# Supplemental data

## Monocyte gene expression in childhood obesity is associated with obesity and complexity of atherosclerosis in adults

Keustermans GC, Kofink D, Eikendal A, de Jager W, Meerding J, Nuboer R, Waltenberger J, Kraaijeveld AO, Jukema JW, Sels JW, Garssen J, Prakken BJ, Asselbergs FW, Kalkhoven E, Hoefer IE, Pasterkamp G, Schipper HS

**Supplemental table 1** Significantly different genes between obese and lean children in total study population (n = 51)

| | **Log Fold change** | **Crude p-value** | **FDR-adjusted p-value** | **Beta** |
|---|---|---|---|---|
| **ACBD6** | -0.16 | <0.0001 | 0.03 | 3.35 |
| **ANXA2P1** | 0.25 | <0.0001 | 0.04 | 1.75 |
| **APOF** | 0.23 | <0.0001 | 0.03 | 2.07 |
| **ATP5D** | -0.16 | <0.0001 | 0.03 | 2.31 |
| **C16orf13** | -0.17 | <0.0001 | 0.05 | 1.33 |
| **C20orf201** | -0.15 | <0.0001 | 0.04 | 1.98 |
| **CCT7** | -0.29 | <0.0001 | 0.03 | 2.47 |
| **CD99** | 0.29 | <0.0001 | 0.04 | 1.85 |
| **CDKN1C** | -0.41 | <0.0001 | 0.05 | 1.32 |
| **CHCHD10** | -0.17 | <0.0001 | 0.04 | 1.86 |
| **CKS1B** | -0.30 | <0.0001 | 0.03 | 2.46 |
| **COX15** | -0.32 | <0.0001 | 0.04 | 1.57 |
| **DCTD** | -0.14 | <0.0001 | 0.03 | 2.88 |
| **DIS3L** | -0.32 | <0.0001 | 0.04 | 1.92 |
| **ECSIT** | -0.21 | <0.0001 | 0.03 | 3.69 |
| **EEF1D** | -0.17 | <0.0001 | 0.03 | 3.04 |
| **EMP2** | 0.14 | <0.0001 | 0.03 | 2.36 |
| **F13A1** | 0.62 | <0.0001 | 0.03 | 3.70 |
| **FAM195A** | -0.35 | <0.0001 | 0.03 | 2.42 |
| **FERMT3** | 0.11 | <0.0001 | 0.03 | 3.29 |
| **FOXK1** | -0.19 | <0.0001 | 0.04 | 1.89 |
| **GABRR3** | -0.09 | <0.0001 | 0.03 | 2.57 |
| **GALM** | -0.17 | <0.0001 | 0.04 | 1.47 |
| **GMDS** | -0.20 | <0.0001 | 0.04 | 1.57 |
| **GTDC1** | -0.10 | <0.0001 | 0.04 | 1.73 |
| **HMBS** | -0.27 | <0.0001 | 0.03 | 2.76 |
| **IFNA1** | -0.09 | <0.0001 | 0.03 | 2.07 |
| **IMPDH2** | -0.28 | <0.0001 | 0.02 | 4.98 |
| **LGALS3** | 0.31 | <0.0001 | 0.03 | 2.80 |
| **LNPEP** | -0.12 | 0.0001 | 0.05 | 1.22 |
| **LOC100130604** | 0.36 | <0.0001 | 0.03 | 2.18 |
| **LOC100131387** | 0.16 | <0.0001 | 0.03 | 2.19 |
| **LOC100132598** | -0.08 | 0.0001 | 0.05 | 1.19 |
| **LOC651452** | 0.07 | <0.0001 | 0.03 | 2.38 |
| **LOC652683** | -0.10 | <0.0001 | 0.03 | 2.10 |
| **LOC653778** | 0.40 | <0.0001 | 0.04 | 1.84 |
| **LOC654121** | 0.20 | <0.0001 | 0.03 | 2.65 |
| **LOC730278** | 0.31 | <0.0001 | 0.03 | 2.51 |
| **LOC730740** | 0.16 | <0.0001 | 0.03 | 3.24 |
| **LRPPRC** | -0.21 | <0.0001 | 0.03 | 3.15 |
| **LSM4** | -0.23 | 0.0001 | 0.05 | 1.20 |
| **MAP6D1** | -0.33 | <0.0001 | 0.03 | 2.78 |

| | | | | |
|---|---|---|---|---|
| **ME1** | 0.27 | <0.0001 | 0.02 | 4.37 |
| **METTL2B** | 0.14 | <0.0001 | 0.03 | 2.86 |
| **MRPS15** | -0.16 | <0.0001 | 0.05 | 1.30 |
| **NDUFB2** | -0.22 | <0.0001 | 0.04 | 1.63 |
| **NDUFS7** | -0.23 | <0.0001 | 0.05 | 1.28 |
| **NME1-NME2** | -0.23 | <0.0001 | 0.03 | 3.42 |
| **PID1** | -0.44 | <0.0001 | 0.03 | 2.07 |
| **PKN1** | -0.15 | <0.0001 | 0.03 | 2.07 |
| **POLR2I** | -0.20 | 0.0001 | 0.05 | 1.22 |
| **PPP1R12A** | 0.25 | <0.0001 | 0.04 | 1.48 |
| **QPRT** | -0.32 | <0.0001 | 0.00 | 8.56 |
| **SAR1A** | 0.32 | <0.0001 | 0.04 | 1.75 |
| **SH3BGRL3** | 0.26 | <0.0001 | 0.03 | 3.24 |
| **SLC30A4** | 0.19 | <0.0001 | 0.03 | 2.48 |
| **SNHG7** | -0.39 | <0.0001 | 0.02 | 4.61 |
| **SNORD113-1** | -0.08 | <0.0001 | 0.04 | 1.73 |
| **SRM** | -0.17 | <0.0001 | 0.04 | 1.42 |
| **TMEM134** | -0.19 | <0.0001 | 0.02 | 4.54 |
| **TMEM160** | -0.28 | <0.0001 | 0.04 | 1.77 |
| **UBA6** | 0.36 | <0.0001 | 0.04 | 1.53 |
| **USP49** | 0.55 | <0.0001 | 0.04 | 1.56 |
| **UTP14A** | -0.16 | <0.0001 | 0.05 | 1.37 |
| **ZFP36L1** | 0.40 | <0.0001 | 0.04 | 1.96 |
| **ZNF581** | -0.17 | <0.0001 | 0.04 | 1.51 |
| **ZWILCH** | -0.12 | <0.0001 | 0.03 | 2.62 |

