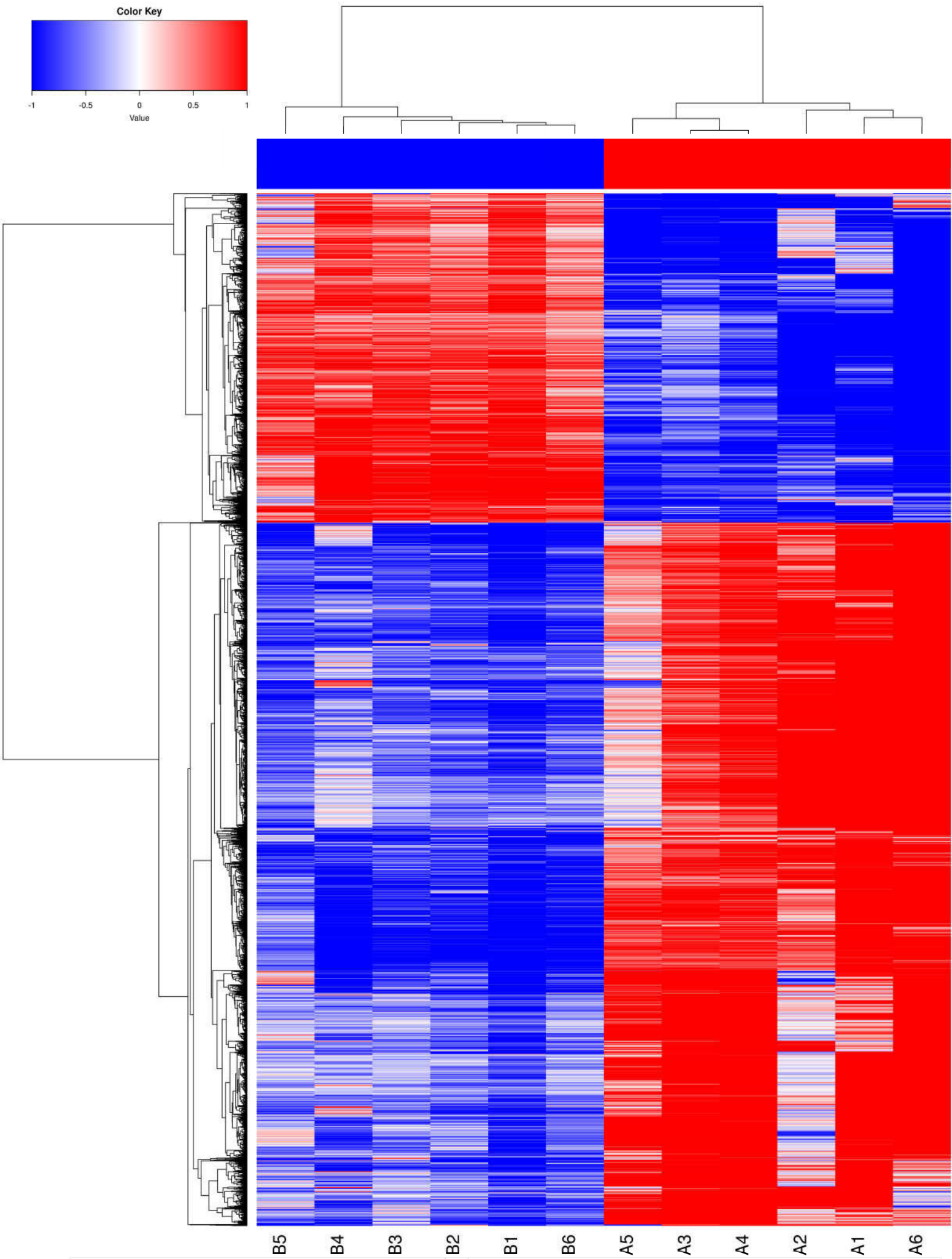
