# Supplementary Information

## A Systems Biology approach to determine cell-specific gene regulatory effects of genetic associations in multiple sclerosis

International Multiple Sclerosis Genetics Consortium*

GWAS summary statistics

GWAS genotype-level individual data

## I. SNP to Gene

### Step 1a

1. Identify independently associated SNPs
2. Select SNPs in LD (r2>0.8, 0.5 or 0.1)
3. Pull RegulomeDB full records for selected SNPs

### Step 1b

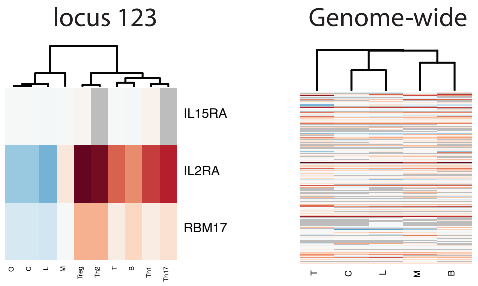
1. Aggregate RegulomeDB data into cell specific signals (T cells, monocytes, etc)
2. Aggregate RegulomeDB data into major regulatory signals (activation, represssion, etc)

### Step 2

Compute predicted regulatory effect (PRE) for each gene within associated loci

- Add all positive and negative regulatory effects for a given gene
- Weight evidence by number of experiments in ENCODE and REP

### PRE Visualization

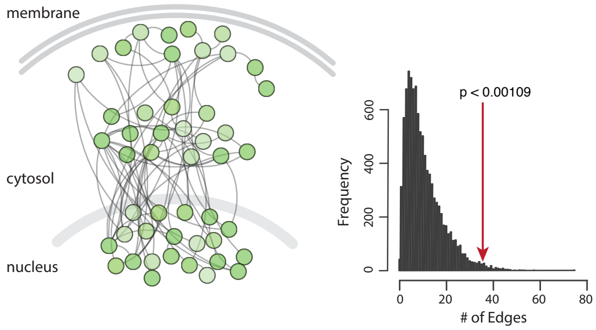


## II. Gene to Pathway

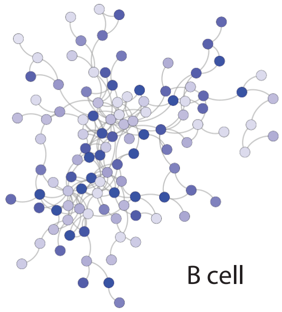
### Step 3

1. integrate cell-specific PRE with protein interaccion network (PPI)
2. create cell-specific interactomes of MS-associated genes
3. compute significance of network by permutation

### cell-specific network Visualization (population level)



### individualized cell-specific MS-risk network



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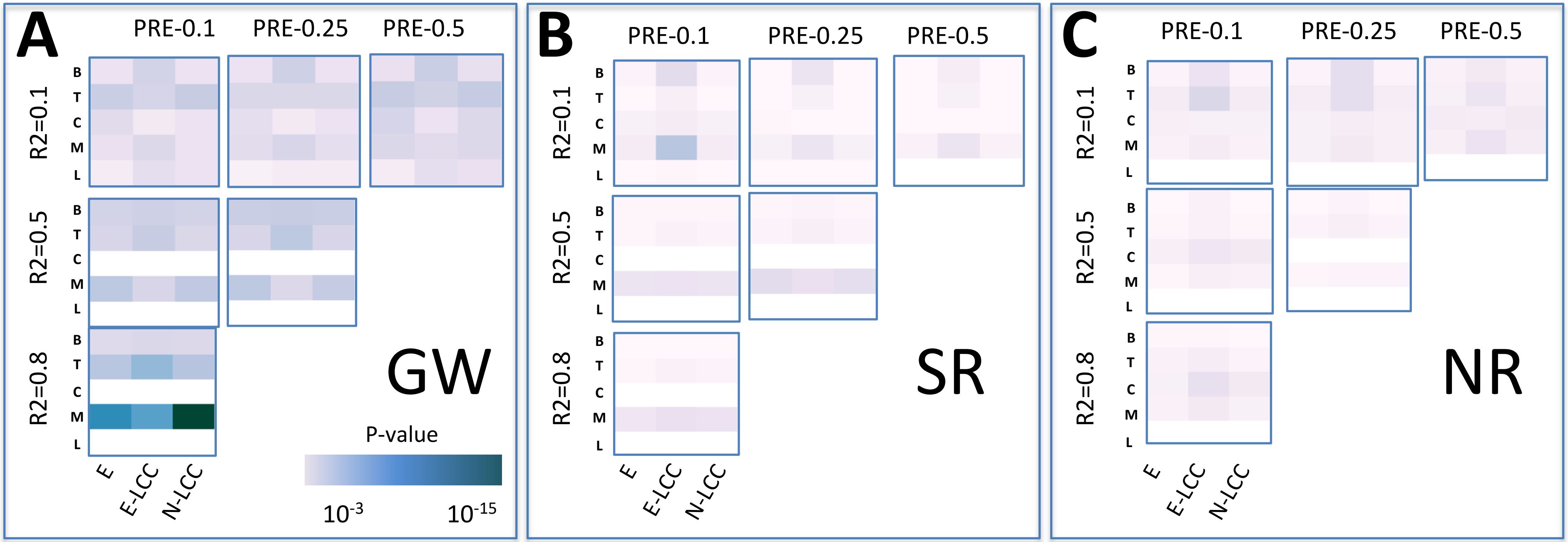
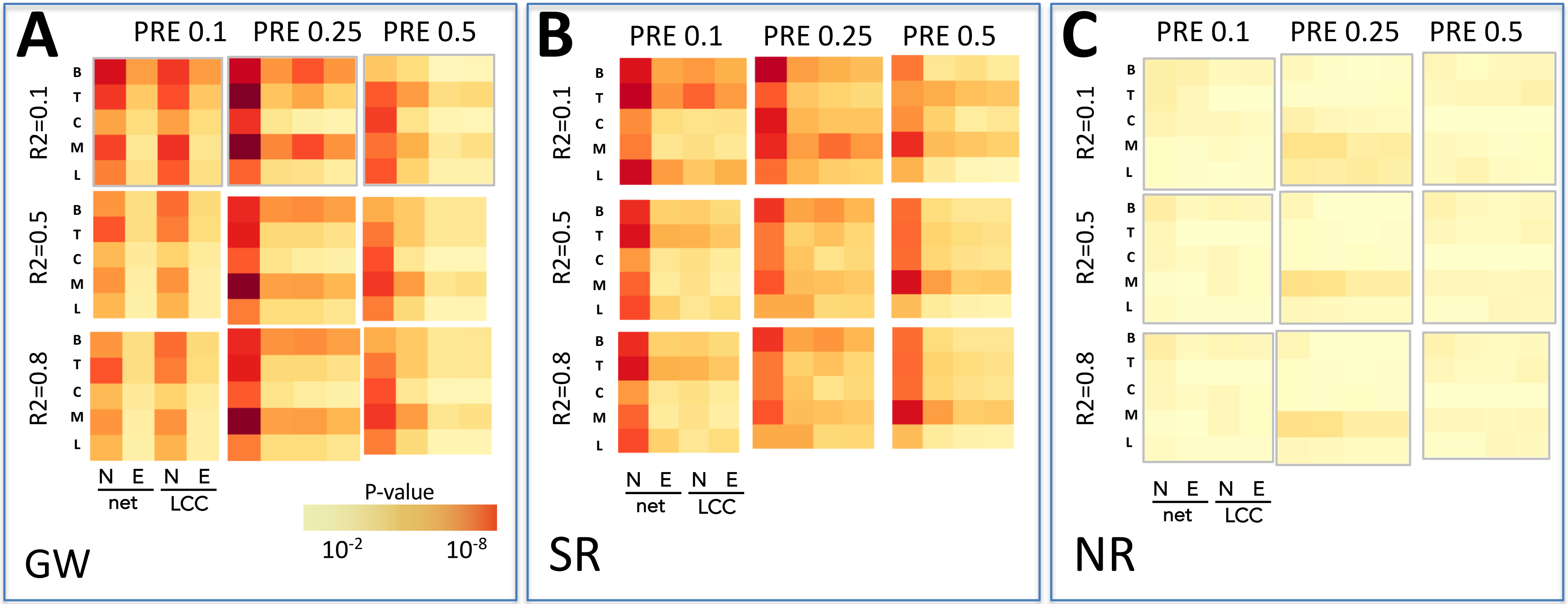
Supplementary Figure 1

**Supplementary Figure 1. Overview of our approach.** Both summary statistics and genotype-level data were incorporated into the pipeline. The algorithm consists of two stages: I. SNP to Gene (steps 1 and 2) and II. Gene to pathway (step 3). Step 1 consists in selecting individual SNPs, and those in LD. Subsequently, RegulomeDB records for all selected SNPs are parsed and organized in discrete regulatory signals (activation, repression, etc) and discrete cell type (B cell, T cell, etc) where the regulatory effect has been documented. Step 2 consists in computing an aggregate score for each nearby gene from all regulatory signals. This predicted regulatory effect (PRE) is then used to prioritize each gene within a region and construct a local protein interactome based on an established protein interaction network. Finally, the resulting network is evaluated for statistical significance and visualized both at the population and individual level.



Supplementary Figure 2

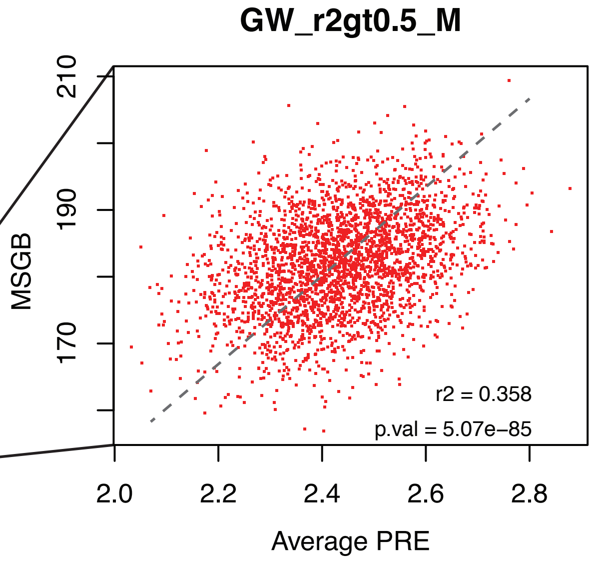
**Supplementary Figure 2. Sensitivity analysis of cell-specific sub-networks.** Basic topological measures such as the number of edges of the entire sub-network (E) and the number of nodes (N-ECC) and edges (E-LCC) in the largest connected component were computed for networks generated using different PRE thresholds (10th, 25th, and 50th percentiles), and association $r^2$ cut-offs (0.1, 0.5 and 0.8) for each cell type (B: B cells; T: T cells; C: CNS; M: monocytes; L: lung) at each level of confidence (GW, SR and NR). Each colored cell represents the significance of each tested network metric. Panel A shows that significant networks were obtained across a wide spectrum of conditions (the lower value observed at the 99th percentile is due to the small networks resulting from using that extreme PRE threshold). Panels B and C show that the significance of generated networks with SR and NR variants is much lower than with GW variants.