**Supplemental table 2** Association between genes and obesity status in total study population (n = 51)

| | **Model 1*†**<br>β (95% CI) | **p value** | **Model 2*†**<br>β (95% CI) | **p value** |
|---|---|---|---|---|
| **ACBD6** | -0.16 (-0.22, -0.10) | <0.0001 | -0.16 (-0.22, -0.09) | <0.0001 |
| **ANXA2P1** | 0.26 (0.16, 0.37) | <0.0001 | 0.25 (0.13, 0.36) | <0.0001 |
| **APOF** | 0.22 (0.12, 0.32) | <0.0001 | 0.23 (0.12, 0.33) | <0.0001 |
| **ATP5D** | -0.17 (-0.23, -0.10) | <0.0001 | -0.16 (-0.23, -0.09 ) | <0.0001 |
| **C16orf13** | -0.15 (-0.23, -0.07) | 0.0004 | -0.17 (-0.26, -0.09) | <0.0001 |
| **C20orf201** | -0.16 (-0.22, -0.09) | <0.0001 | -0.15 (-0.22, -0.08) | 0.0001 |
| **CCT7** | -0.28 (-0.40, -0.16) | <0.0001 | -0.29 (-0.42, -0.16) | <0.0001 |
| **CD99** | 0.26 (0.13, 0.39) | 0.0002 | 0.29 (0.16, 0.43) | <0.0001 |
| **CDKN1C** | -0.40 (-0.59, -0.22) | <0.0001 | -0.41 (-0.61, -0.21) | 0.0001 |
| **CHCHD10** | -0.19 (-0.26, -0.11) | <0.0001 | -0.17 (-0.25, -0.09) | <0.0001 |
| **CKS1B** | -0.28 (-0.41, -0.16) | <0.0001 | -0.30 (-0.43, -0.16) | <0.0001 |
| **COX15** | -0.29 (-0.43, -0.15) | <0.0001 | -0.32 (-0.47, -0.17) | 0.0001 |
| **DCTD** | -0.16 (-0.22, -0.11) | <0.0001 | -0.14 (-0.20, -0.08) | <0.0001 |
| **DIS3L** | -0.31 (-0.45, -0.18) | <0.0001 | -0.32 (-0.46, -0.17) | <0.0001 |
| **ECSIT** | -0.21 (-0.29, -0.13) | <0.0001 | -0.21 (-0.30, -0.13) | <0.0001 |
| **EEF1D** | -0.15 (-0.22, -0.08) | <0.0001 | -0.17 (-0.24, -0.10) | <0.0001 |
| **EMP2** | 0.12 (0.06, 0.18) | 0.0002 | 0.14 (0.08, 0.20) | <0.0001 |
| **F13A1** | 0.64 (0.41, 0.88) | <0.0001 | 0.62 (-0.37, 0.88) | <0.0001 |
| **FAM195A** | -0.34 (-0.48, -0.19) | <0.0001 | -0.35 (-0.51, -0.20) | <0.0001 |
| **FERMT3** | 0.11 (0.07, 0.15) | <0.0001 | 0.11 (0.07, 0.15) | <0.0001 |
| **FOXK1** | -0.19 (-0.27, -0.11) | <0.0001 | -0.19 (-0.28, -0.10) | <0.0001 |
| **GABRR3** | -0.08 (-0.12, -0.05) | <0.0001 | -0.09 (-0.13, -0.05) | <0.0001 |
| **GALM** | -0.18 (-0.26, -0.11) | <0.0001 | -0.17 (-0.26, -0.09) | 0.0001 |
| **GMDS** | -0.18 (-0.27, -0.09) | 0.0001 | -0.20 (-0.29, -0.10) | <0.0001 |
| **GTDC1** | -0.10 (-0.14, -0.06) | <0.0001 | -0.10 (-0.15, -0.06) | <0.0001 |
| **HMBS** | -0.25 (-0.36, -0.15) | <0.0001 | -0.27 (-0.38, -0.15) | <0.0001 |
| **IFNA1** | -0.08 (-0.11, -0.04) | 0.0003 | -0.09 (-0.13, -0.05) | <0.0001 |
| **IMPDH2** | -0.29 (-0.39, -0.19) | <0.0001 | -0.28 (-0.39, -0.18) | <0.0001 |
| **LGALS3** | 0.35 (0.22, 0.48) | <0.0001 | 0.31 (0.18, 0.44) | <0.0001 |
| **LNPEP** | -0.13 (-0.18, -0.07) | <0.0001 | -0.12 (-0.18, -0.06) | 0.0001 |
| **LOC100130604** | 0.38 (0.23, 0.53) | <0.0001 | 0.36 (0.20, 0.53) | <0.0001 |
| **LOC100131387** | 0.17 (0.11, 0.24) | <0.0001 | 0.16 (0.09, 0.23) | <0.0001 |
| **LOC100132598** | -0.08 (-0.11, -0.04) | <0.0001 | -0.08 (-0.12, -0.04) | <0.0001 |
| **LOC651452** | 0.06 (0.04, 0.09) | <0.0001 | 0.07 (0.04, 0.10) | <0.0001 |
| **LOC652683** | -0.09 (-0.13, -0.05) | <0.0001 | -0.10 (-0.14, -0.05) | <0.0001 |
| **LOC653778** | 0.39 (0.21, 0.56) | <0.0001 | 0.40 (0.21, 0.59) | <0.0001 |
| **LOC654121** | 0.20 (0.13, 0.28) | <0.0001 | 0.20 (-0.11, 0.28) | <0.0001 |
| **LOC730278** | 0.32 (0.19, 0.45) | <0.0001 | 0.31 (0.18, 0.45) | <0.0001 |
| **LOC730740** | 0.17 (0.11, 0.23) | <0.0001 | 0.16 (0.09, 0.23) | <0.0001 |
| **LRPPRC** | -0.21 (-0.30, -0.13) | <0.0001 | -0.21 (-0.30, -0.12) | <0.0001 |
| **LSM4** | -0.22 (-0.33, -0.12) | <0.0001 | -0.23 (-0.34, -0.12) | 0.0001 |
| **MAP6D1** | -0.36 (-0.49, -0.23) | <0.0001 | -0.33 (-0.48, -0.19) | <0.0001 |

