

Supplementary figure legends

Figure S1. The overall study design, including the number of subjects/samples in each phase and analysis methods. The identification of obesity-specific CpG was conducted in a three-phased case-control study with phase I discovery in 450 subjects and phase II-III replication in 377 and 75 subjects. Obesity-specific CpGs were prioritized with fat-blood methylome comparison and methylome-transcriptome analysis in fat tissue and cells.

Figure S2. Venn-diagram of 48 DMPs discovered and replicated in blood samples of multi-phased analyses. Probes/genes were categorized with additional prioritization methods of blood-fat consistency in methylation (blue), correlations between DNA methylation and gene expression in fat tissues (green), and DMPs in childhood obesity (yellow).

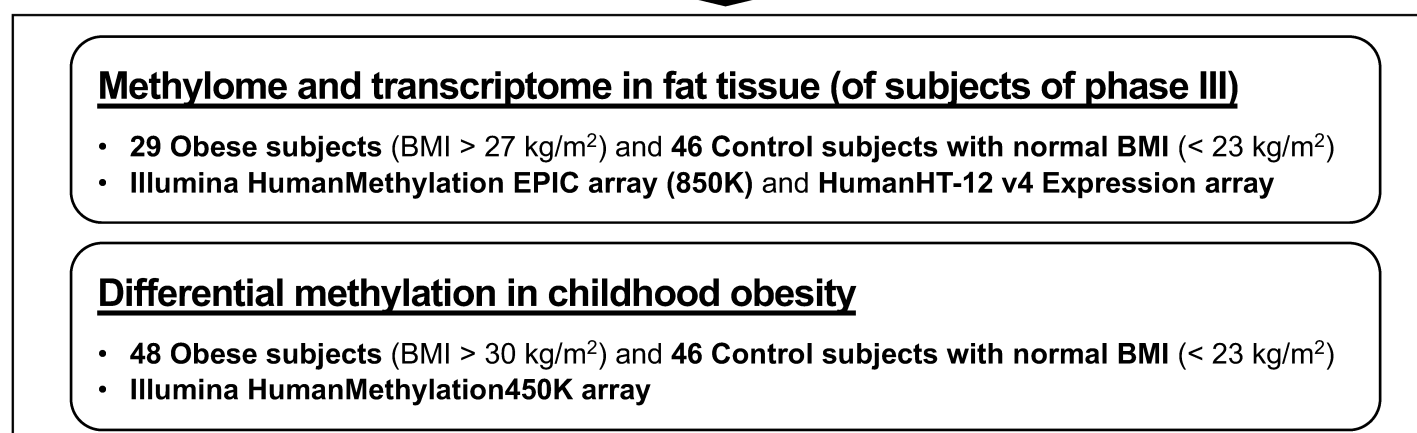
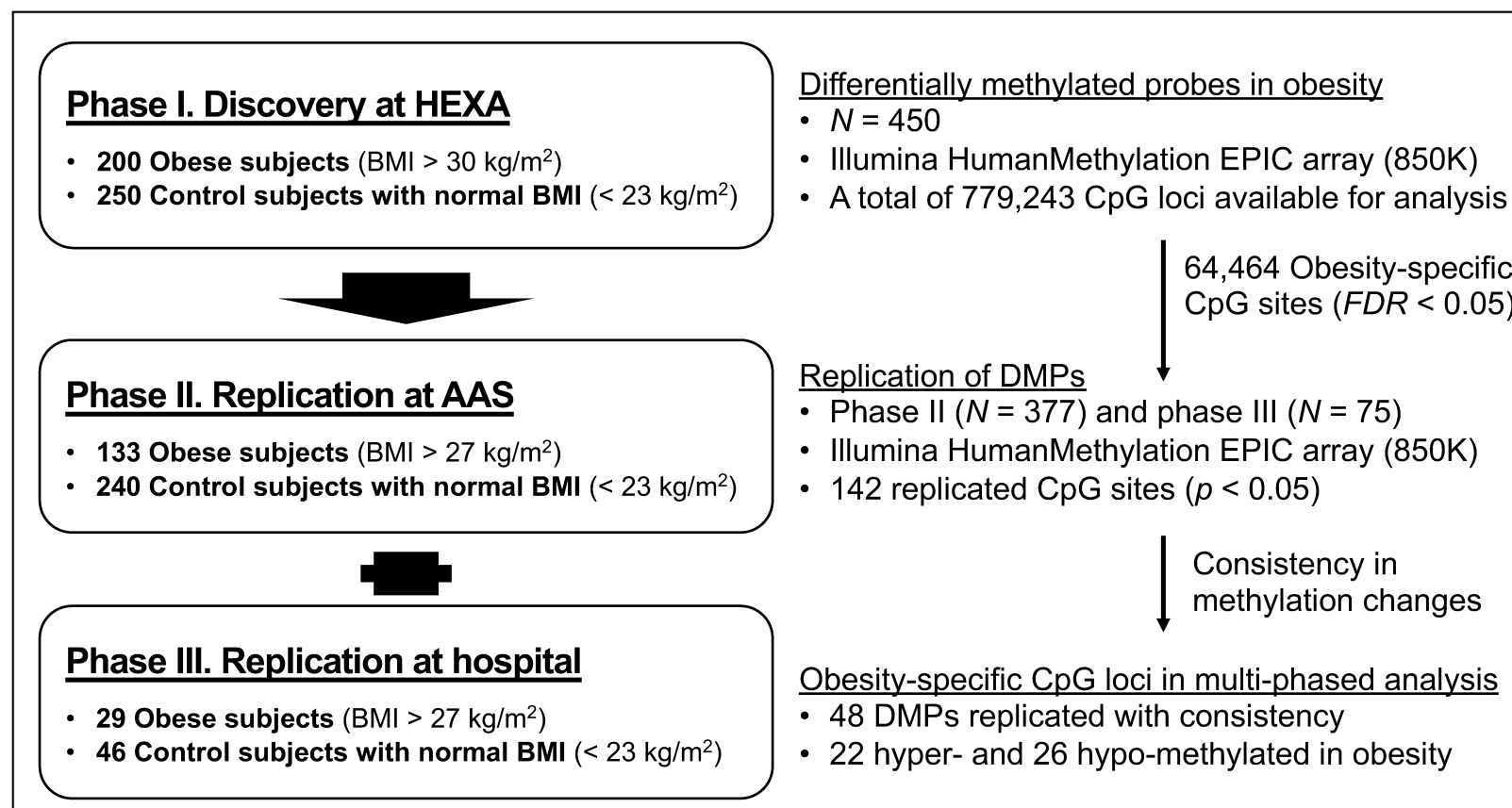
Figure S3. Volcano plot of $-\log_{10}(p\text{-value})$ against \log_2 fold change of delta beta value, representing the methylation difference between obese and lean group in phase I analysis ($N = 450$). Circled probes are 48 differentially methylated in multi-phased case-control analyses, with 22 blue circles indicating probes showing correlations in DMP-DEG analysis, including 7 probes with differences in both blood and fat tissue (red-filled circles).