Supplementary Figure 3

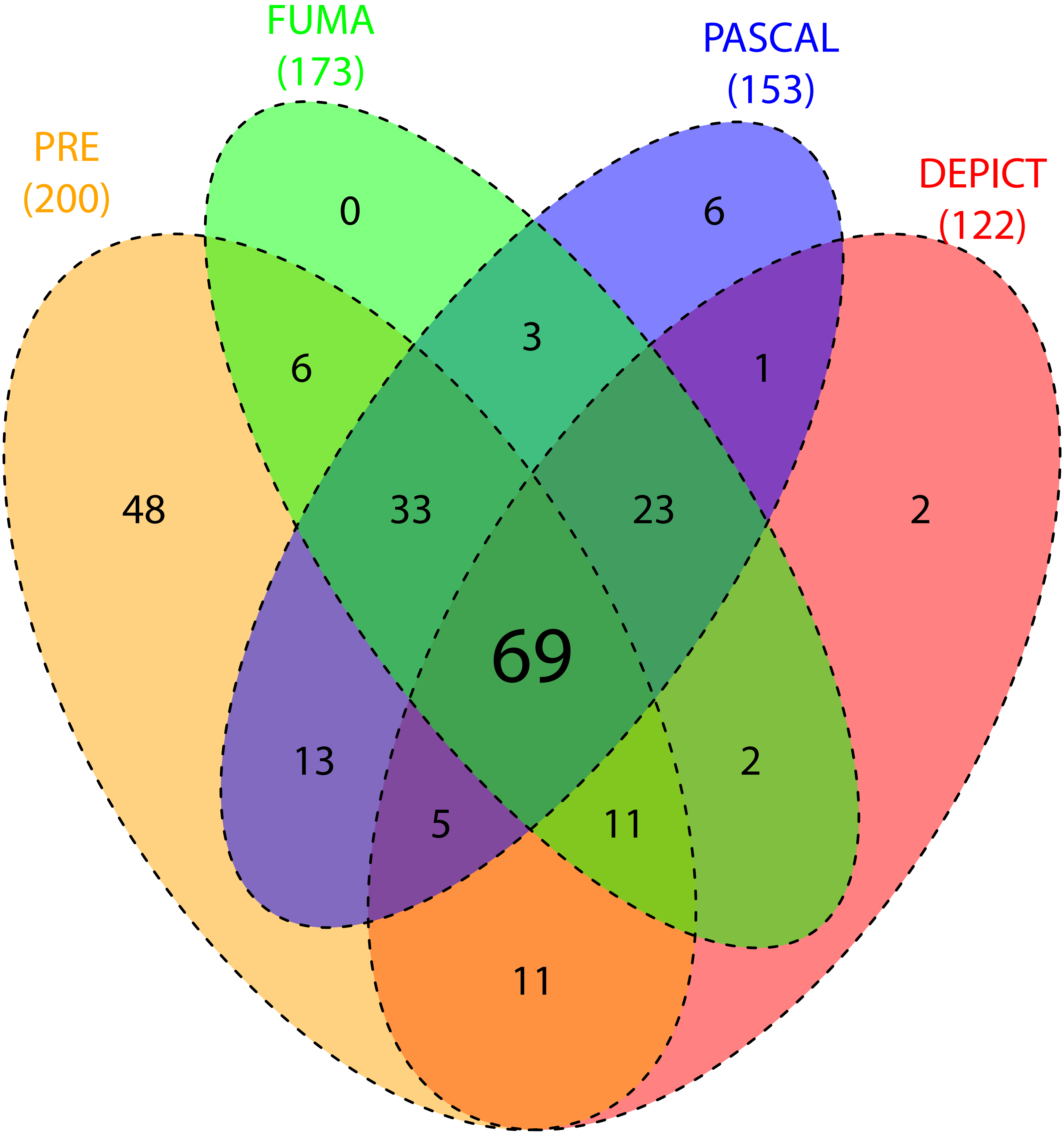
**Supplementary Figure 3. Sensitivity analysis of individual-level networks.** Basic topological measures such as the number of nodes (N) and edges (E) of the entire sub-network and the number of nodes (N-ECC) and edges (E-LCC) in the largest connected component were computed for networks generated using different PRE thresholds (10th, 25th, and 50th percentiles), and association $r^2$ cut-offs (0.1, 0.5 and 0.8) for each cell type (B: B cells; T: T cells; C: CNS; M: monocytes; L: lung) at each level of confidence (GW, SR and NR). Then, each metric was compared between cases and controls by means of T-test (1-tailed) to test the hypothesis that on average more significant networks are obtained for patients than for healthy controls. Each colored cell represents the significance of each tested network metric. Panel A shows that significant networks were obtained across a wide spectrum of conditions (the lower value observed at the 50th percentile is due to that only small networks result from using that extreme PRE threshold). Panel B shows that using variants from SR regions yields networks with significant differences between cases and controls. Panel C show that NR regions do not result in significant differences between cases and controls.

| Cell Type | Corr (r) | pval |
|---|---|---|
| B | 0.286 | $8.18\ 10^{-54}$ |
| T | 0.338 | $9.27\ 10^{-76}$ |
| C | 0.158 | $2.10\ 10^{-17}$ |
| L | 0.162 | $3.73\ 10^{-18}$ |
| M | 0.358 | $5.07\ 10^{-85}$ |



Supplementary Figure 4

**Supplementary Figure 4: Individual PREs correlate with global polygenic risk scores:** Cell-specific predicted regulatory effects (PRE) of 2,370 MS cases were correlated with their corresponding polygenic risk scores (MS genetic burden, MSGB). The table shows all correlations between MSGC and PRE for each cell type discussed in this paper. A representative scatter plot shows individual values of MSGB (Y-axis) and average PRE for monocytes (X-axis).



Supplementary Figure 5

**Supplementary Figure 5: Comparison of gene prioritization across three methods:** SNP to gene operations were computed in FUMA, DEPICT, and PASCAL and the results were compared to those obtained in this work. For 69 out of 200 loci the prioritized genes were the same across all methods. The method presented here produced a gene output for every association and shared the most genes with the other three methods (119 with FUMA, 96 with DEPICT, and 120 with PASCAL).

**Supplementary Table 1. Feature comparison with other pathway methods**

| Method | PRE | DEPICT | FUMA | PASCAL |
|---|---|---|---|---|
| SNP to gene mapping per cell/tissue type | Yes | No | Yes | No |
| Cell type/Tissue specific gene prioritization | Yes | No | Yes | No |
| Leverages SNP Regulatory information | Yes | No | Yes | No |
| Takes into account SNPs in LD | Yes | Yes | Yes | Yes |
| Requires SNP p-values as input | No | No | Yes | Yes |
| SNP filtering based on predicted functional annotations from tools | No | No | Yes | No |
| Genes assignment by proximity | No | Yes | yes | Yes |
| Needs predefined gene sets | Yes | Yes | Yes | Yes |
| computes individual regulatory burden | Yes | No | No | No |
| Enrichment analysis of prioritized genes in biological pathways | Yes | Yes | Yes | Yes |
| Default restriction based on MAF | No | Yes | Yes | Yes |