| | | | | |
|---|---|---|---|---|
| **ME1** | 0.27 (0.17, 0.38) | <0.0001 | 0.27 (0.17, 0.38) | <0.0001 |
| **METTL2B** | 0.13 (0.08, 0.19) | <0.0001 | 0.14 (0.08, 0.21) | <0.0001 |
| **MRPS15** | -0.17 (-0.24, -0.10) | <0.0001 | -0.16 (-0.24, -0.08) | 0.0001 |
| **NDUFB2** | -0.22 (-0.32, -0.13) | <0.0001 | -0.22 (-0.33, -0.12) | <0.0001 |
| **NDUFS7** | -0.24 (-0.34, -0.14) | <0.0001 | -0.23 (-0.34, -0.12) | 0.0001 |
| **NME1-NME2** | -0.23 (-0.31, -0.14) | <0.0001 | -0.23 (-0.32, -0.13) | <0.0001 |
| **PID1** | -0.43 (-0.62, -0.25) | <0.0001 | -0.44 (-0.65, -0.24) | <0.0001 |
| **PKN1** | -0.14 (-0.20, -0.08) | <0.0001 | -0.15 (-0.22, -0.08) | <0.0001 |
| **POLR2I** | -0.21 (-0.30, -0.12) | <0.0001 | -0.20 (-0.30, -0.11) | 0.0001 |
| **PPP1R12A** | 0.27 (0.16, 0.38) | <0.0001 | 0.25 (0.13, 0.37) | 0.0001 |
| **QPRT** | -0.31 (-0.40, -0.22) | <0.0001 | -0.32 (-0.42, -0.22) | <0.0001 |
| **SAR1A** | 0.33 (0.19, 0.46) | <0.0001 | 0.32 (0.17, 0.47) | <0.0001 |
| **SH3BGRL3** | 0.25 (0.14, 0.36) | <0.0001 | 0.26 (0.15, 0.38) | <0.0001 |
| **SLC30A4** | 0.16 (0.09, 0.24) | <0.0001 | 0.19 (0.11, 0.27) | <0.0001 |
| **SNHG7** | -0.37 (-0.51, -0.24) | <0.0001 | -0.39 (-0.54, -0.24) | <0.0001 |
| **SNORD113-1** | -0.07 (-0.10, -0.03) | 0.0003 | -0.08 (-0.12, -0.05) | <0.0001 |
| **SRM** | -0.18 (-0.25, -0.10) | <0.0001 | -0.17 (-0.25, -0.09) | <0.0001 |
| **TMEM134** | -0.19 (-0.26, -0.13) | <0.0001 | -0.19 (-0.26, -0.12) | <0.0001 |
| **TMEM160** | -0.28 (-0.40, -0.16) | <0.0001 | -0.28 (-0.42, -0.15) | <0.0001 |
| **UBA6** | 0.33 (0.17, 0.49) | 0.0002 | 0.36 (0.19, 0.54) | 0.0001 |
| **USP49** | 0.55 (0.31, 0.79) | <0.0001 | 0.55 (0.29, 0.81) | 0.0001 |
| **UTP14A** | -0.14 (-0.21, -0.07) | 0.0002 | -0.16 (-0.23, -0.08) | 0.0001 |
| **ZFP36L1** | 0.44 (0.27, 0.62) | <0.0001 | 0.40 (0.22, 0.59) | <0.0001 |
| **ZNF581** | -0.18 (-0.25, -0.10) | <0.0001 | -0.17 (-0.25, -0.09) | <0.0001 |
| **ZWILCH** | -0.11 (-0.16, -0.06) | <0.0001 | -0.12 (-0.17, -0.07) | <0.0001 |

* Model 1: crude, Model 2: adjusted for age and sex (reference category: lean)

† Values are linear regression coefficients (β) with 95% confidence intervals (CI)