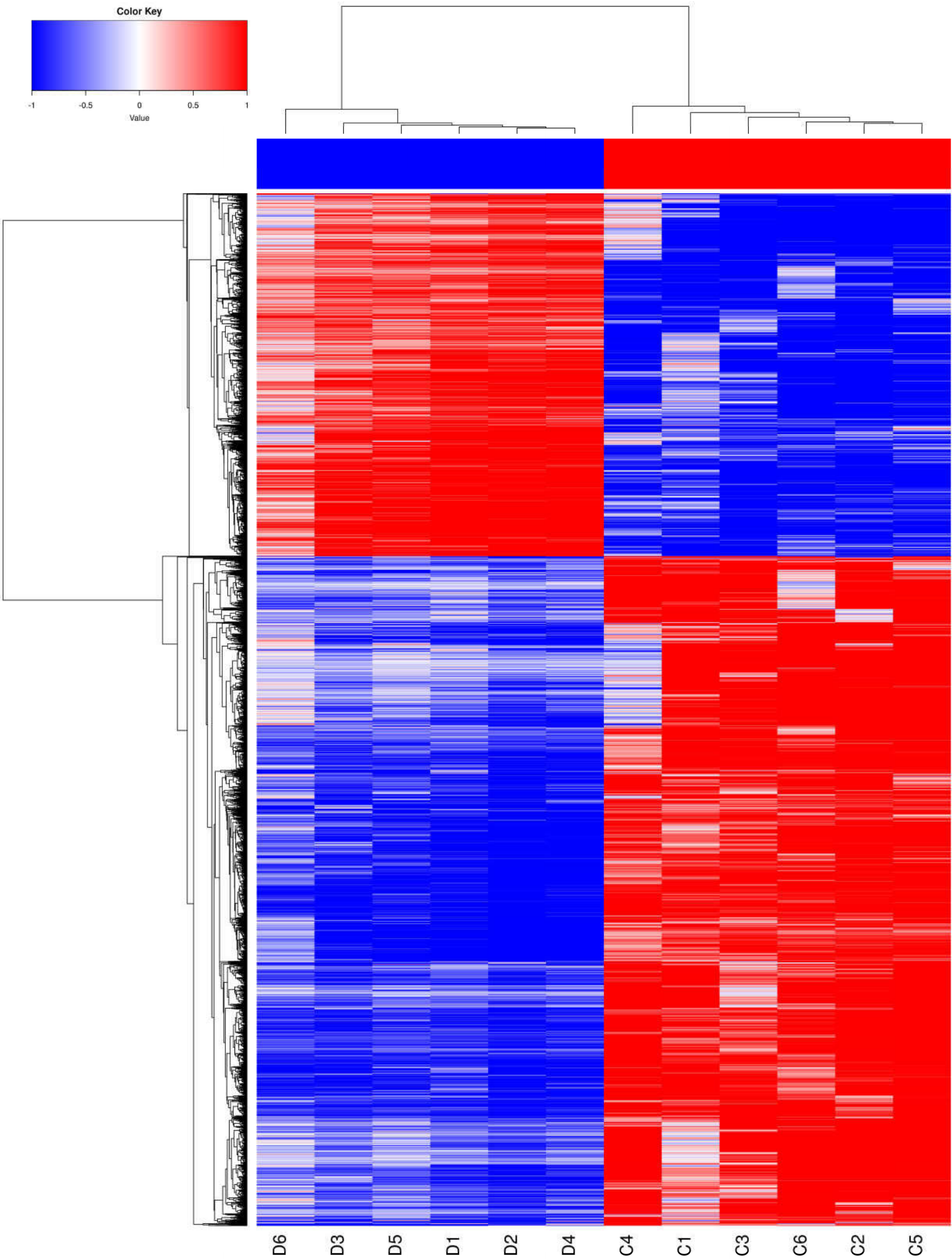