**Supplementary Table 2. Comparison of results with other pathway methods**

| Effect | PRE | Depict | Fuma |
|---|---|---|---|
| chr11:118783424 | DDX6 | NA | NA |
| chr11:14868316 | RRAS2 | NA | NA |
| chr13:100026952 | MIR548AN\|TM9SF2 | NA | NA |
| chr14:88523488 | GALC | NA | NA |
| chr16:11213951 | CLEC16A | NA | NA |
| chr16:11353879 | CLEC16A | NA | NA |
| chr1:154983036 | FLAD1 | NA | NA |
| chr1:32738415 | FAM167B\|LCK | NA | NA |
| chr2:112492986 | ANAPC1\|MERTK | NA | NA |
| chr3:100848597 | LOC152225\|SENP7\|ZPLD1 | NA | NA |
| chr3:112693983 | CD200R1 | NA | NA |
| chr3:121765368 | IQCB1 | NA | NA |
| chr3:121783015 | IQCB1 | NA | NA |
| chr5:40429250 | DAB2\|PTGER4 | NA | NA |
| chr6:119215402 | FAM184A\|MCM9 | NA | NA |
| chr6:130348257 | L3MBTL3 | NA | NA |
| chr6:14691215 | CD83\|JARID2\|NA | NA | NA |
| chr7:50328339 | C7orf72\|IKZF1 | NA | NA |
| chr8:129177769 | LINC00977\|MIR1208\|PCAT1\|POU5F1B | NA | NA |
| chr8:95851818 | INTS8 | NA | NA |
| rs10063294 | CAPSL\|IL7R | IL7R | IL7R |
| rs1014486 | IL12A\|LINC01100 | IL12A | IL12A |
| rs10191360 | CXCR4\|DARS\|THSD7B | CXCR4 | CXCR4 |
| rs10230723 | C7orf72\|IKZF1 | NA | NA |
| rs10245867 | JAZF1\|JAZF1-AS1 | JAZF1 | JAZF1 |
| rs1026916 | STAT3 | STAT3 | STAT5A\|STAT3\|PTRF |
| rs10271373 | ZC3HAV1\|ZC3HAV1L | ZC3HAV1 | ZC3HAV1L\|ZC3HAV1 |
| rs1076928 | STK38 | ETV7\|KCTD20 | ETV7\|PXT1\|KCTD20 |
| rs1077667 | C3\|TNFSF14 | TNFSF14 | TNFSF14\|C3 |
| rs10801908 | CD58 | CD58 | CD58 |
| rs1087056 | ZEB1-AS1\|ZNF438 | ZNF438 | NA |
| rs10936182 | IL12A\|LINC01100 | IL12A | NA |
| rs10936602 | LRRC31\|MYNN | NA | ACTRT3\|MYNN\|LRRC34\|LRRIQ4\|LRRC31 |
| rs10951042 | CARD11\|CHST12\|SDK1 | CARD11 | NA |
| rs10951154 | HOXA1\|NA | NA | HOXA1\|HOXA2 |
| rs11079784 | NPEPPS | NPEPPS | ITGB3\|ITGB3\|EFCAB13\|NPEPPS\|KPNB1\|TBKBP1 |
| rs11083862 | NA | NA | SAE1 |
| rs11125803 | CENPO | NCOA1 | PTRHD1\|CENPO\|ADCY3 |
| rs1112718 | HHEX\|IDE | HHEX | IDE\|KIF11\|HHEX |
| rs11161550 | BCL10\|C1orf52\|LOC646626 | BCL10 | NA |
| rs11231749 | PLCB3\|VEGFB | CCDC88B\|RPS6KA4\|GPR137 | NUDT22\|DNAJC4\|VEGFB\|FKBP2\|PPP1R14B\|PLCB3\|BAD\|GPR137\|KCNK4\|TEX40\|ESRRA\|TRMT112\|PRDX5\|CCDC88B\|RPS6KA4 |
| rs11256593 | IL15RA\|IL2RA | IL2RA | RBM17 |
| rs11578655 | DPH6\|SLC30A7 | NA | EXTL2\|SLC30A7\|DPH5\|NA |
| rs11749040 | DAB2\|PTGER4 | PTGER4 | NA |
| rs1177228 | KIAA1841\|PUS10 | PUS10 | PUS10\|PEX13\|KIAA1841 |
| rs11809700 | EVI5\|FAM69A | NA | RPL5\|FAM69A\|GFI1\|EVI5 |
| rs11852059 | FRMD6\|GNG2 | GNG2 | GNG2 |
| rs11899404 | MIR4262\|NA\|TRIB2 | NA | NA |
| rs11919880 | CCR4\|GLB1 | CCR4 | TRIM71\|CCR4 |
| rs12133753 | EVI5\|FAM69A | TGFBR3 | TGFBR3 |
| rs12147246 | TRAF3 | TRAF3 | TRAF3 |
| rs12211604 | RREB1 | NA | RREB1 |
| rs12365699 | DDX6 | CXCR5 | DDX6\|CXCR5 |
| rs12434551 | ZFP36L1 | ZFP36L1 | ZFP36L1 |
| rs12478539 | HAAO\|ZFP36L2 | NA | NA |
| rs1250551 | ZMIZ1 | ZMIZ1 | ZMIZ1 |
| rs12588969 | TRAF3 | TRAF3 | TRAF3 |
| rs12609500 | SMARCA4 | NA | SMARCA4 |
| rs12614091 | CD28\|CTLA4\|RAPH1 | CD28 | CD28 |
| rs12622670 | FBXO48\|PLEK | PLEK | PLEK |
| rs12722559 | IL15RA\|IL2RA | NA | IL2RA\|RBM17 |
| rs12832171 | TNFRSF1A\|U47924.1 | NA | NA |
| rs12925972 | DYNLRB2\|WWOX | NA | WWOX |
| rs12971909 | HDGFRP2\|NA\|UBXN6 | NA | UBXN6\|HDGFL2 |
| rs13066789 | LPP | NA | LPP |
| rs13136820 | CHRNA9\|RHOH | NA | NA |
| rs1323292 | RGS1 | RGS1 | RGS1 |
| rs13327021 | CMC1\|EOMES | EOMES | EOMES |
| rs13385171 | MIR4778\|SPRED2 | NA | SPRED2 |
| rs13414105 | LBH | NA | NA |
| rs1365120 | PRR5L | PRR5L | PRR5L |
| rs137955 | ENTHD1\|GRAP2 | ENTHD1\|GRAP2 | ENTHD1\|GRAP2 |
| rs1399180 | GATA3\|GATA3-AS1\|TAF3 | GATA3 | GATA3 |
| rs140522 | ODF3B\|SCO2 | SCO2 | NCAPH2\|SCO2\|TYMP\|ODF3B |
| rs1415069 | EVI5\|FAM69A | EVI5\|FAM69A | RPL5\|FAM69A |
| rs1465697 | SLC6A16 | CD37\|DKKL1 | SLC6A16\|CD37\|TEAD2\|DKKL1\|CCDC155\|PTH2\|GFY |
| rs17051321 | NDNF\|TNIP3 | TNIP3 | TNIP3 |
| rs1738074 | RSPH3\|TAGAP | TAGAP | RSPH3\|TAGAP |
| rs17724508 | DYNLRB2\|WWOX | NA | NA |
| rs17741873 | CAMK2G | PLAU | CAMK2G\|PLAU\|C10orf55 |
| rs17780048 | IL20RA\|IL22RA2 | TNFAIP3 | TNFAIP3 |
| rs1800693 | TNFRSF1A\|U47924.1 | NA | PLEKHG6\|TNFRSF1A\|SCNN1A |
| rs1801133 | CLCN6 | NA | C1orf167\|MTHFR |
| rs2084007 | JADE2\|TCF7 | JADE2 | JADE2 |
| rs2150879 | VMP1 | VMP1 | VMP1\|TUBD1\|RPS6KB1\|NA\|RNFT1 |
| rs2248137 | BCAS1 | NA | CYP24A1 |
| rs2269434 | MADD | SPI1\|DDB2\|NR1H3\|ACP2 | DDB2\|ACP2\|NR1H3\|MADD\|MYBPC3\|SPI1\|RAPSN |
| rs2286974 | CLEC16A | NA | CIITA\|DEXI\|CLEC16A |
| rs2289746 | CBLB | CBLB | CBLB |
| rs2317231 | CD5L\|FCRL1\|FCRL3 | FCRL1\|FCRL3 | FCRL3\|FCRL2\|FCRL1 |
| rs2327586 | AHI1\|MYB | MYB | MYB |
| rs2331964 | IQCB1 | IQCB1 | FBXO40\|HCLS1\|IQCB1\|EAF2 |
| rs2364485 | TNFRSF1A\|U47924.1 | NA | LTBR |
| rs244656 | JADE2\|TCF7 | TCF7 | TCF7 |
| rs2469434 | CD226\|NA | CD226 | DOK6\|CD226 |
| rs249677 | NDFIP1 | NDFIP1 | NDFIP1 |
| rs2546890 | LOC285626 | IL12B | IL12B |
| rs2585447 | BCAS1 | NA | CYP24A1 |
| rs2590438 | LPP | BCL6 | NA |
| rs2705616 | AFF1\|LOC100506746 | AFF1 | C4orf36\|AFF1 |
| rs2726479 | PPA2 | TET2 | TET2\|PPA2 |
| rs2836438 | ERG | TMPRSS3\|ERG | ERG |
| rs28703878 | PKIA | PKIA | NA |
| rs28834106 | SMARCA4 | NA | KEAP1 |
| rs2986736 | TNFRSF25 | TNFRSF25 | ESPN\|TNFRSF25\|PLEKHG5 |
| rs3184504 | HECTD4 | SH2B3\|TRAFD1 | SH2B3\|ATXN2\|BRAP\|ACAD10\|NA\|ALDH2\|MAPKAPK5\|NAA25\|TRAFD1\|HECTD4\|RPL6\|PTPN11 |
| rs32658 | TNFAIP8 | TNFAIP8 | TNFAIP8 |
| rs34026809 | DDX6 | CXCR5 | ARCN1\|PHLDB1\|TREH |
| rs34536443 | SMARCA4 | NA | ZGLP1\|FDX1L\|NA\|NA\|RAVER1\|TYK2\|CDC37\|PDE4A |
| rs34681760 | PAPD7 | NA | PAPD7 |
| rs34695601 | BATF\|FLVCR2 | BATF | BATF |
| rs34723276 | DPH5\|SLC30A7 | NA | NA |
| rs34947566 | CLEC16A | RMI2\|CLEC16A | RMI2\|TNP2\|PRM3\|PRM2\|PRM1\|LOC400499 |
| rs35218683 | IFITM3 | IFITM3 | NA |
| rs354033 | ZNF746 | ZNF746 | ZNF746 |
| rs35486093 | BCL10\|C1orf52\|LOC646626 | BCL10 | C1orf52\|BCL10 |
| rs35540610 | SP110\|SP140 | SP140\|SP110 | SP110\|SP140 |
| rs35703946 | IRF8\|LINC01082 | IRF8 | NA |
| rs3737798 | CD48\|VANGL2 | NA | VANGL2 |
| rs3809627 | GDPD3 | TBX6\|PPP4C\|YPEL3 | ALDOA\|PPP4C\|TBX6\|YPEL3\|GDPD3\|MAPK3 |
| rs3923387 | PLEC | PARP10\|GRINA\|PLEC | PLEC\|PARP10\|GRINA\|SPATC1 |
| rs405343 | SOX8\|SSTR5-AS1 | NA | NA |
| rs4262739 | ETS1 | ETS1 | ETS1 |
| rs4325907 | LOC152225\|SENP7\|ZPLD1 | ZPLD1 | NA |
| rs438613 | CMC1\|EOMES | NA | NA |
| rs4409785 | FAM76B\|SESN3 | NA | NA |
| rs4728142 | IRF5\|KCP | IRF5 | IRF5 |
| rs4796224 | GGNBP2 | NA | ZNHIT3\|MYO19\|PIGW\|GGNBP2\|DHRS11\|MRM1 |
| rs4808760 | MAST3 | IFI30\|MAST3 | IL12RB1\|MAST3\|PIK3R2\|PIK3R2\|IFI30\|MPV17L2\|RAB3A\|PDE4C |
| rs4812772 | TOX2 | TOX2 | TOX2 |
| rs4820955 | LIMK2 | NA | NA |
| rs483180 | PHGDH | NA | PHGDH |
| rs4896153 | AHI1\|MYB | NA | AHI1 |
| rs4939490 | CD5\|CD6 | CD6 | CD6 |
| rs4940730 | MALT1 | ALPK2 | ALPK2 |
| rs531612 | SART1 | CTSW\|C11orf68 | FIBP\|CCDC85B\|FOSL1\|C11orf68\|DRAP1\|SART1\|EIF1AD\|BANF1\|CST6\|CATSPER1 |
| rs55858457 | CARD11\|CHST12\|SDK1 | NA | CHST12 |
| rs56095240 | FAM76B\|SESN3 | NA | NA |
| rs57116599 | ANAPC1\|MERTK | MERTK | MERTK\|TMEM87B |
| rs5756405 | CSF2RB\|NCF4 | CSF2RB | CSF2RB\|NCF4 |
| rs58166386 | EPS15L1 | NA | EPS15L1\|CALR3\|NA\|C19orf44 |
| rs58394161 | EVI5\|FAM69A | NA | C1orf146\|GLMN\|GFI1\|EVI5 |
| rs59655222 | C1orf106\|KIF21B | KIF21B | C1orf106\|KIF21B\|CACNA1S |
| rs6020055 | PTPN1 | SLC9A8 | SLC9A8 |
| rs6032662 | CD40\|NCOA5\|SLC12A5 | CD40\|NCOA5 | SLC12A5\|NCOA5\|CD40 |
| rs60600003 | ELMO1 | ELMO1 | ELMO1 |
| rs6072343 | NA | NA | TOP1\|PLCG1\|ZHX3\|LPIN3\|EMILIN3 |
| rs61708525 | PLXNC1 | PLXNC1 | PLXNC1 |
| rs61863928 | ADO\|ZNF365 | ADO | NA |
| rs61884005 | RRAS2 | RRAS2\|PDE3B | RRAS2\|COPB1\|PSMA1\|PSMA1 |
| rs62013236 | CTSH | CTSH | CTSH\|RASGRF1 |
| rs62420820 | IL20RA\|IL22RA2 | IL22RA2 | NA |
| rs631204 | IL20RA\|IL22RA2 | NA | NA |
| rs6427540 | CD48\|VANGL2 | SLAMF1 | SLAMF1\|CD48 |
| rs6496663 | IQGAP1 | IQGAP1 | GABARAPL3\|ZNF774\|IQGAP1 |
| rs6533052 | UBE2D3 | SLC9B2\|UBE2D3 | MANBA\|UBE2D3\|CISD2\|SLC9B1\|SLC9B2 |
| rs6564681 | DYNLRB2\|WWOX | NA | NA |
| rs6589706 | DDX6 | CXCR5 | CXCR5 |
| rs6589939 | UBASH3B | UBASH3B | UBASH3B |
| rs6670198 | TNFRSF14\|UBE2D3 | TNFRSF14\|C1orf93 | TNFRSF14\|FAM213B\|MMEL1\|TTC34 |
| rs6672420 | RUNX3\|SYF2 | RUNX3 | RUNX3 |
| rs67111717 | LMAN2 | RGS14 | LMAN2\|RGS14\|SLC34A1 |
| rs6738544 | NA\|STAT4 | STAT4 | STAT4 |
| rs6742 | ZGPAT | NA | ZGPAT\|NA\|LIME1\|NA\|SLC2A4RG\|ZBTB46 |
| rs6789653 | ZBTB38 | RASA2\|ZBTB38 | NA |

| | | | |
|---|---|---|---|
| rs67934705 | NA | NA | NA |
| rs6837324 | TEC\|TXK | TXK\|TEC | TXK\|TEC |
| rs6911131 | FUCA2\|LOC285740 | PHACTR2 | PHACTR2 |
| rs6990534 | LINC00977\|MIR1208\|PCAT1\|POU5F1B | PVT1 | NA |
| rs701006 | TSFM | CYP27B1\|MARCH9\|METTL21B\|B4GALNT1\|OS9 | DTX3\|ARHGEF25\|SLC26A10\|B4GALNT1\|OS9\|AGAP2\|AGAP2-AS1\|TSPAN31\|CDK4\|MARCH9\|CYP27B1\|METTL1\|METTL21B\|NA\|TSFM\|AVIL\|CTDSP2 |
| rs719316 | ATXN1 | ATXN1 | ATXN1 |
| rs7222450 | MAP3K14 | NA | NA |
| rs7260482 | PVR | PVR | IGSF23\|PVR\|CEACAM19 |
| rs72922276 | JAK1 | JAK1 | RAVER2\|JAK1 |
| rs72928038 | BACH2 | BACH2 | BACH2 |
| rs72989863 | MARCH1 | MARCH1 | MARCH1 |
| rs73414214 | SYPL1 | NA | SYPL1 |
| rs735542 | LINC00977\|MIR1208\|PCAT1\|POU5F1B | NA | NA |
| rs760517 | CSF2RB\|NCF4 | NCF4 | NCF4 |
| rs7731626 | ANKRD55\|NA | NA | ANKRD55 |
| rs7855251 | NANS | NA | TRIM14 |
| rs7975763 | MPHOSPH9 | RILPL2\|PITPNM2 | ABCB9\|OGFOD2\|ARL6IP4\|PITPNM2\|MPHOSPH9\|C12orf65\|CDK2AP1\|SBNO1\|SETD8\|RILPL2 |
| rs7977720 | CLEC2D\|CLECL1 | CLECL1\|CLEC2D | CLEC2D\|CLECL1 |
| rs802730 | NA | NA | PTPRK |
| rs8062446 | NLRC5 | NLRC5 | NLRC5 |
| rs883871 | GSDMB | NA | THRA\|NR1D1 |
| rs9308424 | BATF3\|UBE2D3 | BATF3 | BATF3 |
| rs9568402 | DLEU7\|ST13P4 | NA | DLEU1 |
| rs9591325 | DLEU7\|ST13P4 | NA | DLEU1 |
| rs9610458 | MAPK1 | PPM1F | YPEL1\|MAPK1\|PPM1F\|TOP3B |
| rs962052 | NA\|RBM43\|RND3 | NA | NA |
| rs9808753 | IL10RB | IFNGR2 | IFNGR2\|TMEM50B |
| rs983494 | CD48\|VANGL2 | SLAMF7 | SLAMF7 |
| rs9843355 | ARHGAP31 | CD80\|ARHGAP31\|POGLUT1\|TMEM39A | ARHGAP31\|TMEM39A\|POGLUT1\|TIMMDC1\|CD80 |
| rs9863496 | KCNH8\|SATB1 | SATB1 | NA |
| rs9878602 | FOXP1 | FOXP1 | FOXP1 |
| rs9900529 | GRB2 | GRB2\|GGA3\|MIF4GD\|SLC25A19\|TSEN54 | SLC25A19\|GRB2 |
| rs9909593 | GSDMB | GSDMB\|IKZF3\|ORMDL3 | GRB7\|IKZF3\|ZPBP2\|GSDMB\|ORMDL3\|LRRC3C |
| rs9955954 | MALT1 | MALT1 | MALT1 |
| rs9992763 | LEF1\|RPL34-AS1 | LEF1 | LEF1 |