**Supplemental table 3** Monocyte gene expression and cardiometabolic parameters in the total pediatric population

| | | ***Genes*** | | | | |
|---|---|---|---|---|---|---|
| | | **HMBS** | **IMPDH2** | **LRPPRC** | **TMEM134** | **ZWILCH** |
| ***Cardiovascular risk factors*** | | | | | | |
| Systolic BP | β | -2.52 | 11.46 | -0.66 | -3.13 | -26.43 |
| | 95% CI | -18.87, 13.84 | -6.47, 29.38 | -21.39, 20.07 | -29.94, 23.67 | -63.45, 10.59 |
| QUICKI | β | -0.01 | 0.03 | -0.06 | 0.06 | -0.02 |
| | 95% CI | -0.06, 0.05 | -0.02, 0.09 | -0.13, 0.001 | -0.02, 0.14 | -0.14, 0.10 |
| ***Monocytes*** | | | | | | |
| Total monocyte nr | β | -0.06 | -0.25 | -0.15 | -0.18 | -0.51 |
| | 95% CI | -0.33, 0.20 | -0.54, 0.04 | -0.49, 0.18 | -0.61, 0.24 | -1.11, 0.09 |
| $CD14^{++}CD16^{-}$ nr | β | -5.08 | -25.98 | -12.28 | -25.81 | -54.99 |
| | 95% CI | -32.18, 22.01 | -55.11, 3.15 | -46.14, 21.58 | -68.19, 16.56 | -114.69, 4.71 |
| $CD14^{++}CD16^{+}$ nr | β | -0.26 | -2.16 | -5.55 | 2.48 | -7.97 |
| | 95% CI | -6.86, 6.34 | -9.47, 5.15 | -13.66, 2.56 | -7.98, 12.93 | -22.85, 6.91 |
| $CD14^{++}CD16^{-}$ CD11b MFI | β | -2442 | -3071 | -10184 * | -5021.0 | -19312 * |
| | 95% CI | -10380, 5495 | -12069, 5927 | -18305, -2062 | -18839, 8797 | -36097, -2527 |
| $CD14^{++}CD16^{+}$ CD11b MFI | β | 362 | -1705 | -6765 | 2012 | -8736 |
| | 95% CI | -7767, 8491 | -1094, 7507 | -15456, 1925 | -12154, 16178 | -26844, 9373 |
| ***Adipokines*** | | | | | | |
| Adiponectin | β | 13.56 | 10.41 | 10.33 | 20.66 | 36.01 * |
| | 95% CI | -1.79, 28.90 | -7.67, 28.49 | -9.17, 29.83 | -3.96, 45.29 | 1.43, 70.60 |
| Chemerin | β | -0.84 * | -0.25 | -0.27 | -1.24 * | -0.14 |
| | 95% CI | -1.60, -0.09 | -1.13, 0.63 | -1.26, 0.76 | -2.45, -0.03 | -1.96, 1.68 |
| Leptin | β | -7.05 | 106.93 | 27.60 | 116.45 | 311.12 |
| | 95% CI | -204.94, 190.85 | -110.29, 324.16 | -220.06, 275.26 | -195.93, 428.84 | -130.88, 753.11 |
| TNF-R2 | β | 0.11 | 1.01 * | 0.48 | 1.02 | 1.86 |
| | 95% CI | -0.77, 0.99 | 0.08, 1.94 | -0.62, 1.57 | -0.34, 2.39 | -0.07, 3.79 |

The association of the 5 validated genes with a selection of cardiometabolic parameters was studied using a linear regression model. Linear regression coefficients (β) with 95% confidence intervals (95% CI) for the monocyte genes are shown, adjusted for age, sex and BMI-SD. *$p<0.05$, § $p<0.01$. MFI: median fluorescence intensity, nr: number, QUICKI: quantitative insulin sensitivity index, Systolic BP: systolic blood pressure.

**Supplemental table 4** Monocyte gene expression and cardiometabolic parameters in the obese pediatric subgroup

| | | ***Genes*** | | | | |
|---|---|---|---|---|---|---|
| | | **HMBS** | **IMPDH2** | **LRPPRC** | **TMEM134** | **ZWILCH** |
| ***Cardiovascular risk factors*** | | | | | | |
| Systolic BP | β | -1.41 | 20.72 * | 11.22 | -5.82 | -25.87 |
| | 95% CI | -19.59, 16.78 | 1.25, 40.19 | -15.87, 38.30 | -38.63, 26.99 | -74.00, 22.26 |
| QUICKI | β | -0.03 | -0.03 | -0.08 * | -0.01 | -0.14 * |
| | 95% CI | -0.09, 0.02 | -0.09, 0.04 | -0.16, -0.001 | -0.12, 0.09 | -0.28, -0.001 |
| ***Monocytes*** | | | | | | |
| Total monocyte nr | β | 0.02 | -0.17 | -0.05 | 0.02 | -0.35 |
| | 95% CI | -0.37, 0.41 | -0.61, 0.28 | -0.64, 0.54 | -0.69, 0.72 | -1.39, 0.70 |
| CD14$^{++}$CD16$^{-}$ nr | β | 4.15 | 1.09 | -3.80 | 12.66 | -6.53 |
| | 95% CI | -5.81, 14.11 | -10.44, 12.62 | -18.78, 11.18 | -4.75, 30.07 | -33.05, 19.98 |
| CD14$^{++}$CD16$^{+}$ nr | β | 6.98 | -15.09 | 1.94 | -4.53 | -36.60 |
| | 95% CI | -33.07, 47.02 | -60.64, 30.46 | -57.94, 61.82 | -76.39, 67.34 | -141.66, 68.47 |
| CD14$^{++}$CD16$^{-}$ | β | 3389 | -8455 | -15385 * | 10387 | -24070 |
| CD11b MFI | 95% CI | -9927, 16705 | -12017, 14902 | -29859, -912 | -18329, 39102 | -62508, 14369 |
| CD14$^{++}$CD16$^{+}$ | β | 2323 | -839 | -19214 § | 17823 | -23782 |
| CD11b MFI | 95% CI | -11681, 16326 | -14954, 13275 | -33658, -4771 | -11611, 47257 | -64228, 16665 |
| ***Adipokines*** | | | | | | |
| Adiponectin | β | 16.47 | 7.72 | -0.55 | 16.56 | 23.05 |
| | 95% CI | -0.54, 33.48 | -13.85, 29.29 | -27.07, 26.01 | -16.04, 49.17 | -24.31, 70.40 |
| Chemerin | β | -1.09 * | -0.17 | -0.28 | -2.68 § | -1.17 |
| | 95% CI | -2.14, -0.03 | -1.46, 1.12 | -1.95, 1.40 | -4.45, -0.92 | -4.13, 1.78 |
| Leptin | β | 580 | 238 | 144 | 377 | 759 |
| | 95% CI | -265, 380 | -120, 596 | -333, 621 | -186, 939 | -46, 1563 |
| TNF-R2 | β | 0.16 | 1.28 * | 0.58 | 1.17 | 1.19 |
| | 95% CI | -0.99, 1.30 | 0.07, 2.49 | -1.10, 2.26 | -0.83, 3.17 | -1.80, 4.17 |

The association of the 5 validated genes with a selection of cardiometabolic parameters was studied using a linear regression model. Linear regression coefficients (β) with 95% confidence intervals (95% CI) for the monocyte genes are shown, adjusted for age and sex. *p<0.05, § p<0.01. MFI: median fluorescence intensity, nr: number, QUICKI: quantitative insulin sensitivity index, Systolic BP: systolic blood pressure.

