Appendix Table 1 Different proteins between HFrecEF patients and controls

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cytokines | Mean\_HFrecEF | Mean\_control | HFrecEF vs control FC | P value |
| TSLP | 499.04 | 2852.6 | 0.17 | 0.01 |
| GLI-3 | 77.96 | 444.78 | 0.18 | 0.03 |
| IL-17F | 969.44 | 3570.98 | 0.27 | 0.04 |
| Desmin | 165.64 | 528.62 | 0.31 | 0.01 |
| GDF-8 | 1028.07 | 3146.35 | 0.33 | 0.02 |
| CD39L3 | 318.8 | 833.94 | 0.38 | 0.03 |
| GATA-5 | 247.39 | 585.46 | 0.42 | 0.04 |
| HIF-1a | 660.62 | 1586.14 | 0.42 | 0 |
| NQO-1 | 337.35 | 772.07 | 0.44 | 0.02 |
| CES2 | 935.58 | 1999.49 | 0.47 | 0.04 |
| MSP | 5022.45 | 10445.36 | 0.48 | 0.03 |
| Cf10 | 4110.48 | 8327.72 | 0.49 | 0.04 |
| TPP1 | 2219.3 | 4403.18 | 0.5 | 0.01 |
| IGFBP-3 | 9335.55 | 18703.05 | 0.5 | 0.04 |
| TLR1 | 2671.17 | 4916.69 | 0.54 | 0.04 |
| ADA | 1018.26 | 1877.31 | 0.54 | 0 |
| Ret | 2746.35 | 4846.07 | 0.57 | 0.03 |
| IL-20 | 944.08 | 1670.47 | 0.57 | 0.02 |
| IL-31 | 2523.6 | 4323.26 | 0.58 | 0.03 |
| GFR alpha-1 | 2474.9 | 4192.71 | 0.59 | 0.01 |
| Glypican 1 | 2263.7 | 3846.65 | 0.59 | 0.03 |
| Flt-3L | 5442.63 | 9003.91 | 0.6 | 0.01 |
| TLR3 | 2368.66 | 3937.65 | 0.6 | 0.03 |
| GFR alpha-2 | 1198.71 | 1920.66 | 0.62 | 0.02 |
| FGF-9 | 309.75 | 499.38 | 0.62 | 0.03 |
| Syntaxin 6 | 463.83 | 721.03 | 0.64 | 0.02 |
| Epo R | 174.24 | 266.98 | 0.65 | 0.02 |
| CDO1 | 10778.22 | 16553.46 | 0.65 | 0 |
| GALNT10 | 621.44 | 958.6 | 0.65 | 0.02 |
| Galectin-4 | 4460.48 | 6891.71 | 0.65 | 0.03 |
| Visfatin | 651.15 | 977.18 | 0.67 | 0.03 |
| C5a | 1793.58 | 2460.24 | 0.73 | 0.03 |
| FGF-16 | 1798.94 | 2471.14 | 0.73 | 0.01 |
| HIF-1 beta | 348.16 | 479.14 | 0.73 | 0.05 |
| CD99-L2 | 10205.79 | 13643.61 | 0.75 | 0.01 |
| Matrilin-2 | 4605.66 | 6173.24 | 0.75 | 0.04 |
| Semaphorin 6B | 3167.2 | 4168.31 | 0.76 | 0.03 |
| IL-1 R5 | 651.18 | 862.46 | 0.76 | 0.04 |
| Contactin-1 | 3713.89 | 4703.43 | 0.79 | 0.03 |
| Syntaxin 4 | 758.27 | 588.75 | 1.29 | 0.02 |
| Dectin-2 | 303.37 | 225.9 | 1.34 | 0.02 |
| ANG-4 | 648.57 | 476.24 | 1.36 | 0.01 |
| GRAP2 | 452.74 | 322.93 | 1.4 | 0.01 |
| LIF R alpha | 3880.45 | 2735.53 | 1.42 | 0.04 |
| TAFA1 | 838.39 | 551.13 | 1.52 | 0.03 |
| AMIGO2 | 407.77 | 243.26 | 1.68 | 0.03 |
| Kell | 1060.76 | 629.15 | 1.69 | 0.05 |
| CEA | 3403.13 | 2005.25 | 1.7 | 0 |
| SMPD1 | 997.92 | 580.31 | 1.72 | 0.03 |
| TRACP | 3156.91 | 1705.3 | 1.85 | 0.03 |
| ALK-1 | 996.18 | 506.18 | 1.97 | 0.05 |
| IDO | 226.1 | 75.88 | 2.98 | 0.05 |