**Supplementary Table 3. RegulomeDB content**

| Data Type | Types | Features |
|---|---|---|
| Transcription Factor ChIP-seq (ENCODE) | 495 conditions/cell lines | 7,721,822 |
| Transcription Factor ChIP-seq (non-ENCODE) | 32 conditions/cell lines | 397,534 |
| Transcription Factor ChIP-exo | 1 condition | 35,161 |
| Histone Modifications | 284 conditions/cell lines/marks | 23,055,241 |
| Dnase I hypersensitive sites | 114 conditions/cell lines | 20,710,098 |
| FAIRE sites | 25 conditions/cell lines | 4,816,196 |
| Dnase I footprints | 50 cell lines | 128,266,803 |
| Predicted binding (PWMs) | 1158 motifs | 239,713,973 |
| eQTLs | 142,945 SNPs | 142,945 |
| dsQTLs | 6069 SNPs | 6,069 |
| Manual annotations | 6 genomic regions | 282 |
| VISTA enhancers | 1448 enhancers | 1,325 |
| Validated SNPs affecting binding | 855 SNPs | 855 |

| **Key** | |
|---|---|
| Data Type | Type of regulatory feature hosted by RegulomeDB |
| Types | Detailed content for each data type |
| Features | Total amount of regulatory features for data type |

**Supplementary Table 4. ENCODE cell types used in this analysis**

| cell_Line_name | ENCODE_Tier | Description | Tissue | Karyotype |
|---|---|---|---|---|
| GM13976 | 3 | lymphoblastoid cell line, clinically normal; monozygotic twin sister with Cornelia De Lange syndrome is GM13977 | blood | normal |
| GM12878 | 1 | B-lymphocyte, lymphoblastoid, International HapMap Project - CEPH/Utah - European Caucasion, Epstein-Barr Virus | blood | normal |
| CD20+ | 2 | B cells from donors RO01778 and RO01794, newly promoted to tier 2: not in 2011 analysis | blood | normal |
| CD20+_RO01778 | 2 | B cells, caucasian, draw number 1, newly promoted to tier 2: not in 2011 analysis | blood | normal |
| CD20+_RO01794 | 2 | B cells, African American, draw number 1, newly promoted to tier 2: not in 2011 analysis | blood | normal |
| GM10248 | 3 | lymphoblastoid cell line, Clinically normal; 4 paternal cousins have Cornelia de Lange syndrome; 46,XY, t(3;22)(q25.3;p12) | blood | normal |
| GM12878-XiMat | 3 | B-lymphocyte, lymphoblastoid, cloned for maternal X inactivation, International HapMap Project, CEPH/Utah, Epstein-Barr Virus | blood | normal |
| GM12871 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed. | blood | normal |
| GM12872 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM18507 | 3 | lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM06990 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM10847 | 3 | lymphoblastoid, International HapMap Project, CEPH/Utah, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12801 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12812 | 3 | B-Lymphocyte, Lymphoblastoid, International HapMap Project, CEPH/Utah, Treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12813 | 3 | B-Lymphocyte, Lymphoblastoid, International HapMap Project, CEPH/Utah, Treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12864 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12865 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12866 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed. | blood | normal |
| GM12867 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12868 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed. | blood | normal |
| GM12869 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed. | blood | normal |
| GM12870 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed. | blood | normal |
| GM12873 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12874 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12875 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1459, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12891 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1463, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM12892 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, CEPH/Utah pedigree 1463, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM15510 | 3 | lymphoblastoid NIGMS Human Genetic Cell Repository, DNA Polymorphism Discovery Resource Collection, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM18505 | 3 | lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM18526 | 3 | lymphoblastoid, International HapMap Project, Han Chinese in Beijing, China, treatment: Epstein-Barr Virus transformed | blood | normal |
| PBMC | 3 | peripheral blood mononuclear cells | blood | normal |
| GM19099 | 3 | lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM19193 | 3 | lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM19238 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM18951 | 3 | lymphoblastoid, International HapMap Project, Japanese in Tokyo, Japan, treatment: Epstein-Barr Virus transformed | blood | normal |
| H0287 | 3 | EBV-transformed lymphoblastoid cell line (LCL) was derived from peripheral blood donated by a normal healthy male. | blood | normal |
| Lymphoblastoid | 3 | parental cell type to lymphoblastoid cell lines | blood | normal |
| Lymphoblastoid_cell_line | 3 | parental cell type to lymphoblastoid cell lines | blood | normal |
| H0287 | 3 | EBV-transformed lymphoblastoid cell line (LCL) was derived from peripheral blood donated by a normal healthy male. | blood | normal |
| GM19239 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| GM19240 | 3 | B-lymphocyte, lymphoblastoid, International HapMap Project, Yoruba in Ibadan, Nigera, treatment: Epstein-Barr Virus transformed | blood | normal |
| H0287 | 3 | EBV-transformed lymphoblastoid cell line (LCL) was derived from peripheral blood donated by a normal healthy male. | blood | normal |
| Frontal_cortex_OC | 3 | Primary ventromedial prefrontal cortex, from KPBBB donor IDs 673 (Rep B1) and 913 (Rep B2) | frontal cortex | normal |
| H1-neurons | 2 | neurons derived from H1 embryonic stem cells, newly promoted to tier 2: not in 2011 analysis | neurons | normal |
| HAc | 3 | astrocytes-cerebellar | cerebellar | normal |
| NH-A | 3 | astrocytes (also called Astrocy) | brain | normal |
| Pons_OC | 3 | Primary frozen pons mid-brain tissue from NICHD donor IDs 1104 (Rep B1), 602 (Rep B2), 1442 (Rep B3) | pons mid-brain | normal |
| BC_Brain_H11058N | 3 | brain, donor H11058N, age 66, Asian, DNA extract | brain | normal |
| Cerebellum_OC | 3 | Primary frozen cerebellum tissue from NICHD donor IDs 1104 (Rep B1), 602 (Rep B2), 1442 (Rep B3), all Caucasian | cerebellum | normal |
| Cerebrum_frontal_OC | 3 | Primary frozen frontal cerebrum tissue from NICHD donor IDs 1104 (Rep B1), 602 (Rep B2), 1442 (Rep B3), all Caucasian | frontal cerebrum | normal |
| HA-sp | 3 | astrocytes spinal cord | spinal cord | normal |
| HA-h | 3 | astrocytes-hippocampal | brain hippocampus | normal |
| IMR90 | 2 | fetal lung fibroblasts, newly promoted to tier 2: not in 2011 analysis | lung | normal |
| AG04450 | 3 | fetal lung fibroblast | lung | normal |
| BC_Lung_01-11002 | 3 | lung, donor 01-11002, age 83, caucasian, DNA and RNA extract | lung | normal |
| BC_Lung_H12817N | 3 | lung, donor H12817N, age 71, caucasian, DNA and RNA extract | lung | normal |
| HPF | 3 | pulmonary fibroblasts isolated from lung tissue | lung | normal |
| Lung_BC | 3 | lung, parental cell type to donors 01-11002 and H12817N | lung | normal |
| Lung_OC | 3 | Primary frozen lung tissue from NICHD donor IDs 1104 (Rep B1 DNase), 602 (Rep B2 DNase), 1442 (Rep B3 DNase) and CF Center donor IDs DD006I (Rep B1 FAIRE) and DD007I (Rep B2 FAIRE) | Lung | normal |
| NHLF | 3 | lung fibroblasts | lung | normal |
| WI-38 | 3 | embryonic lung fibroblast cells, hTERT immortalized, includes Raf1 construct | embryonic lung | normal |
| FibroP_AG08396 | 3 | fibroblasts taken from individuals with Parkinson's disease | lung fibroblast | normal |
| hMNC-CB | 3 | Mononuclear Cells (umbilical cord blood-single donor) from two individuals, hMNC-CB_9111701.6 and hMNC-CB_8072802.6 | blood | normal |
| hMNC-CB_8072802.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |

|  |  |  |  |  |
|---|---|---|---|---|
| Monocytes-CD14+ | 2 | Monocytes-CD14+ are CD14-positive cells from human leukapheresis production, from donor RO 01746 (draw 1 ID is RO 01746, draw 2 ID is RO 01826), newly promoted to tier 2: not in 2011 analysis | monocytes | normal |
| Monocytes-CD14+_RO01746 | 2 | Monocytes-CD14+ are CD14-positive cells from human leukapheresis production, from donor RO 01746 (draw 1 ID is RO 01746, draw 2 ID is RO 01826), Monocytes-CD14+_RO01746 and Monocytes-CD14+_RO01826 are being used as replicates, newly promoted to tier 2: not in 2011 analysis | monocytes | normal |
| Monocytes-CD14+_RO01826 | 2 | Monocytes-CD14+ are CD14-positive cells from human leukapheresis production, Monocytes-CD14+_RO01826 is a second draw being used as a replicate for Monocytes-CD14+_RO01746, newly promoted to tier 2: not in 2011 analysis | monocytes | normal |
| GC_B_cell | 3 | Germinal center B cells (CD77+) isolated from de-identified tonsillectomy | tonsil | normal |
| BC_Stomach_H12817N | 3 | stomach, donor H12817N, age 71, caucasian, DNA and RNA extract | stomach | normal |
| Endometrium_OC | 3 | Endometrium isolated from uterine lining | endometrium | normal |
| Fibrobl_GM03348 | 3 | skin fibroblast | skin | normal |
| FibroP | 3 | fibroblasts taken from individuals with Parkinson's disease, AG20443, AG08395 and AG08396 were pooled for this sample | skin | normal |
| GM04503 | 3 | adult twin pair fibroblasts, monozygotic twin of GM04504 | skin | normal |
| GM04504 | 3 | adult twin pair fibroblasts, monozygotic twin of GM04503, 13% of the cells examined show random chromosome loss | skin | normal |
| HFF-Myc | 3 | foreskin fibroblast cells expressing canine cMyc | foreskin | normal |
| HGF | 3 | gingival fibroblasts | gingiva | normal |
| HIPEpiC | 3 | iris pigment epithelial cells | epithelium | normal |
| HWP | 3 | Undifferentiated White Preadipocytes from two individuals, HWP_0092205 and HWP_8120201.5, subcutaneous adipose tissue from abdomen / upper arm | adipose | normal |
| HWP_0092205 | 3 | Undifferentiated White Preadipocytes from abdomen | subcutaneous adipose tissue | normal |
| Melano | 3 | epidermal melanocytes | skin | normal |
| FibroP_AG20443 | 3 | fibroblasts taken from individuals with Parkinson's disease | skin fibroblast | normal |
| HFL11W | 3 | fetal liver 11 weeks, consented fetal liver samples were isolated from legally aborted fetuses at 11 weeks gestation | liver | normal |
| HFL24W | 3 | fetal liver 24 weeks, consented fetal liver samples were isolated from legally aborted fetuses at 24 weeks gestation | liver | normal |
| HHSEC | 3 | hepatic sinusoidal endothelial cells | liver | normal |
| iPS_CWRU1 | 3 | iPS cells derived from MSC658 fibroblast | induced pluripotent cell (iPS) | normal |
| HMVEC-LBl | 3 | blood microvascular endothelial cells, lung-derived | blood vessel | normal |
| HMVEC-LLy | 3 | lymphatic microvascular endothelial cells, lung-derived | blood vessel | normal |
| TBEC | 3 | trachea and bronchial epithelial cells from frush lung tissue provided by National Disease Research Interchange, passage 2 primary, non-immortalized cells, donor was 21 years old | epithelium | normal |
| BC_Testis_N30 | 3 | testis, donor N30, age 41, Asian, DNA extract | testis | normal |
| HMEC | 3 | mammary epithelial cells | breast | normal |
| HMEpC | 3 | Mammary Epithelial Cells (placeholder, waiting on second lot/donor from PromoCell) | mammary gland | normal |
| HMEpC_6022801.3 | 3 | Mammary Epithelial Cells | mammary gland | normal |
| Myometr | 3 | myometrial cells | myometrium | normal |
| HMF | 3 | mammary fibroblasts | mammary | normal |
| PBMC | 3 | peripheral blood mononuclear cells | blood | normal |
| HBVP | 3 | brain vascular pericytes | blood vessel | normal |
| BC_Bladder_01-11002 | 3 | urinary bladder, donor 01-11002, age 83, caucasian, DNA extract | urinary bladder | normal |
| BC_Uterus_BN0765 | 3 | uterus, donor BN0765, age 44, Asian, DNA extract | uterus | normal |
| BJ | 3 | skin fibroblast, "The line was established from skin taken from normal foreskin." - ATCC. (PMID: 9916803) | skin | normal |
| HAEpiC | 3 | amniotic epithelial cells | epithelium | normal |
| BC_Leukocyte_UHN00204 | 3 | peripheral blood mononuclear cell, donor UHN00204, age 54, caucasian, DNA extract | blood | normal |
| hMNC-CB_9111701.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |
| hMNC-PB | 3 | Mononuclear Cells (peripheral blood-single donor) from two individuals, hMNC-PB_0022330.9 and hMNC-PB_0082430.9 | blood | normal |
| hMNC-PB_0022330.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| hMNC-PB_0082430.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| Naive_B_cell | 3 | Naive B cells (IgD+) isolated from de-identified tonsillectomy | tonsil | normal |
| HBMEC | 3 | brain microvascular endothelial cells | blood vessel | normal |
| HBVSMC | 3 | brain vascular smooth muscle cells. | blood vessel | normal |
| HCPEpiC | 3 | choroid plexus epithelial cells | epithelium | normal |
| BC_Leukocyte_UHN00204 | 3 | peripheral blood mononuclear cell, donor UHN00204, age 54, caucasian, DNA extract | blood | normal |
| hMNC-CB | 3 | Mononuclear Cells (umbilical cord blood-single donor) from two individuals, hMNC-CB_9111701.6 and hMNC-CB_8072802.6 | blood | normal |
| hMNC-CB_8072802.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |
| hMNC-CB_9111701.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |
| hMNC-PB | 3 | Mononuclear Cells (peripheral blood-single donor) from two individuals, hMNC-PB_0022330.9 and hMNC-PB_0082430.9 | blood | normal |
| hMNC-PB_0022330.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| hMNC-PB_0082430.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| HUVEC | 2 | umbilical vein endothelial cells | blood vessel | normal |
| AG04449 | 3 | fetal buttock/thigh fibroblast | skin | normal |
| AG09319 | 3 | gum tissue fibroblasts from apparently heathly 24 year old | gingival | normal |
| AoAF | 3 | aortic adventitial fibroblast cells | blood vessel | normal |
| AoSMC | 3 | aortic smooth muscle cells | blood vessel | normal |
| BC_Adipose_UHN00001 | 3 | adipose tissue, donor UHN0001, age 35, African American, DNA extract | adipose tissue | normal |
| BC_Adrenal_Gland_H12803N | 3 | adrenal gland, donor H12803N, age 88, caucasian, DNA extract | adrenal gland | normal |
| BC_Breast_02-03015 | 3 | breast, donor 02-03015, age 21, caucasian, DNA extract | breast | normal |
| BC_Colon_01-11002 | 3 | colon, donor 01-11002, age 83, caucasian, DNA and RNA extract | colon | normal |
| BC_Colon_H12817N | 3 | colon, donor H12817N, age 71, caucasian, DNA and RNA extract | colon | normal |

| | | | | |
|---|---|---|---|---|
| BC_Esophagus_01-11002 | 3 | esophagus, donor 01-11002, age 83, caucasian, DNA and RNA extract | esophagus | normal |
| BC_Esophagus_H12817N | 3 | esophagus, donor H12817N, age 71, caucasian, DNA extract | esophagus | normal |
| BC_Jejunum_H12817N | 3 | jejunum, donor H12817N, age 71, caucasian, DNA and RNA extract | jejunum | normal |
| BC_Kidney_01-11002 | 3 | kidney, donor 01-11002, age 83, caucasian, DNA and RNA extract | kidney | normal |
| BC_Kidney_H12817N | 3 | kidney, donor H12817N, age 71, caucasian, DNA and RNA extract | kidney | normal |
| BC_Left_Ventricle_N41 | 3 | left ventricle, donor N41, age 26, Asian, DNA extract | left ventricle | normal |
| BC_Liver_01-11002 | 3 | liver, donor 01-11002, age 83, caucasian, DNA and RNA extract | liver | normal |
| BC_Pancreas_H12817N | 3 | pancreas, donor H12817N, age 71, caucasian, DNA and RNA extract | pancreas | normal |
| BC_Penis_H12817N | 3 | penis, donor H12817N, age 71, caucasian, DNA extract | penis | normal |
| BC_Pericardium_H12529N | 3 | pericardium, donor H12529N, age 70, caucasian, DNA extract | pericardium | normal |
| BC_Placenta_UHN00189 | 3 | placenta, donor UHN00189, age 29 | placenta | normal |
| BC_Prostate_Gland_H12817N | 3 | prostate gland, donor H12817N, age 71, caucasian, DNA extract | prostate gland | normal |
| BC_Rectum_N29 | 3 | rectum, donor N29, age 29, Asian, DNA extract | rectum | normal |
| BC_Skeletal_Muscle_01-11002 | 3 | skeletal muscle, donor 01-11002, age 83, caucasian, DNA and RNA extract | skeletal muscle | normal |
| BC_Skeletal_Muscle_H12817N | 3 | skeletal muscle, donor H12817N, age 71, caucasian, DNA and RNA extract | skeletal muscle | normal |
| BC_Skin_01-11002 | 3 | skin, donor 01-11002, age 83, caucasian, DNA extract | skin | normal |
| BC_Small_Intestine_01-11002 | 3 | small intestine, donor 01-11002, age 83, caucasian, DNA and RNA extract | small intestine | normal |
| BC_Spleen_H12817N | 3 | spleen, donor H12817N, age 71, caucasian, DNA and RNA extract | spleen | normal |
| BC_Stomach_01-11002 | 3 | stomach, donor 01-11002, age 83, caucasian, DNA extract | stomach | normal |
| bone_marrow_HS27a | 3 | HS27a Human Marrow Stromal Cells are fibroblastoid cells immortalized with HPV16 E6/E7 genes as described in Roecklein and Torok-Storb, 1995 Blood 85:997-1005, insert DNA is LXSN-16 E6E7 packaged in PA31. | bone marrow | normal |
| bone_marrow_HS5 | 3 | HS5 Human Marrow Stromal Cells are fibroblastoid cells immortalized with HPV16 E6/E7 genes as described in Roecklein and Torok-Storb, 1995 Blood 85:997-1005, insert DNA is LXSN-16 E6E7 packaged in PA31. | bone marrow | normal |
| bone_marrow_MSC | 3 | These cells are primary fibroblastoid cells obtained from human bone marrow of normal donors as described in Roecklein and Torok-Storb, 1995 Blood 85:997-1005. | bone marrow | normal |
| Breast_OC | 3 | Primary frozen breast tissue from NCTC donor IDs 11-0068A (Rep B1) and 11-0067A (Rep B2), both African American | breast | normal |
| Colon_BC | 3 | colon, parent cell type to donors BC_01-11002 and BC_H12817N | colon | normal |
| Colon_OC | 3 | Primary frozen colon tissue from NCTC donor IDs 10-0005A (Rep B1) and 10-0170A (Rep B2), African American and caucasian | colon | normal |
| Esophagus_BC | 3 | esophagus, parental cell type to donors 01-11002 and H12817N | esophagus | normal |
| Fibrobl | 3 | child fibroblast | skin | normal |
| HAoAF | 3 | Aortic Adventitial Fibroblasts from two individuals, HAoAF_6090101.11 and HAoAF_6111301.9 from tunica adventitia | blood vessel | normal |
| HAoAF_6090101.11 | 3 | Aortic Adventitial Fibroblasts from tunica adventitia | blood vessel | normal |
| HAoAF_6111301.9 | 3 | Aortic Adventitial Fibroblasts from tunica adventitia | blood vessel | normal |
| HAoEC | 3 | Aortic Endothelial Cells (thoracic) from two individuals, HAoEC_7071706.1 and HAoEC_8061102.1 | blood vessel | normal |
| HAoEC_7071706.1 | 3 | Aortic Endothelial Cells | blood vessel | normal |
| HAoEC_8061102.1 | 3 | Aortic Endothelial Cells from throracic | blood vessel | normal |
| HCF | 3 | cardiac fibroblasts | heart | normal |
| HCFaa | 3 | cardiac fibroblasts- adult atrial | heart | normal |
| HCH | 3 | Undifferentiated Chondrocytes from two individuals, HCH_8100808.2 and HCH_0011308.2P from knee joint | cartilage | normal |
| HCH_0011308.2P | 3 | Undifferentiated Chondrocytes from knee joint | cartilage | normal |
| HCH_8100808.2 | 3 | Undifferentiated Chondrocytes from knee joint | cartilage | normal |
| HCM | 3 | cardiac myocytes | heart | normal |
| Heart_OC | 3 | Primary frozen heart tissue from NICHD donor IDs 1104 (Rep B1 DNase), 602 (Rep B2 DNase), 1442 (Rep B3 DNase), 1863 (Rep B1 FAIRE), 4548 (Rep B2 FAIRE) | heart | normal |
| Heart_STL003 | 3 | Standard procurement of heart tissue from a 34 year old caucasian male. | heart | normal |
| HEEpiC | 3 | esophageal epithelial cells | epithelium | normal |
| Hepatocytes | 3 | primary hepatocytes, liver perfused by enzymes to generate single cell suspension | liver | normal |
| HFDPC | 3 | Follicle Dermal Papilla Cells from two individuals, HFDPC_0100503.2 and HFDPC_0102703.3 from lateral scalp (brown, blond) | skin | normal |
| HFDPC_0100503.2 | 3 | Follicle Dermal Papilla Cells from lateral scalp (brown) | skin | normal |
| HFDPC_0102703.3 | 3 | Follicle Dermal Papilla Cells from lateral scalp (blond) | skin | normal |
| HFF | 3 | foreskin fibroblast | foreskin | normal |
| hMSC-AT | 3 | Undifferentiated Mesenchymal Stem Cells from two individuals, hMSC-AT_9061601.12 and hMSC-AT_0102604.12 from subcutaneous abdomen adipose tissue | adipose | normal |
| hMSC-AT_0102604.12 | 3 | Undifferentiated Mesenchymal Stem Cells from subcutaneous abdomen adipose tissue | adipose | normal |
| hMSC-AT_9061601.12 | 3 | Undifferentiated Mesenchymal Stem Cells from abdomen | subcutaneous adipose tissue | normal |
| hMSC-BM | 3 | Undifferentiated Mesenchymal Stem Cells from two individuals, hMSC-BM_0050602.11 and hMSC-BM_0051105.11 from femoral head | bone marrow | normal |
| hMSC-BM_0050602.11 | 3 | Undifferentiated Mesenchymal Stem Cells from femoral head | bone marrow | normal |
| hMSC-BM_0051105.11 | 3 | Undifferentiated Mesenchymal Stem Cells from femoral head | bone marrow | normal |
| hMSC-UC | 3 | Undifferentiated Mesenchymal Stem Cells from two individuals, hMSC-UC_0081101.7 and hMSC-UC_0052501.7 from matrix (Wharton's Jelly) | umbilical cord | normal |
| hMSC-UC_0052501.7 | 3 | Undifferentiated Mesenchymal Stem Cells from matrix (Wharton's Jelly) | umbilical cord | normal |
| hMSC-UC_0081101.7 | 3 | Undifferentiated Mesenchymal Stem Cells from matrix (Wharton's Jelly) | umbilical cord | normal |
| HMVEC-dAd | 3 | adult dermal microvascular endothelial cells. | blood vessel | normal |
| HMVEC-dBl-Ad | 3 | adult blood microvascular endothelial cells, dermal-derived | blood vessel | normal |
| HMVEC-dBl-Neo | 3 | neonatal blood microvascular endothelial cells, dermal-derived | blood vessel | normal |
| HMVEC-dLy-Ad | 3 | adult lymphatic microvascular endothelial cells, dermal-derived | blood vessel | normal |
| HMVEC-dLy-Neo | 3 | neonatal lymphatic microvascular endothelial cells, dermal-derived | blood vessel | normal |