Figure S4. Annotation of cg13424229 to *CPA3* with schematic representation of GATA1 transcription factor cluster (from ENCODE, gray bar boxed in red) in promoter region, alongside with the obesity-DMP, cg13424229. GATA binding motifs (blue A/TGATAA/G) and two CpG sites (cg13424229: red, cg03020424: green) within GATA1 cluster were highlighted.

Figure S5. A genome-wide map of chromatin state annotations defined for 3 types of cells (adipocytes, pancreatic islets, and renal cells) from histone modification ChIP-seq data generated using ChromHMM. Cell-type specific patterns (Weak repressed Polycomb) for adipocytes were defined. Map was visualized in a UCSC genome browser for *CPA3* with promoter regions including cg13424229 and GATA1 binding motif (chr3: 148,578,436 – 148,616,898). State descriptions for each state with an abbreviation are shown to the right of the chromatin state annotation map.

Figure S6. Relative CPA3 expression in T2d and asthma. Relative gene expression was reanalyzed from GEO data on (A) human islets of T2D case and control (GDS3782) and (B) PBMC during exacerbation and at subsequent convalescence phases of asthma (GDS3615)

Figure S1.



CPA3 (cg13424229)

T2D

EWAS

- 1046 type 2 diabetes and 1288 control subjects
- Illumina HumanMethylation EPIC and 450K arrays

GEO

- Reanalysis of GDS3782 (human pancreatic islets)

OBESITY

DNA methylation and gene expression in fat-isolated cells

- 21 pre-adipocytes and 26 adipocytes including samples from 7 same subjects
- Illumina HumanMethylation 450K array and RNA sequencing (Hiseq)

GEO

- Adipocytes from 19 human and 14 mice
- Reanalysis of GDS3601 (human) and GDS2743 (mice)

CHIPseq

- 3 adipocytes, 4 islets and 5 renal cells for chromHMM state definition
- ChIP-seq for 6 histone modification marks (Hiseq)

Asthma

GEO

- Reanalysis of GDS3615 (human peripheral blood mononuclear cells)

Figure S2.