Supplement Figure.1 The chart for total transcript up and down and for the DNA methylation status.



Supplement Figure.2 Heatmaps of differentially methylation positions (DMPs) in both the comparisons. Heatmaps of DMPs for Cpn positive NSCLC vs. Cpn positive adjacent normal (A vs B). "Red" indicates relative hypermethylation, and "Blue" indicates relative hypomethylation.

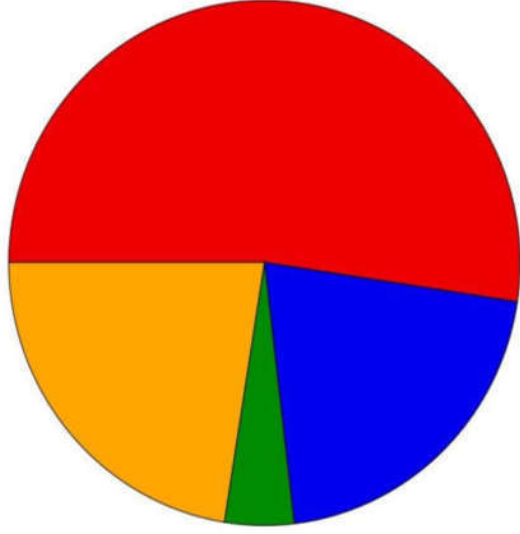


Supplement Figure. 3 Heatmaps of differentially methylated positions (DMPs) in both the comparisons. Cpn negative NSCLC vs. Cpn negative adjacent normal (C vs D) were hierarchically clustered. "Red" indicates relative hypermethylation, and "blue" indicates relative hypomethylation.