Abbreviations:TSLP ,Thymic stromal lymphopoietin; GLI-3, Transcriptional activator GLI3, IL-17F, Interleukin-17F; GDF-8, Growth/differentiation factor 8; CD39L3, Ectonucleoside triphosphate diphosphohydrolase 3; GATA-5, Transcription factor GATA-5; HIF-1a ,Hypoxia-inducible factor 1-alpha; NQO-1, NAD(P)H dehydrogenase [quinone] 1; CES2,Cocaine esterase; MSP, Dye-decolorizing peroxidase msp; Cf10, Coagulation factor X; TPP1, Tripeptidyl-peptidase 1, IGFBP-3, Insulin-like growth factor-binding protein 3; TLR1, Toll-like receptor 1; ADA,Adenosine deaminase; Ret,Proto-oncogene tyrosine-protein kinase receptor Ret; IL-20,Interleukin-20; IL-31, Interleukin-31; IL-31,Toll-like receptor 3; GFR alpha-1，GDNF family receptor alpha-1;Flt-3L,Fms-related tyrosine kinase 3 ligand;TLR3, Toll-like receptor 3;GFR alpha-2,GDNF family receptor alpha-2; FGF-9, Fibroblast growth factor 9; Epo R,Erythropoietin receptor; CDO1, Cysteine dioxygenase type 1; GALNT10, Polypeptide N-acetylgalactosaminyltransferase 10; C5a, Complement C5; FGF-16, Fibroblast growth factor 16; HIF-1 beta, Aryl hydrocarbon receptor nuclear translocator; CD99-L2,CD99 antigen-like protein 2; IL-1 R5,Interleukin-18 receptor 1; Dectin-2,C-type lectin domain family 6 member A; ANG-4, Angiopoietin-4; GRAP2, GRB2-related adapter protein 2; LIF R alpha, Leukemia inhibitory factor receptor; TAFA1, Protein FAM19A1; AMIGO2, Amphoterin-induced protein 2; Kell ,Kell blood group glycoprotein; CEA ,Carcinoembryonic antigen-related cell adhesion molecule 5; SMPD1, Sphingomyelin phosphodiesterase; TRACP, Tartrate-resistant acid phosphatase type 5; ALK-1, Serine/threonine-protein kinase receptor R3; IDO ,Indoleamine 2,3-dioxygenase 1