| | | | | |
|---|---|---|---|---|
| HMVEC-dNeo | 3 | neonatal microvascular endothelial cells (single donor), dermal-derived | blood vessel | normal |
| HNPCEpiC | 3 | non-pigment ciliary epithelial cells | epithelium | normal |
| HOB | 3 | Undifferentiated Osteoblasts from two individuals, HOB_0090202.1 and HOB_0091301 from femoral head | cancellous bone | normal |
| HOB_0090202.1 | 3 | Undifferentiated Osteoblasts from femoral head | cancellous bone | normal |
| HOB_0091301 | 3 | Undifferentiated Osteoblasts from femoral head | cancellous bone | normal |
| HPAEC | 3 | pulmonary artery endothelial cells. | blood vessel | normal |
| HPAEpiC | 3 | pulmonary alveolar epithelial cells | epithelium | normal |
| HPAF | 3 | pulmonary artery fibroblasts | blood vessel | normal |
| HPDE6-E6E7 | 3 | pancreatic duct cells immortalized with E6E7 gene of HPV | pancreatic duct | normal |
| HPdLF | 3 | periodontal ligament fibroblasts | epithelium | normal |
| HPIEpC | 3 | Placental Epithelial Cells amniotic membrane | placenta | normal |
| HPIEpC_9012801.2 | 3 | Placental Epithelial Cells amniotic membrane | placenta | normal |
| HPIEpC_9041503.2 | 3 | Placental Epithelial Cells amniotic membrane | placenta | normal |
| HRCEpiC | 3 | renal cortical epithelial cells | epithelium | normal |
| HRE | 3 | renal epithelial cells | epithelium | normal |
| HRGEC | 3 | renal glomerular endothelial cells | kidney | normal |
| HRPEpiC | 3 | retinal pigment epithelial cells | epithelium | normal |
| HSaVEC | 3 | Saphenous Vein Endothelial Cells from two individuals, HSaVEC_9100101.15 and HSaVEC_0022202.16 from thigh | blood vessel | normal |
| HSaVEC_0022202.16 | 3 | Saphenous Vein Endothelial Cells from thigh | blood vessel | normal |
| HSaVEC_9100101.15 | 3 | Saphenous Vein Endothelial Cells from thigh | blood vessel | normal |
| HSMM | 3 | skeletal muscle myoblasts | muscle | normal |
| HSMMtube | 3 | skeletal muscle myotubes differentiated from the HSMM cell line | muscle | normal |
| HTR8svn | 3 | trophoblast (HTR-8/SVneo) cell line, a thin layer of ectoderm that forms the wall of many mammalian blastulas and functions in the nutrition and implantation of the embryo | blastula | normal |
| HVMF | 3 | villous mesenchymal fibroblast cells | connective | normal |
| HVMF_6091203.3 | 3 | Villous Mesenchymal Fibroblasts from villous tissue | placenta | normal |
| HVMF_6100401.3 | 3 | Villous Mesenchymal Fibroblasts from villous tissue | placenta | normal |
| HWP_8120201.5 | 3 | Undifferentiated White Preadipocytes from upper arm | subcutaneous adipose tissue | normal |
| iPS_hFib2_iPS4 | 3 | induced pluripotent stem cell line 4 derived from skin fibroblast of a 30 year old donor, same donor as iPS_hFib2_iPS5 | induced pluripotent cell (iPS) | normal |
| iPS_hFib2_iPS5 | 3 | induced pluripotent stem cell line 5 derived from skin fibroblast of a 30 year old donor, same donor as iPS_hFib2_iPS4 | induced pluripotent cell (iPS) | normal |
| Kidney_BC | 3 | kidney, parental cell type to donors 01-11002 and H12817N | kidney | normal |
| Kidney_OC | 3 | Primary frozen kidney tissue from NICHD donor IDs 1104 (Rep B1 DNase), 602 (Rep B2 DNase), 1442 (Rep B3 DNase), 1863 (Rep B3 FAIRE) and NCTC donor ID 10-0022A (Rep B1 FAIRE) | kidney | normal |
| LHSR | 3 | prostate epithelial cells (PrEC), multiple human donors, all of whom are HIV-1, Hepatitis B and Hepatitis C negative, treatment: to create LHSR, cells were infected with amphotropic retroviruses encoding the SV40 large T antigen (L), the telomerase catalytic subunit hTERT (H), the SV40 small T antigen (S) and an oncogenic allele of H-ras (R). | epithelium | normal |
| Liver_OC | 3 | Primary frozen liver tissue from NICHD donor IDs 1104 (Rep B1), 602 (Rep B2), 1442 (Rep B3) | liver | normal |
| Liver_STL004 | 3 | Primary liver tissue from the right portion of a standard liver procurement from a 6 year old female. | liver | normal |
| Liver_STL011 | 3 | Primary liver tissue of a standard liver procurement from a 36 year old caucasian male. | liver | normal |
| NHBE | 3 | bronchial epithelial cells | epithelium | normal |
| NHBE_RA | 3 | bronchial epithelial cells with retinoic acid | bronchial epithelium | normal |
| NHDF | 3 | Dermal Fibroblasts from temple / breast | skin | normal |
| NHDF-Ad | 3 | adult dermal fibroblasts | skin | normal |
| NHDF-neo | 3 | neonatal dermal fibroblasts | skin | normal |
| NHDF_0060801.3 | 3 | Dermal Fibroblasts from temple | skin | normal |
| NHDF_7071701.2 | 3 | Dermal Fibroblasts from breast | skin | normal |
| NHEK | 3 | epidermal keratinocytes | skin | normal |
| NHEM.f_M2 | 3 | Epidermal Melanocytes from two individuals, NHEM.f_M2_5071302.2 and NHEM.f_M2_6022001 from foreskin | skin | normal |
| NHEM.f_M2_5071302.2 | 3 | Epidermal Melanocytes (foreskin) | skin | normal |
| NHEM.f_M2_6022001 | 3 | Epidermal Melanocytes (foreskin) | skin | normal |
| NHEM_M2 | 3 | Epidermal Melanocytes (adult) from two individuals, NHEM_M2_7011001.2 and NHEM_M2_7012303 from cheek / temple | skin | normal |
| NHEM_M2_7011001.2 | 3 | Epidermal Melanocytes (adult) from cheek | skin | normal |
| NHEM_M2_7012303 | 3 | Epidermal Melanocytes (adult) from temple | skin | normal |
| Olf_neurosphere | 3 | Human olfactory neurosphere-derived cells from mucosal biopsies | Nasal biopsy | normal |
| Osteobl | 3 | osteoblasts (NHOst) | bone | normal |
| Pancreas_OC | 3 | Primary frozen pancreas tissue from NCTC donor IDs 09-0144A (Rep B1) and 10-0021A (Rep B2) | pancreas | normal |
| PanIslets | 3 | pancreatic islets from 2 donors, the sources of these primary cells are cadavers from National Disease Research Interchange (NDRI) and another sample isolated as in Bucher, P. et al., Assessment of a novel two-component enzyme preparation for human islet isolation and transplantation. Transplantation 79, 917 (2005) | pancreas | normal |
| PBDEFetal | 3 | peripheral blood-derived erythroblasts from 16-19 week human fetal liver | liver | normal |
| PrEC | 3 | prostate epithelial cell line | prostate | normal |
| Prostate_OC | 3 | Primary frozen prostate tissue from NICHD donor IDs 1669 (Rep B1) and 1540 (Rep B2) | prostate | normal |
| Psoas_muscle_OC | 3 | Primary frozen psoas muscle tissue from NICHD donor IDs 1104 (Rep B1 DNase), 602 (Rep B2 DNase), 1442 (Rep B3 DNase), 1540 (Rep B1), 1863 (Rep B2 FAIRE) | psoas muscle | normal |
| RPTEC | 3 | renal proximal tubule epithelial cells | epithelium | normal |
| RWPE1 | 3 | prostate epithelial | prostate | normal |