## **Supplemental table 5** Pathway analysis

| **Name** | **Gene ID** | **Hits in query list** | **Number of genes in pathway** | **Raw p-value** | **P-value (FDR-adjusted)** | **Hits in Query List** |
|---|---|---|---|---|---|---|
| oxidative phosphorylation | GO:0006119 | 5 | 108 | 1,58E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2 |
| purine ribonucleoside monophosphate metabolic process | GO:0009167 | 7 | 279 | 1,63E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,NDUFB2,PID1 |
| purine nucleoside monophosphate metabolic process | GO:0009126 | 7 | 280 | 1,67E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,NDUFB2,PID1 |
| ribonucleoside monophosphate metabolic process | GO:0009161 | 7 | 291 | 2,14E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,NDUFB2,PID1 |
| nucleoside metabolic process | GO:0009116 | 8 | 414 | 2,56E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,DCTD,NDUFB2,PID1 |
| nucleoside monophosphate metabolic process | GO:0009123 | 7 | 304 | 2,83E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,NDUFB2,PID1 |
| nucleotide metabolic process | GO:0009117 | 10 | 694 | 2,88E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,QPRT,COX15,DCTD,NDUFB2,ME1,PID1 |
| nucleoside phosphate metabolic process | GO:0006753 | 10 | 704 | 3,26E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,QPRT,COX15,DCTD,NDUFB2,ME1,PID1 |
| glycosyl compound metabolic process | GO:1901657 | 8 | 436 | 3,70E-05 | 4,24E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH,COX15,DCTD,NDUFB2,PID1 |
| nucleoside biosynthetic process | GO:0009163 | 5 | 131 | 4,02E-05 | 4,24E-03 | ATP5D,CHCHD10,IMPDH2,DCTD,PID1 |
| nucleotide biosynthetic process | GO:0009165 | 7 | 322 | 4,08E-05 | 4,24E-03 | ATP5D,CHCHD10,IMPDH2,QPRT,DCTD,ME1,PID1 |
| glycosyl compound biosynthetic process | GO:1901659 | 5 | 133 | 4,32E-05 | 4,24E-03 | ATP5D,CHCHD10,IMPDH2,DCTD,PID1 |
| nucleoside phosphate biosynthetic process | GO:1901293 | 7 | 325 | 4,33E-05 | 4,24E-03 | ATP5D,CHCHD10,IMPDH2,QPRT,DCTD,ME1,PID1 |
| organonitrogen compound biosynthetic process | GO:1901566 | 14 | 1445 | 5,17E-05 | 4,69E-03 | ATP5D,LRPPRC,EEF1D,CHCHD10,IMPDH2,ZFP36L1,QPRT,MRPS15, SRM,HMBS,COX15,DCTD,ME1,PID1 |
| purine nucleoside monophosphate biosynthetic process | GO:0009127 | 4 | 74 | 6,50E-05 | 4,96E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |
| purine ribonucleoside monophosphate biosynthetic process | GO:0009168 | 4 | 74 | 6,50E-05 | 4,96E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |
| nucleobase-containing small molecule metabolic process | GO:0055086 | 10 | 766 | 6,63E-05 | 4,96E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH2,QPRT,COX15,DCTD,NDUFB2,ME1,PID1 |
| ATP metabolic process | GO:0046034 | 6 | 242 | 7,35E-05 | 5,19E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| purine ribonucleoside metabolic process | GO:0046128 | 7 | 362 | 8,53E-05 | 5,71E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| purine nucleoside metabolic process | GO:0042278 | 7 | 365 | 8,98E-05 | 5,71E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| purine ribonucleoside triphosphate metabolic process | GO:0009205 | 6 | 263 | 1,16E-04 | 6,76E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| ribonucleoside monophosphate biosynthetic process | GO:0009156 | 4 | 86 | 1,17E-04 | 6,76E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| ribonucleoside triphosphate metabolic process | GO:0009199 | 6 | 270 | 1,34E-04 | 7,12E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| purine nucleoside triphosphate metabolic process | GO:0009144 | 6 | 271 | 1,37E-04 | 7,12E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| ribonucleoside metabolic process | GO:0009119 | 7 | 392 | 1,40E-04 | 7,12E-03 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| nucleoside monophosphate biosynthetic process | GO:0009124 | 4 | 94 | 1,65E-04 | 8,07E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |
| nucleoside triphosphate metabolic process | GO:0009141 | 6 | 295 | 2,17E-04 | 9,91E-03 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| purine nucleoside biosynthetic process | GO:0042451 | 4 | 102 | 2,26E-04 | 9,91E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |
| purine ribonucleoside biosynthetic process | GO:0046129 | 4 | 102 | 2,26E-04 | 9,91E-03 | ATP5D,CHCHD10,IMPDH2,PID1 |
| ATP biosynthetic process | GO:0006754 | 3 | 48 | 3,74E-04 | 1,59E-02 | ATP5D,CHCHD10,PID1 |
| ribonucleoside biosynthetic process | GO:0042455 | 4 | 121 | 4,33E-04 | 1,78E-02 | ATP5D,CHCHD10,IMPDH2,PID1 |
| mitochondrial respiratory chain complex I assembly | GO:0032981 | 3 | 56 | 5,90E-04 | 2,21E-02 | NDUFS7,ECSIT,NDUFB2 |
| NADH dehydrogenase complex assembly | GO:0010257 | 3 | 56 | 5,90E-04 | 2,21E-02 | NDUFS7,ECSIT,NDUFB2 |
| mitochondrial respiratory chain complex I biogenesis | GO:0097031 | 3 | 56 | 5,90E-04 | 2,21E-02 | NDUFS7,ECSIT,NDUFB2 |
| purine ribonucleoside triphosphate biosynthetic process | GO:0009206 | 3 | 59 | 6,88E-04 | 2,50E-02 | ATP5D,CHCHD10,PID1 |
| purine nucleoside triphosphate biosynthetic process | GO:0009145 | 3 | 60 | 7,22E-04 | 2,55E-02 | ATP5D,CHCHD10,PID1 |
| ribonucleoside triphosphate biosynthetic process | GO:0009201 | 3 | 65 | 9,12E-04 | 3,11E-02 | ATP5D,CHCHD10,PID1 |
| purine ribonucleotide metabolic process | GO:0009150 | 7 | 537 | 9,28E-04 | 3,11E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| generation of precursor metabolites and energy | GO:0006091 | 6 | 395 | 1,01E-03 | 3,30E-02 | ATP5D,CHCHD10,NDUFS7,COX15,NDUFB2,PID1 |
| ribonucleotide metabolic process | GO:0009259 | 7 | 552 | 1,09E-03 | 3,46E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| purine nucleotide metabolic process | GO:0006163 | 7 | 556 | 1,14E-03 | 3,52E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| ribose phosphate metabolic process | GO:0019693 | 7 | 567 | 1,27E-03 | 3,85E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| mitochondrial respiratory chain complex assembly | GO:0033108 | 3 | 77 | 1,49E-03 | 4,28E-02 | NDUFS7,ECSIT,NDUFB2 |
| nucleoside triphosphate biosynthetic process | GO:0009142 | 3 | 77 | 1,49E-03 | 4,28E-02 | ATP5D,CHCHD10,PID1 |
| nicotinamide nucleotide biosynthetic process | GO:0019359 | 2 | 20 | 1,55E-03 | 4,28E-02 | QPRT,ME1 |
| pyridine nucleotide biosynthetic process | GO:0019363 | 2 | 20 | 1,55E-03 | 4,28E-02 | QPRT,ME1 |
| mitochondrion organization | GO:0007005 | 8 | 770 | 1,70E-03 | 4,60E-02 | LRPPRC,CHCHD10,NDUFS7,MRPS15,LSM4,ECSIT,NDUFB2,PID1 |
| mitochondrial ATP synthesis coupled electron transport | GO:0042775 | 3 | 82 | 1,79E-03 | 4,73E-02 | NDUFS7,COX15,NDUFB2 |
| purine-containing compound metabolic process | GO:0072521 | 7 | 605 | 1,84E-03 | 4,73E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,COX15,NDUFB2,PID1 |
| organophosphate metabolic | GO:0019637 | 10 | 1167 | 1,86E-03 | 4,73E-02 | ATP5D,CHCHD10,NDUFS7,IMPDH2,Q |