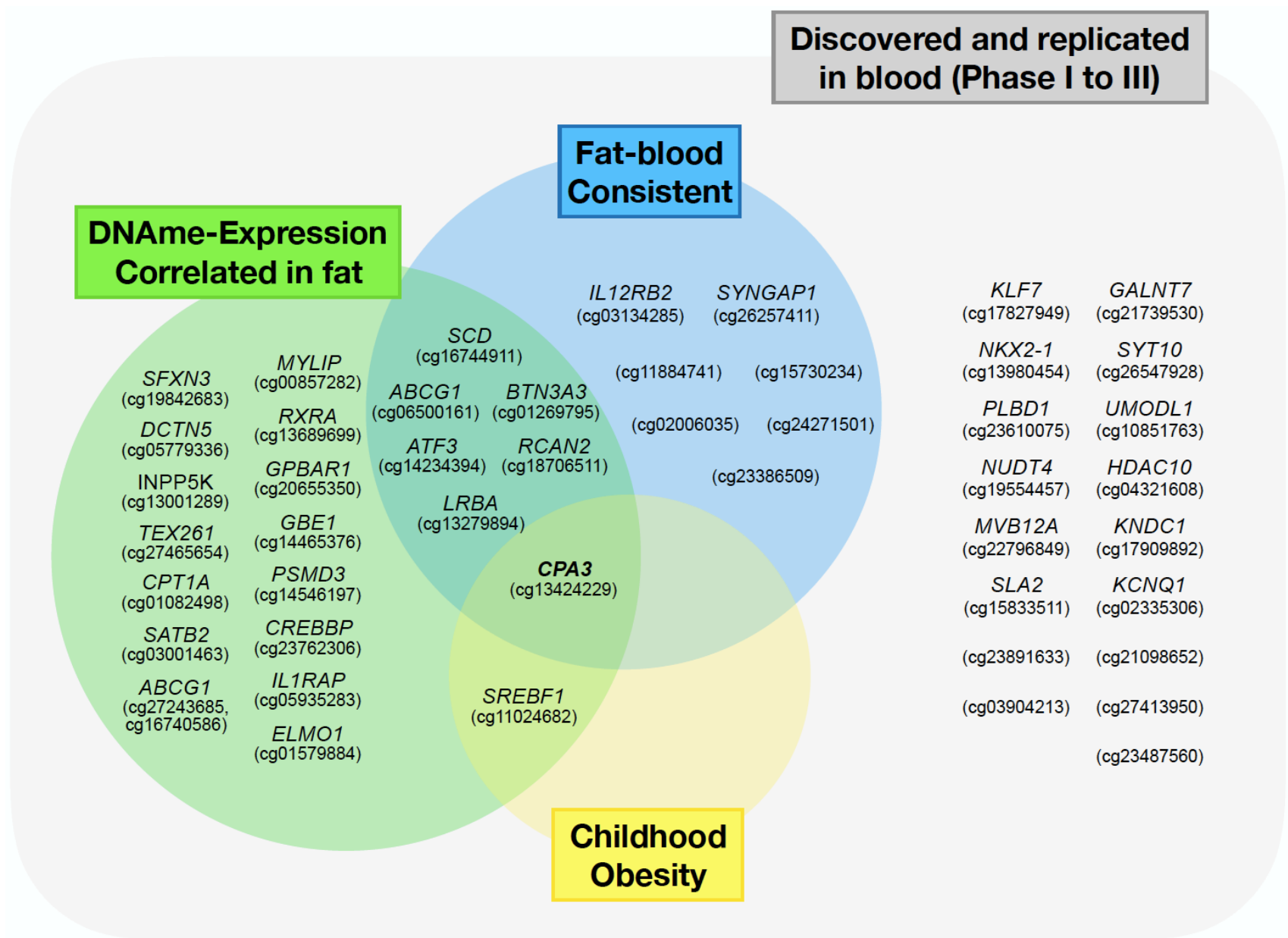


Figure S3.

