SLC30A5, SSH1, TCN2	CDKN1A, EIF5A, HNRNPA2B1, ID2, MSN, MYL6, RPL11, S100A4, STMN1, TPI1
Cellular Growth and Proliferation, Auditory Disease, Cancer	AES, ELF1, HIPK2, HMGA1, HMOX1, IL13RA2, PPAP2A, PPP1R14B, PPP2CB, SENP2, SLC12A2, STAT3, TLE1, TSHR	CAV1, EPN2, FCER1G, FLT1, LY6E, PECAM1, PLD3, PPP1CA, PPP1R10, TENC1

¹ Expression of all genes listed is significantly different between compared groups ($P < 0.01$)