| | | | | | | |
|---|---|---|---|---|---|---|
| process | | | | | | PRT,COX15,DCTD,NDUFB,ME1,PID1 |
| cofactor biosynthetic process | GO:0051188 | 4 | 181 | 1,94E-03 | 4,81E-02 | QPRT,HMBS,COX15,ME1 |
| ATP synthesis coupled electron transport | GO:0042773 | 3 | 85 | 1,98E-03 | 4,81E-02 | NDUFS7,COX15,NDUFB2 |
| organophosphate biosynthetic process | GO:0090407 | 7 | 614 | 2,00E-03 | 4,81E-02 | ATP5D,CHCHD10,IMPDH2,QPRT, DCTD,ME1,PID1 |
| heme biosynthetic process | GO:0006783 | 2 | 23 | 2,05E-03 | 4,82E-02 | HMBS,COX15 |
| organelle inner membrane | GO:0019866 | 8 | 564 | 1,69E-04 | 3,30E-02 | ATP5D,LRPPRC,NDUFS7,MRPS15,COX15,ECSIT,NDUFB2,LGALS3 |

Results of GO Term enrichment analysis. The table lists GO term pathways (> 10 genes) involved in biological processes, the number of overlapping genes in the query gene list and each pathway, the size of each pathway, the nominal p value derived from a hypergeometric test and the corresponding FDR adjusted p-value.

**Supplemental table 6** qPCR Primer sequences

| Gene | Forward | Reverse |
|---|---|---|
| **36B4** | CGGGAAGGCTGTGGTGCTG | GTGAACACAAAGCCCACATTCC |
| **GUSB** | CACCAGGGACCATCCAATACC | GCAGTCCAGCGTAGTTGAAAAA |
| **B2M** | CCAGCAGAGAATGGAAAGTC | GATGCTGCTTACATGTCTCG |
| **ACBD6** | TTGGTGGGCCAGTTATTAGTTC | CCAGTGAAGTAGAGCCCTACC |
| **CHCHD10** | CTACCATGGTCTGAGCTCCC | CATTTGTGTCTTGGGTTATCTGTG |
| **CKS1B** | CGACGACGAGGAGTTTGAGTATC | TTAGGGACCAGCTTGGCTATGT |
| **COX15** | TGGAGTAACTAGGTTGACAGAG | TGGAAATTGCTGGTATCTTTGG |
| **ECSIT** | ACAGGAACCTCCATCTCTCAG | GGACTGTTCAGAGCTATGGGC |
| **FERMT3** | AGCAGATCAATCGCAAGCAG | ATCCCGTACTTGTCCAGTGT |
| **F13A1** | GTGAAGATGATGCTGTGTATCTG | ATGCCATCTTCAAACTGACC |
| **HMBS** | GGCAATGCGGCTGCAA | GGGTACCCACGCGAATCAC |
| **IFNA1** | GCCTCGCCCTTTGCTTTACT | CTGTGGGTCTCAGGGAGATCA |
| **IMPDH2** | GGGCATCATCTCCTCCAGGG | TGCTGCGCTGCAGAATTTCA |
| **LRPPRC** | GAGAGATGCCGGAATTGAGC | CTCGGACTTCTCCACCTTCT |
| **NME-1** | AAGGAGATCGGCTTGTGGTTT | CTGAGCACAGCTCGTGTAATC |
| **NME-2** | CATTGACCTGAAAGACCGAC | ATGATGTTCCTGCCAACCTG |
| **QPRT** | GGGCAGCCTTTCTTCGATG | GGAGCCCATACTTCTCCACCA |
| **TMEM134** | CAGTTCAGCATTGATGATGCC | TTCTCCAGGTTCTGGTAGCG |
| **USP49** | CTCATCCCCTTCTCCCAGAG | TTCCAGGGATAGGTCCCAAA |
| **ZWILCH** | TTGGCTGATGGTTTGAGGAC | TGGTATGAAATCACACTACTGCTC |