Appendix Table 2 Different proteins between HFrEF patients and controls

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cytokines | Mean\_HFrEF | Mean\_contral | HFrEF vs control FC | P value |
| TSLP | 359.78 | 2852.6 | 0.13 | 0 |
| Dopa Decarboxylase | 7491.06 | 18519.93 | 0.4 | 0.01 |
| CD39L3 | 363.87 | 833.94 | 0.44 | 0.04 |
| ST3GAL1 | 530.15 | 1163.31 | 0.46 | 0.03 |
| GDF-8 | 1497.6 | 3146.35 | 0.48 | 0.03 |
| TREML1 | 612.8 | 1199.45 | 0.51 | 0.03 |
| Reg4 | 4414.23 | 8512 | 0.52 | 0.03 |
| Contactin-5 | 1876.36 | 3473.33 | 0.54 | 0.05 |
| TGFa | 3015.43 | 5340.01 | 0.56 | 0.04 |
| Galectin-4 | 3891.1 | 6891.71 | 0.56 | 0.04 |
| Neurocan | 1653.41 | 2955 | 0.56 | 0.03 |
| Flt-3L | 5008.97 | 9003.91 | 0.56 | 0.01 |
| LDL R | 22076.89 | 36934.2 | 0.6 | 0.03 |
| Matriptase | 1125.61 | 1887.76 | 0.6 | 0.03 |
| Visfatin | 606.85 | 977.18 | 0.62 | 0.02 |
| Syntaxin 6 | 453.89 | 721.03 | 0.63 | 0.03 |
| Reg3A | 4823.1 | 7396.3 | 0.65 | 0.05 |
| G-CSF R | 1855.41 | 2810.71 | 0.66 | 0.01 |
| Kallikrein 7 | 677.73 | 977.12 | 0.69 | 0.02 |
| EGF | 13985.74 | 19897.04 | 0.7 | 0.04 |
| Gas6 | 279.21 | 391.75 | 0.71 | 0.02 |
| GALNT10 | 679.8 | 958.6 | 0.71 | 0.01 |
| HS3ST1 | 287.1 | 399.75 | 0.72 | 0.03 |
| LAMP | 3425.45 | 4603.43 | 0.74 | 0.03 |
| GPVI | 5914.76 | 7805.14 | 0.76 | 0.02 |
| GASP-1 | 39718.07 | 51045.82 | 0.78 | 0.05 |
| CDO1 | 13059.35 | 16553.46 | 0.79 | 0.01 |
| HO-1 | 4566.41 | 5621.55 | 0.81 | 0.04 |
| RGM-A | 1064.06 | 1313.11 | 0.81 | 0.03 |
| BCL-2 | 1360.46 | 1682.65 | 0.81 | 0.01 |
| NUDT5 | 426.12 | 320.39 | 1.33 | 0.04 |
| ANG-4 | 636.81 | 476.24 | 1.34 | 0.01 |
| IL-7 R alpha | 42757.57 | 30533.2 | 1.4 | 0.02 |
| CPB1 | 12338.46 | 6962.74 | 1.77 | 0.01 |
| FLRT2 | 633.77 | 340.59 | 1.86 | 0.01 |
| Semaphorin 4C | 744.33 | 361.3 | 2.06 | 0 |
| B4GalT1 | 658.87 | 255.17 | 2.58 | 0.01 |
| BAI1 | 684.67 | 211.66 | 3.23 | 0 |
| PTH1R | 671.04 | 205.46 | 3.27 | 0.02 |
| IL-22BP | 4279.2 | 1023.58 | 4.18 | 0.05 |

Abbreviations:TSLP,Thymic stromal lymphopoietin; CD39L3, Ectonucleoside triphosphate diphosphohydrolase 3;ST3GAL1, CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,3-sialyltransferase 1;GDF-8, Growth/differentiation factor 8; TREML1,Trem-like transcript 1 protein; Reg4, Regenerating islet-derived protein 4; TGFa, Protransforming growth factor alpha; Flt-3L,Fms-related tyrosine kinase 3 ligand; LDL R, Low-density lipoprotein receptor; Reg3A, Regenerating islet-derived protein 3-alpha; G-CSF R, Granulocyte colony-stimulating factor receptor; EGF, Pro-epidermal growth factor; Gas6, Growth arrest-specific protein 6; GALNT10, Polypeptide N-acetylgalactosaminyltransferase 10; HS3ST1, Heparan sulfate glucosamine 3-O-sulfotransferase 1; LAMP, Limbic system-associated membrane protein; GPVI, Platelet glycoprotein VI; GASP-1, G-protein coupled receptor-associated sorting protein 1; CDO1, Cysteine dioxygenase type 1; HO-1,Heme oxygenase 1; RGM-A, Repulsive guidance molecule A; BCL-2,Apoptosis regulator Bcl-2; NUDT5, ADP-sugar pyrophosphatase; ANG-4, Angiopoietin-4; IL-7 R alpha, Interleukin-7 receptor subunit alpha; CPB1,Carboxypeptidase B;FLRT2, Leucine-rich repeat transmembrane protein FLRT2; B4GalT1, Beta-1,4-galactosyltransferase 1; BAI1, Brain-specific angiogenesis inhibitor 1; PTH1R, Parathyroid hormone/parathyroid hormone-related peptide receptor; IL-22BP, Interleukin-22 receptor subunit alpha-2