| | | | | |
|---|---|---|---|---|
| SAEC | 3 | small airway epithelial cells | epithelium | normal |
| Skeletal_Muscle_BC | 3 | skeletal muscle, parental cell type to donors 01-11002 and H12817N | skeletal muscle | normal |
| SkMC | 3 | Skeletal Striated Muscle Cells from two individuals, SkMC_9011302 SkMC_8121902.17 from M. pectoralis / Mm. intercostales | muscle | normal |
| SKMC | 3 | skeletal muscle cells | muscle | normal |
| SkMC_8121902.17 | 3 | Skeletal Muscle Cells from Mm. intercostales | striated muscle | normal |
| SkMC_9011302 | 3 | Skeletal Muscle Cells from M. pectoralis | striated muscle | normal |
| Small_intestine_OC | 3 | Primary frozen small intestine tissue from NCTC donor IDs 10-0063A (Rep B1) and 09-0143A (Rep B2) | small intestine | normal |
| Spleen_OC | 3 | Primary frozen spleen tissue from NICHD donor IDs 1863 (Rep B1) and 4548 (Rep B2) | spleen | normal |
| Stellate | 3 | hepatic stellate cells, liver that was perfused with collagenase and sellected for hepatic stellate cells by density gradient | liver | normal |
| Stomach_BC | 3 | stomach, parental cell type to donors 01-11002 and H12817N | stomach | normal |
| Urothelia | 3 | primary ureter cell culture of urothelial cells derived from a 12 year-old girl and immortalized by transfection with a temperature-sensitive SV-40 large T antigen gene | urothelium | normal |
| Decidua | 3 | decidua cells (part of the mucous membrane lining uterus), Fetal membranes were collected from women who underwent planned cesarean delivery at term, before labor and without rupture of membranes | cervix | normal |
| HAL | 3 | adult liver, genomic DNA purified from surgically excised adult human liver | liver | normal |
| FibroP_AG08395 | 3 | fibroblasts taken from individuals with Parkinson's disease | skin fibroblast | normal |
| CD34+_Mobilized | 3 | hematopoietic progenitor cells- mobilized, from donor RO01679. | blood | normal |
| CD34+_Mobilized | 3 | hematopoietic progenitor cells- mobilized, from donor RO01679. | blood | normal |
| LHCN-M2 | 2 | skeletal myoblasts derived from satellite cells from the pectoralis major muscle of a 41 year old caucasian heart transplant donor, immortalized with lox-hygro-hTERT ("LH"), and Cdk4-neo ("CN"), Zhu et al. (2007) in Aging Cell, vol. 6, pp 515-523, newly promoted to tier 2: not in 2011 analysis. | skeletal muscle myoblast | normal |
| Chorion | 3 | chorion cells (outermost of two fetal membranes), fetal membranes were collected from women who underwent planned cesarean delivery at term, before labor and without rupture of membranes. | fetal membrane | normal |
| HConF | 3 | conjunctival fibroblast | eye | normal |
| HEK293 | 3 | embryonic kidney, cells contain Adenovirus 5 DNA (PMID: 11967234) | kidney | normal |
| HEK293-T-REx | 3 | embryonic kidney cells transformed with Adenovirus 5 DNA stably expressing tetracycline repressor, HEK293 (ATCC number CRL-1573) is the parental cell line, hypotriploid, XXX | kidney | normal |
| HEK293T | 3 | embryonic kidney that expresses SV40 large T antigen, HEK293 (ATCC number CRL-1573) is the parental cell line | kidney | normal |
| HSMM_emb | 3 | embryonic myoblast | muscle | normal |
| HSMM_FSHD | 3 | primary myoblast from Facioscapulohumeral Muscular Dystrophy (FSHD) patients, muscle needle biopsies | muscle | normal |
| HSMMtube_emb | 3 | embryonic myotube | muscle | normal |
| HSMMtube_FSHD | 3 | myotube from Facioscapulohumeral Muscular Dystrophy (FSHD) patient, muscle needle biopsies | muscle | normal |
| iPS | 3 | induced pluripotent stem cell derived from skin fibroblast | induced pluripotent stem cell | normal |
| iPS_NIHi11 | 3 | iPS cells derived from AG20443 fibroblast | induced pluripotent cell (iPS) | normal |
| iPS_NIHi7 | 3 | iPS cells derived from AG08395 fibroblast | induced pluripotent cell (iPS) | normal |
| Ishikawa | 3 | endometrial adenocarcinoma | uterus | normal |
| MCF10A-Er-Src | 3 | mammary gland, non-tumorigenic epithelial, inducible cell line, derived from the MCF-10A parental cells and contain ER-Src, a derivative of the Src kinase oncoprotein (v-Src) that is fused to the ligand-binding domain of the estrogen receptor (ER) | breast | normal |
| PanIsletD | 3 | dedifferentiated human pancreatic islets from the National Disease Research Interchange (NDRI), same source as PanIslets | pancreas | normal |
| PBDE | 3 | peripheral blood-derived erythroblasts | blood | normal |
| pHTE | 3 | primary tracheal epithelial cells | epithelium | normal |
| ProgFib | 3 | fibroblasts, Hutchinson-Gilford progeria syndrome (cell line HGPS, HGADFN167, progeria research foundation) | skin | normal |
| prostate | 3 | prostate tissue purchased for CSHL project | prostate | normal |
| BC_Leukocyte_UHN00204 | 3 | peripheral blood mononuclear cell, donor UHN00204, age 54, caucasian, DNA extract | blood | normal |
| hMNC-CB | 3 | Mononuclear Cells (umbilical cord blood-single donor) from two individuals, hMNC-CB_9111701.6 and hMNC-CB_8072802.6 | blood | normal |
| hMNC-CB_8072802.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |
| hMNC-CB_9111701.6 | 3 | Mononuclear Cells, umbilical cord blood-single donor | blood | normal |
| hMNC-PB | 3 | Mononuclear Cells (peripheral blood-single donor) from two individuals, hMNC-PB_0022330.9 and hMNC-PB_0082430.9 | blood | normal |
| hMNC-PB_0022330.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| hMNC-PB_0082430.9 | 3 | Mononuclear Cells, peripheral blood-single donor | blood | normal |
| CD34+_Mobilized | 3 | hematopoietic progenitor cells- mobilized, from donor RO01679. | blood | normal |
| PBMC | 3 | peripheral blood mononuclear cells | blood | normal |
| Adult_CD4_naive | 3 | CD4+ cells isolated from human blood and enriched for naive populations | blood | normal |
| Adult_CD4_Th0 | 3 | CD4+ cells isolated from human blood and enriched for Th0 populations | blood | normal |
| CD4+_Naive_Wb11970640 | 3 | CD4+ naive sorted cells, donor is Caucasian, male 26 year old, primary pheresis of single normal subject | blood | normal |
| CD4+_Naive_Wb78495824 | 3 | CD4+ naive sorted cells, donor is Causasian, female 35 year old, primary pheresis of single normal subject | blood | normal |
| Cord_CD4_naive | 3 | CD4+ cells isolated from cord blood and enriched for naive populations | blood | normal |
| Cord_CD4_Th0 | 3 | CD4+ cells isolated from cord blood and enriched for Th0 populations | blood | normal |
| Adult_CD4_Th1 | 3 | CD4+ cells isolated from human blood and enriched for Th1 populations | blood | normal |
| Cord_CD4_Th1 | 3 | CD4+ cells isolated from cord blood and enriched for Th1 populations | blood | normal |
| Th1_Wb54553204 | 3 | Th1 cells in vivo isolation, donor is Caucasian, male 33 year old, primary pheresis of single normal subject | blood | normal |
| Th1 | 3 | primary Th1 T cells | blood | normal |
| Th17 | 3 | T helper cells expressing IL-17, primary pheresis of single normal subject | blood | normal |
| Th2_Wb33676984 | 3 | Th2 cells in vivo isolation, donor is Asian, female 26 year old, primary pheresis of single normal subject | blood | normal |
| Th2_Wb54553204 | 3 | Th2 cells in vivo isolation, donor is Caucasian, male 33 year old, primary pheresis of single normal subject | blood | normal |
| Th2 | 3 | primary Th2 T cells | blood | normal |
| Treg_Wb83319432 | 3 | T regulatory cells in vivo isolation, donor is Caucasian, male 28 year old, primary pheresis of single normal subject | blood | normal |

| **Key** | |
|---|---|
| cell_Line_name | Cell line name |
| ENCODE_Tier | ENCODE tier (phase) |
| Description | Description of ENCODE cell line |
| Tissue | Tissue or cell type |
| Karyotype | Karyotype (Normal or cancer) |
| Cell Bucket for analysis | Major cell type associated to cell line for this analysis |
| B: | B cells |
| T: | T cells |
| M: | Monocytes/macrophages |
| O: | Other |
| L: | Lung |

**Supplementary Table 5. Epigenomic Roadmap Project cells used in this analysis**

| Standardized Epigenome name | Epigenome name (from EDACC Release 9 directory) | ANATOMY | TYPE | Cell Bucket for Aanalysis |
|---|---|---|---|---|
| Primary B cells from cord blood | CD19_Primary_Cells_Cord_BI | BLOOD | PrimaryCell | B |
| Primary B cells from peripheral blood | CD19_Primary_Cells_Peripheral_UW | BLOOD | PrimaryCell | B |
| GM12878 Lymphoblastoid Cell Line | GM12878_Lymphoblastoid | BLOOD | CellLine | B |
| Brain Cingulate Gyrus | Brain_Cingulate_Gyrus | BRAIN | PrimaryTissue | C |
| Brain Dorsolateral Prefrontal Cortex | Brain_Dorsolateral_Prefrontal_Cortex | BRAIN | PrimaryTissue | C |
| Brain Germinal Matrix | Brain_Germinal_Matrix | BRAIN | PrimaryTissue | C |
| Brain Hippocampus Middle | Brain_Hippocampus_Middle | BRAIN | PrimaryTissue | C |
| Brain Inferior Temporal Lobe | Brain_Inferior_Temporal_Lobe | BRAIN | PrimaryTissue | C |
| Brain Substantia Nigra | Brain_Substantia_Nigra | BRAIN | PrimaryTissue | C |
| Cortex derived primary cultured neurospheres | Neurosphere_Cultured_Cells_Cortex_Derived | BRAIN | PrimaryCell | C |
| Fetal Brain Female | Fetal_Brain_Female | BRAIN | PrimaryTissue | C |
| Brain Angular Gyrus | Brain_Angular_Gyrus | BRAIN | PrimaryTissue | C |
| Brain Anterior Caudate | Brain_Anterior_Caudate | BRAIN | PrimaryTissue | C |
| Fetal Brain Male | Fetal_Brain_Male | BRAIN | PrimaryTissue | C |
| Ganglion Eminence derived primary cultured neurospheres | Neurosphere_Cultured_Cells_Ganglionic_Eminence_Derived | BRAIN | PrimaryCell | C |
| H9 Derived Neuronal Progenitor Cultured Cells | H9_Derived_Neuronal_Progenitor_Cultured_Cells | ESC_DERIVED | CellLineDerived | C |
| H1 Derived Neuronal Progenitor Cultured Cells | H1_Derived_Neuronal_Progenitor_Cultured_Cells | ESC_DERIVED | CellLineDerived | C |
| H9 Derived Neuron Cultured Cells | H9_Derived_Neuron_Cultured_Cells | ESC_DERIVED | CellLineDerived | C |
| H1 Derived Mesenchymal Stem Cells | H1_Derived_Mesenchymal_Stem_Cells | ESC_DERIVED | CellLineDerived | L |
| IMR90 fetal lung fibroblasts Cell Line | IMR90_Cell_Line | LUNG | CellLine | L |
| NHLF Lung Fibroblast Primary Cells | NHLF_Lung_Fibroblasts | LUNG | PrimaryCell | L |
| Fetal Lung | Fetal_Lung | LUNG | PrimaryTissue | L |
| Lung | Lung | LUNG | PrimaryTissue | L |
| Monocytes-CD14+ RO01746 Primary Cells | Monocytes-CD14+_RO01746 | BLOOD | PrimaryCell | M |
| Primary monocytes from peripheral blood | CD14_Primary_Cells | BLOOD | PrimaryCell | M |
| Fetal Adrenal Gland | Fetal_Adrenal_Gland | ADRENAL | PrimaryTissue | O |
| Primary hematopoietic stem cells | CD34_Primary_Cells | BLOOD | PrimaryCell | O |
| Primary hematopoietic stem cells G-CSF-mobilized Female | Mobilized_CD34_Primary_Cells_Female | BLOOD | PrimaryCell | O |
| Primary hematopoietic stem cells G-CSF-mobilized Male | Mobilized_CD34_Primary_Cells_Male | BLOOD | PrimaryCell | O |
| Primary hematopoietic stem cells short term culture | CD34_Cultured_Cells | BLOOD | PrimaryCell | O |
| Primary mononuclear cells from peripheral blood | Peripheral_Blood_Mononuclear_Primary_Cells | BLOOD | PrimaryCell | O |
| Primary neutrophils from peripheral blood | CD15_Primary_Cells | BLOOD | PrimaryCell | O |
| Osteoblast Primary Cells | Osteoblasts | BONE | PrimaryCell | O |
| Breast Myoepithelial Primary Cells | Breast_Myoepithelial_Cells | BREAST | PrimaryCell | O |
| Breast variant Human Mammary Epithelial Cells (vHMEC) | Breast_vHMEC | BREAST | PrimaryCell | O |
| HMEC Mammary Epithelial Primary Cells | HMEC_Mammary_Epithelial | BREAST | PrimaryCell | O |
| HUES6 Cell Line | HUES6_Cell_Line | ESC | CellLine | O |
| ES-UCSF4  Cell Line | 4star | ESC | CellLine | O |
| ES-I3 Cell Line | ES-I3_Cell_Line | ESC | CellLine | O |
| ES-WA7 Cell Line | ES-WA7_Cell_Line | ESC | CellLine | O |
| H1 Cell Line | H1_Cell_Line | ESC | CellLine | O |
| H9 Cell Line | H9_Cell_Line | ESC | CellLine | O |
| HUES48 Cell Line | HUES48_Cell_Line | ESC | CellLine | O |
| HUES64 Cell Line | HUES64_Cell_Line | ESC | CellLine | O |
| H1 BMP4 Derived Mesendoderm Cultured Cells | H1_BMP4_Derived_Mesendoderm_Cultured_Cells | ESC_DERIVED | CellLineDerived | O |
| H1 BMP4 Derived Trophoblast Cultured Cells | H1_BMP4_Derived_Trophoblast_Cultured_Cells | ESC_DERIVED | CellLineDerived | O |
| hESC Derived CD184+ Endoderm Cultured Cells | hESC_Derived_CD184+_Endoderm_Cultured_Cells | ESC_DERIVED | CellLineDerived | O |
| hESC Derived CD56+ Ectoderm Cultured Cells | hESC_Derived_CD56+_Ectoderm_Cultured_Cells | ESC_DERIVED | CellLineDerived | O |
| hESC Derived CD56+ Mesoderm Cultured Cells | hESC_Derived_CD56+_Mesoderm_Cultured_Cells | ESC_DERIVED | CellLineDerived | O |
| Adipose Derived Mesenchymal Stem Cell Cultured Cells | Adipose_Derived_Mesenchymal_Stem_Cell_Cultured_Cells | FAT | PrimaryCell | O |
| Adipose Nuclei | Adipose_Nuclei | FAT | PrimaryTissue | O |
| Mesenchymal Stem Cell Derived Adipocyte Cultured Cells | Mesenchymal_Stem_Cell_Derived_Adipocyte_Cultured_Cells | FAT | CellLineDerived | O |
| Colon Smooth Muscle | Colon_Smooth_Muscle | GI_COLON | PrimaryTissue | O |
| Colonic Mucosa | Colonic_Mucosa | GI_COLON | PrimaryTissue | O |
| Sigmoid Colon | Sigmoid_Colon | GI_COLON | PrimaryTissue | O |
| Duodenum Mucosa | Duodenum_Mucosa | GI_DUODENUM | PrimaryTissue | O |
| Duodenum Smooth Muscle | Duodenum_Smooth_Muscle | GI_DUODENUM | PrimaryTissue | O |
| Esophagus | Esophagus | GI_ESOPHAGUS | PrimaryTissue | O |
| Fetal Intestine Large | Fetal_Intestine_Large | GI_INTESTINE | PrimaryTissue | O |
| Fetal Intestine Small | Fetal_Intestine_Small | GI_INTESTINE | PrimaryTissue | O |
| Small Intestine | Small_Intestine | GI_INTESTINE | PrimaryTissue | O |
| Rectal Mucosa Donor 29 | Rectal_Mucosa.Donor_29 | GI_RECTUM | PrimaryTissue | O |
| Rectal Mucosa Donor 31 | Rectal_Mucosa.Donor_31 | GI_RECTUM | PrimaryTissue | O |
| Rectal Smooth Muscle | Rectal_Smooth_Muscle | GI_RECTUM | PrimaryTissue | O |
| Gastric | Gastric | GI_STOMACH | PrimaryTissue | O |
| Stomach Mucosa | Stomach_Mucosa | GI_STOMACH | PrimaryTissue | O |
| Stomach Smooth Muscle | Stomach_Smooth_Muscle | GI_STOMACH | PrimaryTissue | O |
| Fetal Heart | Fetal_Heart | HEART | PrimaryTissue | O |
| Left Ventricle | Left_Ventricle | HEART | PrimaryTissue | O |
| Right Atrium | Right_Atrium | HEART | PrimaryTissue | O |
| Right Ventricle | Right_Ventricle | HEART | PrimaryTissue | O |
| iPS-20b Cell Line | iPS-20b_Cell_Line | IPSC | CellLine | O |
| iPS DF 6.9 Cell Line | iPS_DF_6.9_Cell_Line | IPSC | CellLine | O |
| iPS DF 19.11 Cell Line | iPS_DF_19.11_Cell_Line | IPSC | CellLine | O |
| iPS-15b Cell Line | iPS-15b_Cell_Line | IPSC | CellLine | O |
| iPS-18 Cell Line | iPS-18_Cell_Line | IPSC | CellLine | O |
| Fetal Kidney | Fetal_Kidney | KIDNEY | PrimaryTissue | O |
| Liver | Adult_Liver | LIVER | PrimaryTissue | O |
| Psoas Muscle | Psoas_Muscle | MUSCLE | PrimaryTissue | O |
| Fetal Muscle Trunk | Fetal_Muscle_Trunk | MUSCLE | PrimaryTissue | O |
| HSMM Skeletal Muscle Myoblasts Cell Line | HSMM_Skeletal_Muscle_Myoblasts | MUSCLE | CellLine | O |
| Muscle Satellite Cultured Cells | Muscle_Satellite_Cultured_Cells | MUSCLE | PrimaryCell | O |
| Skeletal Muscle Female | Skeletal_Muscle_Female | MUSCLE | PrimaryTissue | O |
| Skeletal Muscle Male | Skeletal_Muscle_Male | MUSCLE | PrimaryTissue | O |
| Fetal Muscle Leg | Fetal_Muscle_Leg | MUSCLE_LEG | PrimaryTissue | O |
| Ovary | Ovary | OVARY | PrimaryTissue | O |
| Pancreas | Pancreas | PANCREAS | PrimaryTissue | O |
| Pancreatic Islets | Pancreatic_Islets | PANCREAS | PrimaryTissue | O |
| Placenta | Fetal_Placenta | PLACENTA | PrimaryTissue | O |
| Placenta Amnion | Placenta_Amnion | PLACENTA | PrimaryTissue | O |
| NHDF-Ad Adult Dermal Fibroblast Primary Cells | NHDF-Ad_Adult_Dermal_Fibroblasts | SKIN | PrimaryCell | O |
| NHEK-Epidermal Keratinocyte Primary Cells | NHEK-Epidermal_Keratinocytes | SKIN | PrimaryCell | O |
| Foreskin Fibroblast Primary Cells skin01 | Penis_Foreskin_Fibroblast_Primary_Cells_skin01 | SKIN | PrimaryCell | O |
| Foreskin Fibroblast Primary Cells skin02 | Penis_Foreskin_Fibroblast_Primary_Cells_skin02 | SKIN | PrimaryCell | O |
| Foreskin Keratinocyte Primary Cells skin02 | Penis_Foreskin_Keratinocyte_Primary_Cells_skin02 | SKIN | PrimaryCell | O |
| Foreskin Keratinocyte Primary Cells skin03 | Penis_Foreskin_Keratinocyte_Primary_Cells_skin03 | SKIN | PrimaryCell | O |