**Supplemental table 7** qPCR validation data

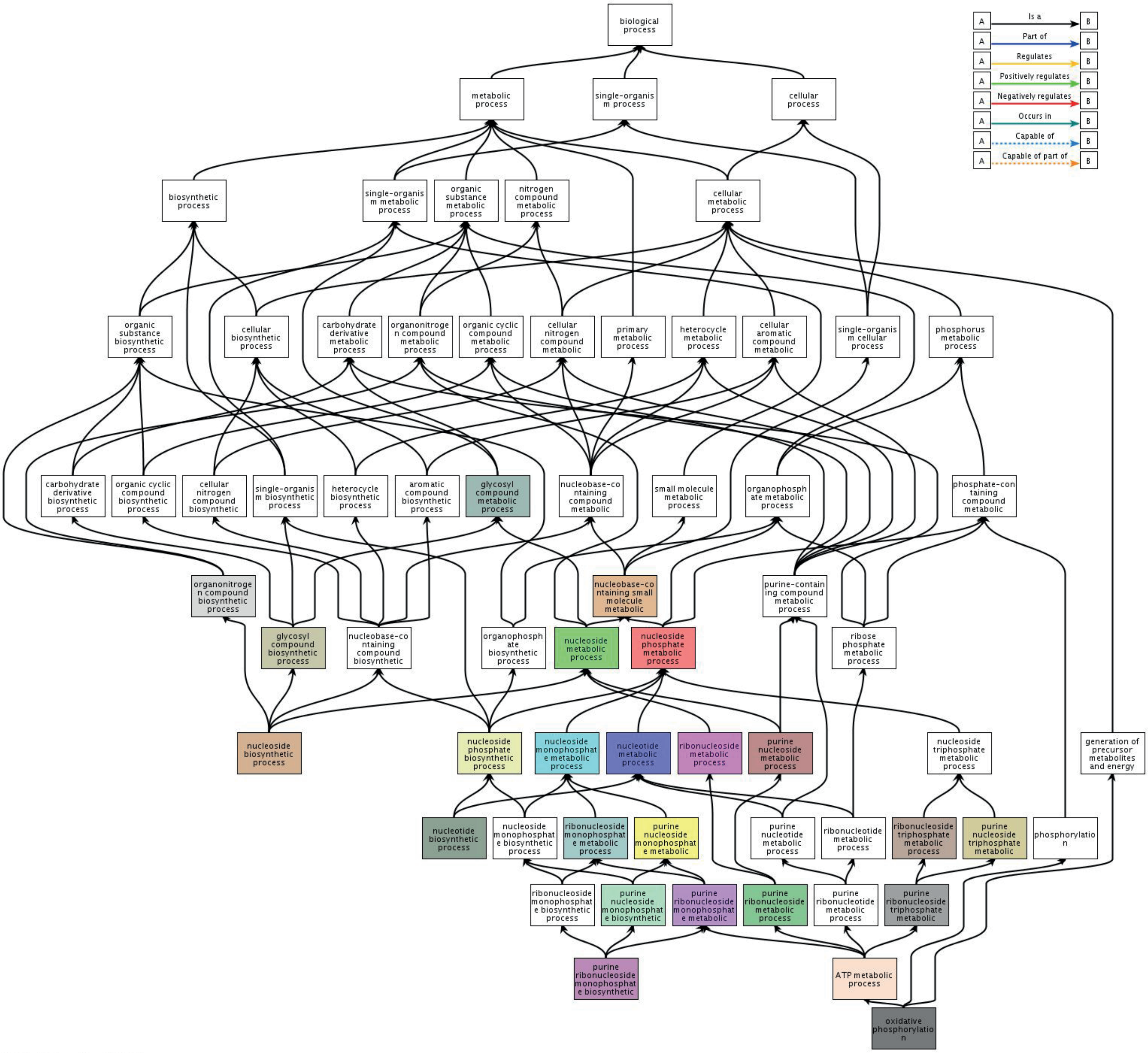
| Gene | Fold Induction obese group<br>(95% CI difference in fold induction) | P-value |
|---|---|---|
| **ACBD6** | 0.59 (-0.18 to 1.0) | 0.17 |
| **CHCHD10** | 1.13 (-0.63 to 0.37) | 0.60 |
| **CKS1B** | 0.85 (-0.19 to 0.48) | 0.38 |
| **COX15** | 1.13 (-0.97 to 0.72) | 0.76 |
| **ECSIT** | 1.35 (-0.87 to 0.16) | 0.17 |
| **FERMT3** | 1.04 (-0.44 to 0.36) | 0.85 |
| **F13A1** | 1.28 (-0.88 to 0.32) | 0.35 |
| **HMBS** | 0.62 (0.087 to 0.68) | 0.01 |
| **IFNA1** | 1.23 (-1.04 to 0.59) | 0.58 |
| **IMPDH2** | 0.64 (-0.014 to 0.74) | 0.06 |
| **LRPPRC** | 0.60 (0.14 to 0.68) | 0.005 |
| **NME-1** | 0.71 (-0.071 to 0.65) | 0.11 |
| **NME-2** | 0.85 (-0.58 to 0.89) | 0.68 |
| **QPRT** | 0.73 (-0.39 to 0.94) | 0.41 |
| **TMEM134** | 0.32 (0.079 to 1.28) | 0.028 |
| **USP49** | 0.84 (-0.28 to 0.60) | 0.47 |
| **ZWILCH** | 0.45 (0.18 to 0.92) | 0.005 |