Appendix Table 3 Different proteins between HFrecEF patients and HFrEF patients

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cytokines | Mean\_HFrecEF | Mean\_HFrEF | HFrEF vs HFrecEF FC | P value |
| ACE-2 | 307.15 | 440.59 | 1.43 | 0.03 |
| AFP | 23138.4 | 14015.06 | 0.61 | 0 |
| B4GalT1 | 341.57 | 658.87 | 1.93 | 0 |
| BAI1 | 236.74 | 684.67 | 2.89 | 0 |
| BMPR-IA | 430.51 | 354.12 | 0.82 | 0.04 |
| Calreticulin | 336.14 | 511.69 | 1.52 | 0.03 |
| CDO1 | 10778.22 | 13059.35 | 1.21 | 0.03 |
| cIAP-2 | 541.82 | 992.4 | 1.83 | 0.04 |
| CNTF R alpha | 3569.05 | 4733.91 | 1.33 | 0.01 |
| EDA-A2 | 161.12 | 279.76 | 1.74 | 0.05 |
| Eotaxin-2 | 10594.97 | 15789.73 | 1.49 | 0.05 |
| Epo R | 174.24 | 272.67 | 1.56 | 0 |
| GBA3 | 533.11 | 962.15 | 1.8 | 0.05 |
| GRAP2 | 452.74 | 323.26 | 0.71 | 0.01 |
| HepaCAM | 737.55 | 353 | 0.48 | 0.01 |
| HO-1 | 6238.91 | 4566.41 | 0.73 | 0.01 |
| ICAM-1 | 121939.72 | 153166.08 | 1.26 | 0.04 |
| IL-17C | 261.94 | 367.34 | 1.4 | 0.01 |
| Kallikrein 12 | 2178.28 | 1146.51 | 0.53 | 0.04 |
| Kell | 1060.76 | 589.65 | 0.56 | 0.03 |
| KIR2DL3 | 297.28 | 506.24 | 1.7 | 0.01 |
| OSCAR | 497.64 | 253.8 | 0.51 | 0.02 |
| PP | 401.56 | 333.37 | 0.83 | 0.03 |
| ROR2 | 825.59 | 1087.42 | 1.32 | 0.01 |
| TPP1 | 2219.3 | 4845.28 | 2.18 | 0.01 |
| TRAIL R2 | 1908.92 | 1486.94 | 0.78 | 0.01 |

Abbreviations: ACE-2, Angiotensin-converting enzyme 2; AFP, Alpha-fetoprotein; B4GalT1, Beta-1,4-galactosyltransferase 1; BAI1, Brain-specific angiogenesis inhibitor 1; BMPR-IA, Bone morphogenetic protein receptor type-1A; CDO1, Cysteine dioxygenase type 1; cIAP-2,Baculoviral IAP repeat-containing protein 3; CNTF R alpha, Ciliary neurotrophic factor receptor subunit alpha; EDA-A2, Ectodysplasin-A; Eotaxin-2, C-C motif chemokine 24; Epo R, Erythropoietin receptor; GBA3, Cytosolic beta-glucosidase; GRAP2, GRB2-related adapter protein 2; HepaCAM, Hepatocyte cell adhesion molecule; HO-1,Heme oxygenase 1; ICAM-1,Intercellular adhesion molecule 1; IL-17C, Interleukin-17C; Kell ,Kell blood group glycoprotein; KIR2DL3,Killer cell immunoglobulin-like receptor 2DL3; OSCAR ,Osteoclast-associated immunoglobulin-like receptor; PP, Pancreatic prohormone; ROR2,Tyrosine-protein kinase transmembrane receptor ROR2; TPP1, Tripeptidyl-peptidase 1; TRAIL R2,Tumor necrosis factor receptor superfamily member 10B