| | | | | |
|---|---|---|---|---|
| Foreskin Melanocyte Primary Cells skin01 | Penis_Foreskin_Melanocyte_Primary_Cells_skin01 | SKIN | PrimaryCell | O |
| Foreskin Melanocyte Primary Cells skin03 | Penis_Foreskin_Melanocyte_Primary_Cells_skin03 | SKIN | PrimaryCell | O |
| Spleen | Spleen | SPLEEN | PrimaryTissue | O |
| Bone Marrow Derived Cultured Mesenchymal Stem Cells | Bone_Marrow_Derived_Mesenchymal_Stem_Cell_Cultured_Cells | STROMAL_CONNECTIVE | PrimaryCell | O |
| Mesenchymal Stem Cell Derived Chondrocyte Cultured Cells | Chondrocytes_from_Bone_Marrow_Derived_Mesenchymal_Stem_Cell_Cultured_Cells | STROMAL_CONNECTIVE | PrimaryCell | O |
| Thymus | Thymus | THYMUS | PrimaryTissue | O |
| Aorta | Aorta | VASCULAR | PrimaryTissue | O |
| HUVEC Umbilical Vein Endothelial Primary Cells | HUVEC_Umbilical_Vein_Endothelial_Cells | VASCULAR | PrimaryCell | O |
| Primary Natural Killer cells from peripheral blood | CD56_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T CD8+ memory cells from peripheral blood | CD8_Memory_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T CD8+ naive cells from peripheral blood | CD8_Naive_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T cells effector/memory enriched from peripheral blood | CD4+_CD25int_CD127+_Tmem_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T cells from cord blood | CD3_Primary_Cells_Cord_BI | BLOOD | PrimaryCell | T |
| Primary T cells from peripheral blood | CD3_Primary_Cells_Peripheral_UW | BLOOD | PrimaryCell | T |
| Primary T helper cells from peripheral blood | CD4+_CD25-_Th_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper cells PMA-I stimulated | CD4+_CD25-_IL17-_PMA-Ionomycin_stimulated_MACS_purified_Th_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper memory cells from peripheral blood 1 | CD4+_CD25-_CD45RO+_Memory_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper memory cells from peripheral blood 2 | CD4_Memory_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper naive cells from peripheral blood | CD4_Naive_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper naive cells from peripheral blood | CD4+_CD25-_CD45RA+_Naive_Primary_Cells | BLOOD | PrimaryCell | T |
| Primary T helper 17 cells PMA-I stimulated | CD4+_CD25-_IL17+_PMA-Ionomcyin_stimulated_Th17_Primary_Cells | BLOOD | PrimaryCell | Th17 |
| Primary T regulatory cells from peripheral blood | CD4+_CD25+_CD127-_Treg_Primary_Cells | BLOOD | PrimaryCell | Treg |

**Key**

| | |
|---|---|
| Standardized Epigenome name | Name of cell line |
| Epigenome name (from EDACC Release 9 directory) | alias |
| ANATOMY | cell type or tissue of procedence |
| TYPE | primary or established cell line |
| Cell Bucket for Aanalysis | Major cell type associated to cell line for this analysis |
| B: | B cells |
| T: | T cells |
| M: | Monocytes/macrophages |
| O: | Other |
| L: | Lung |

**Supplementary Table 6. Assignment of regulatory features into broad categories for this analysis**

| Histone modification or variant | Putative functions |
|---|---|
| H2az | Histone protein variant (H2A.Z) associated with regulatory elements with dynamic chromatin |
| H3k4me1 | Mark of regulatory elements associated with enhancers and other distal elements, but also enriched downstream of transcription starts |
| H3k04me1 | Mark of regulatory elements associated with enhancers and other distal elements, but also enriched downstream of transcription starts |
| H3k4me2 | Mark of regulatory elements associated with promoters and enhancers |
| H3k04me2 | Mark of regulatory elements associated with promoters and enhancers |
| H3k4me2 | Mark of regulatory elements associated with promoters and enhancers |
| H3k04me2 | Mark of regulatory elements associated with promoters and enhancers |
| H3k4me3 | Mark of regulatory elements primarily associated with promoters/transcription starts |
| H3k04me3 | Mark of regulatory elements primarily associated with promoters/transcription starts |
| H3k04me3Ohtam | Mark of regulatory elements primarily associated with promoters/transcription starts |
| H3k9ac | Mark of active regulatory elements with preference for promoters |
| H3k09ac | Mark of active regulatory elements with preference for promoters |
| H3k9me1 | Preference for the 5’ end of genes |
| H3k09me1 | Preference for the 5’ end of genes |
| H3k9me3 | Repressive mark associated with constitutive heterochromatin and repetitive elements |
| H3k09me3 | Repressive mark associated with constitutive heterochromatin and repetitive elements |
| H3k27ac | Mark of active regulatory elements; may distinguish active enhancers and promoters from their inactive counterparts |
| H3k27ac | Mark of active regulatory elements; may distinguish active enhancers and promoters from their inactive counterparts |
| H3k27me3 | Repressive mark established by polycomb complex activity associated with repressive domains and silent developmental genes |
| H3k36me3 | Elongation mark associated with transcribed portions of genes, with preference for 3’ regions after intron 1 |
| H3k79me2 | Transcription-associated mark, with preference for 5’ end of genes |
| H4k20me1 | Preference for 5’ end of genes |
| | |
| Active TSS | |
| Flanking Active TSS | |
| Transcr. at gene 5' and 3' | Transcription/Elongation marker observed |
| Strong transcription | Transcription/Elongation marker observed |
| Weak transcription | Transcription/Elongation marker observed |
| Genic enhancers | |
| Enhancers | |
| ZNF genes & repeats | ZNF genes harbor 3' repeats and have promoter and elongation markers. However, they don't seem to promote any gene activity tested. |
| Heterochromatin | Dead zone |
| Bivalent/Poised TSS | Inactive Promoter |
| Flanking Bivalent TSS/Enh | Inactive Enhancer |
| Bivalent Enhancer | Inactive Enhancer |
| Repressed PolyComb | |
| Weak Repressed PolyComb | |
| Quiescent/Low | No/low marker activity |

| **Key** | |
|---|---|
| Histone modification or variant | Type of regulatory element or histone modification |
| Putative functions | predicted regulatory function |
| Bucket_for_analysis | Major regulatory function associated to element for this analysis |