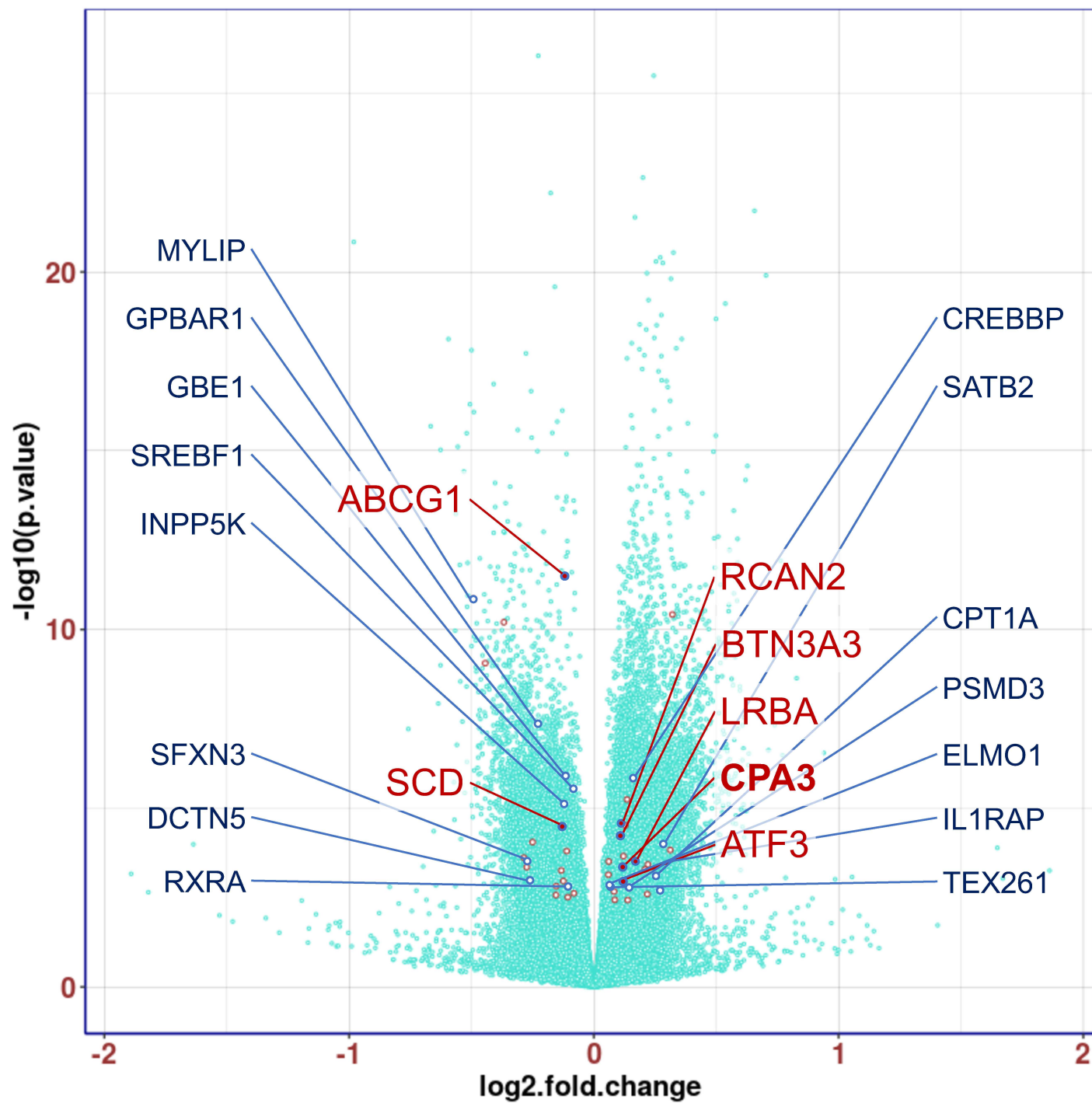
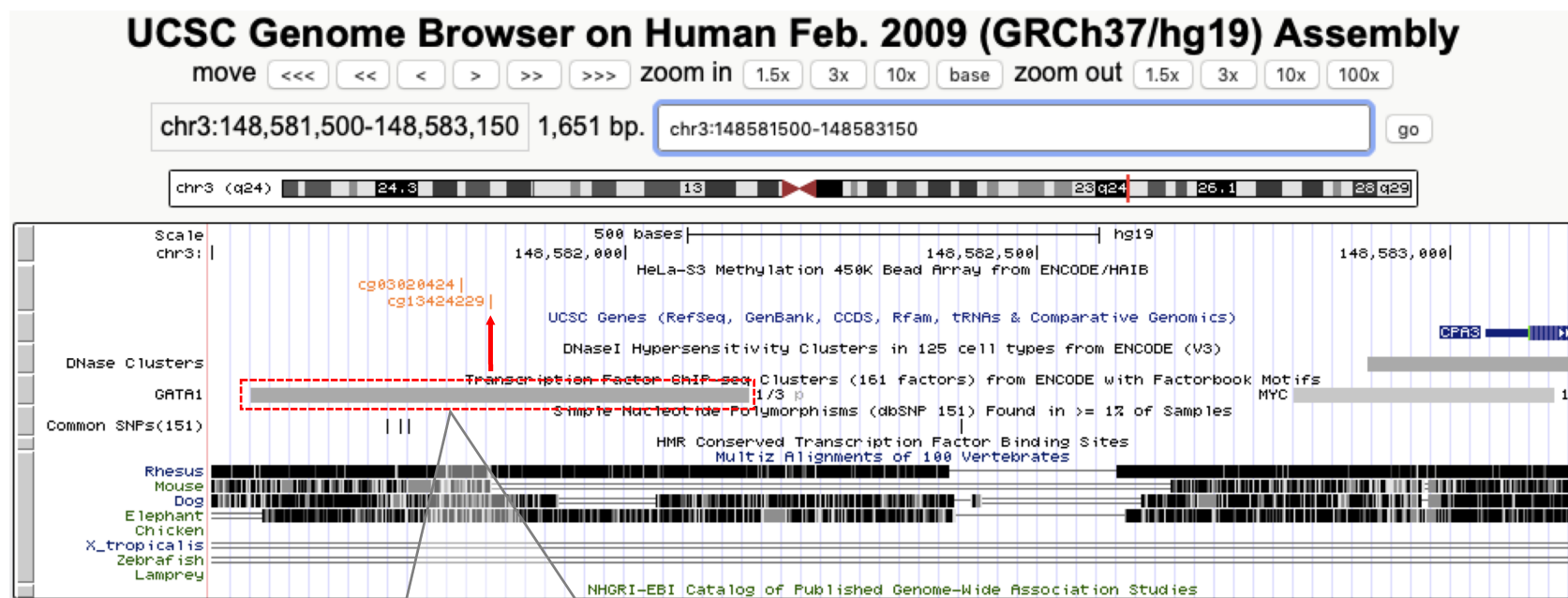


Figure S4.