**Supplemental table 8** Clinical characteristics of the adult cohort at risk

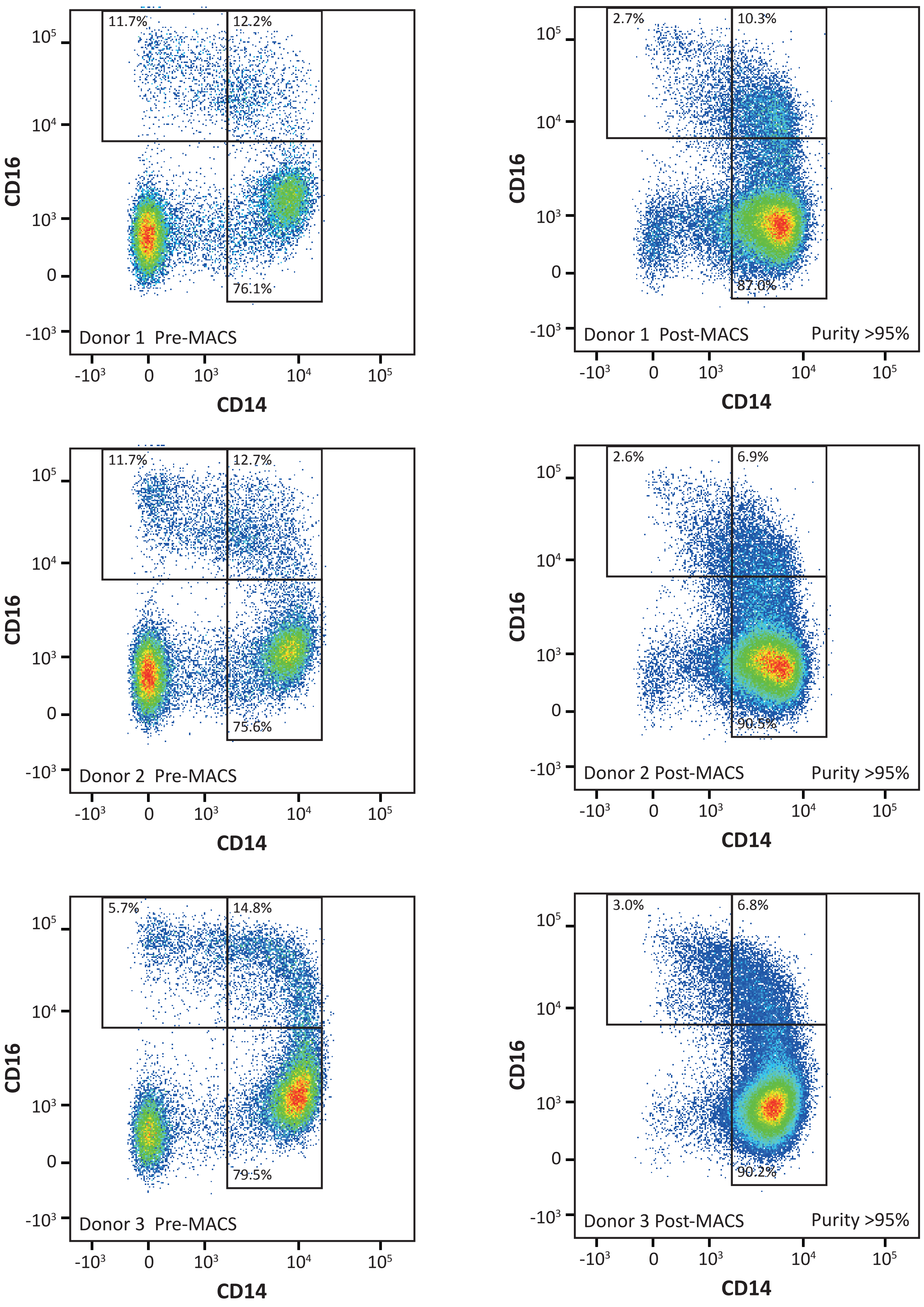
| **Variables** | |
|---|---|
| Age, years | 62.4 (10.1) |
| Male sex | 262 (74.6) |
| BMI, kg/m2 | 27.4 (4.3) |
| Obese (BMI>30) | 80 (23.3) |
| Hypertension | 229 (65.2) |
| Hypercholesterolemia | 230 (65.5) |
| Diabetes mellitus | 75 (21.4) |
| Current smoker | 71 (20.2) |
| Positive family history | 151 (43.0) |
| prior MI | 111 (31.6) |
| prior PCI | 130 (37.0) |
| prior CABG | 32 (9.1) |
| SYNTAX score* | 13 (6-22) |

Baseline characteristics of the adults with cardiovascular risk (n=351). Discrete variables are given as absolute count (%), continuous variables as mean (SD) or as median (IQR). *median (IQR).

# Supplemental figure 1 - Nodal map



# Supplemental figure 2 - Magnetic bead sorting



The monocyte subsets of 3 random patients before and after magnetic bead sorting are shown. Purity of the monocyte fraction after magnetic bead sorting was >95%.