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(1547) TTTT
(1551) TCACTGTTCC CTGGTCAAAA GTATCTTTAG TCAAAAGCAA TGGAGCAAGC
(1601) ATTTGCTTTG GGAGTTCCTA GTGCTGGTGA GCTTGCCAG TGTCAGAAGC
(1651) ATGAAGGCAT TTGTAAGACC CTCCTCTTCC TTACCTGCAA GGCTGGAGCC
(1701) GGAAAATCCA TTTGGGGAAA TAAAAAAAAG TCCCGAGTTC TACCACACAC
(1751) CCATCAGATA GAGAAGAATG GAATTACTGC TGCTGTATAT ATAACAGGGG
(1801) CGTGTCTCCA ACCACACTAT TTTGATAGTA CATAAGCGTG ACTCTGAGAA
(1851) GTTTTATCTA CAGTCAGCTA TACGTTTGTC AATGTGAAGA GGTGGTTTTT
(1901) AAAAAGGAAA TTCTAATAAG TTAAGTATT AGATAAATTC ACTTACTCTT
(1951) TTAGGTTACC TATGATTCTA GGTAAGGTG TTATTCTCCC ATAATTAACC
(2001) AAGTTGTGTT CAAGACTAAA CATCCCTCCA GAGATGGTTG TGAATGGTCT
(2051) ATAGGTGGCT TTCATTAATT CAACTCTCAA AAGGCATTAT TTGGCAATTA
(2101) CAGCATCCAG GCTCTGAAGA CAGTGTCCA TTAATAAACA TTACAGCATT
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Figure S5.

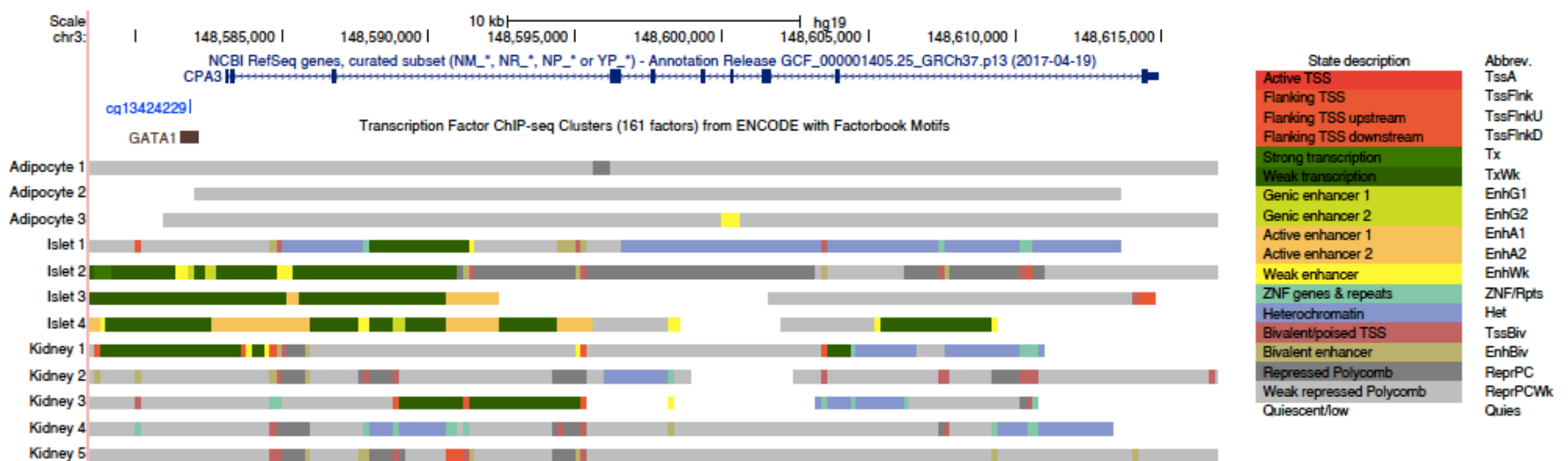


Figure S6.