Hypermethylated

A Cpn+

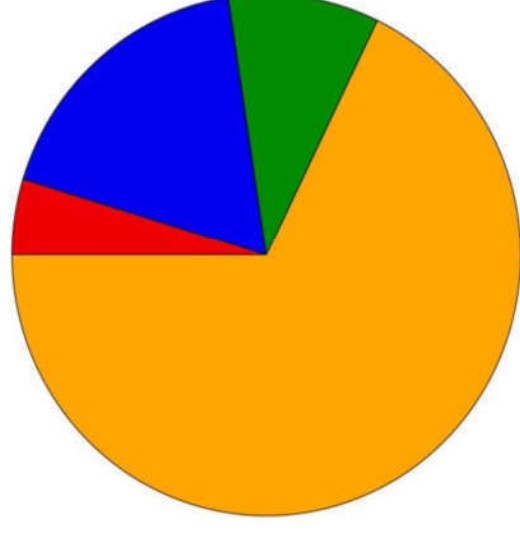
N=3619



Hypomethylated

B Cpn+

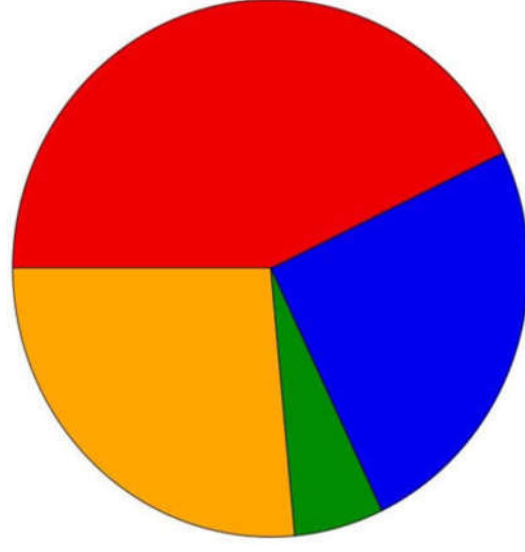
N=1690



Hypermethylated

C Cpn-

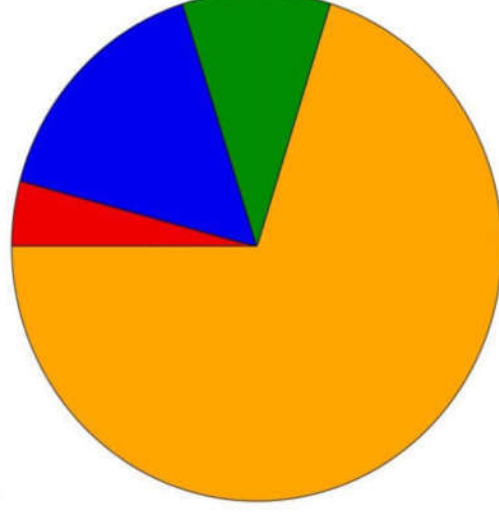
N=4032



Hypomethylated

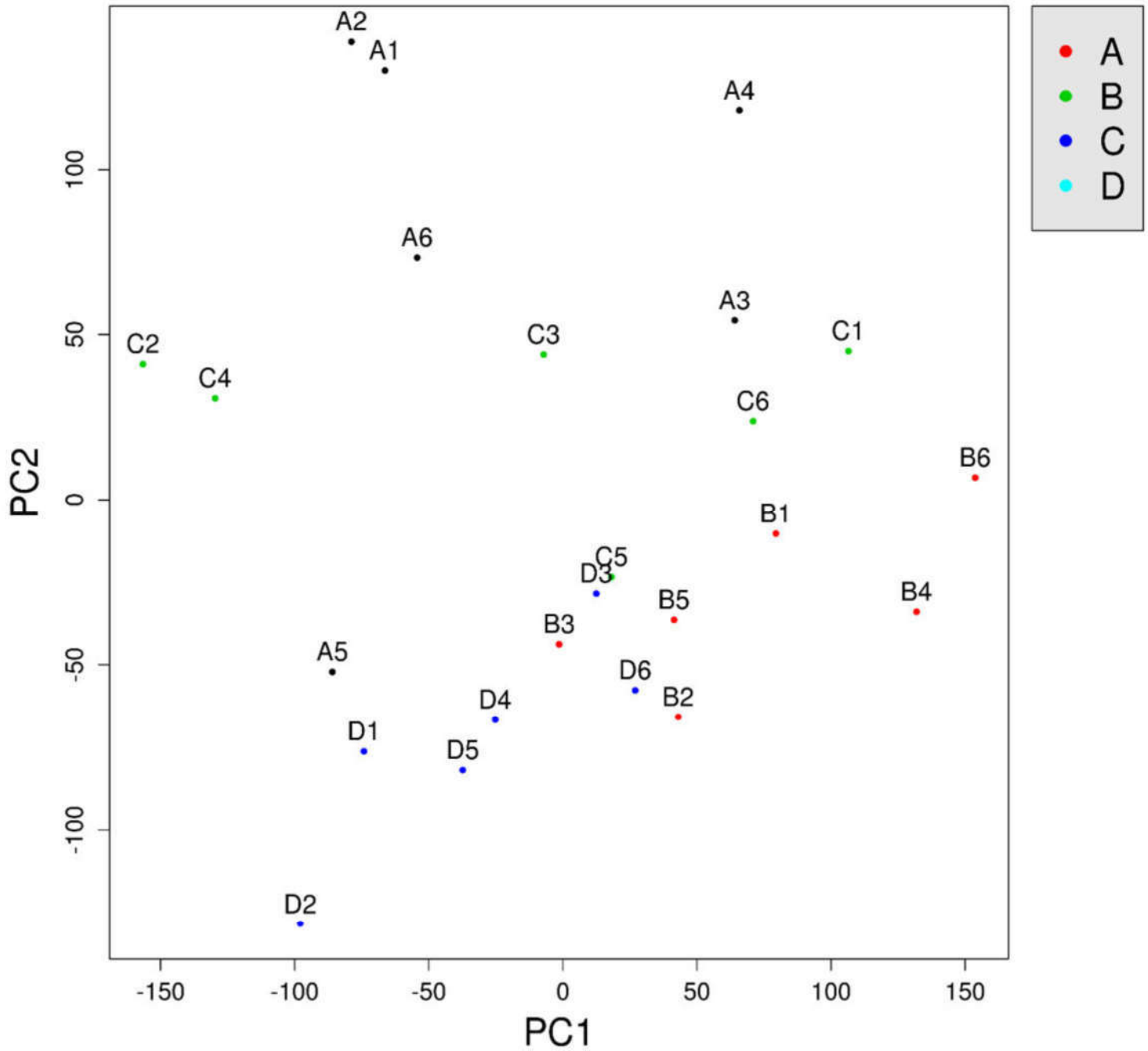
D Cpn-

N=2181

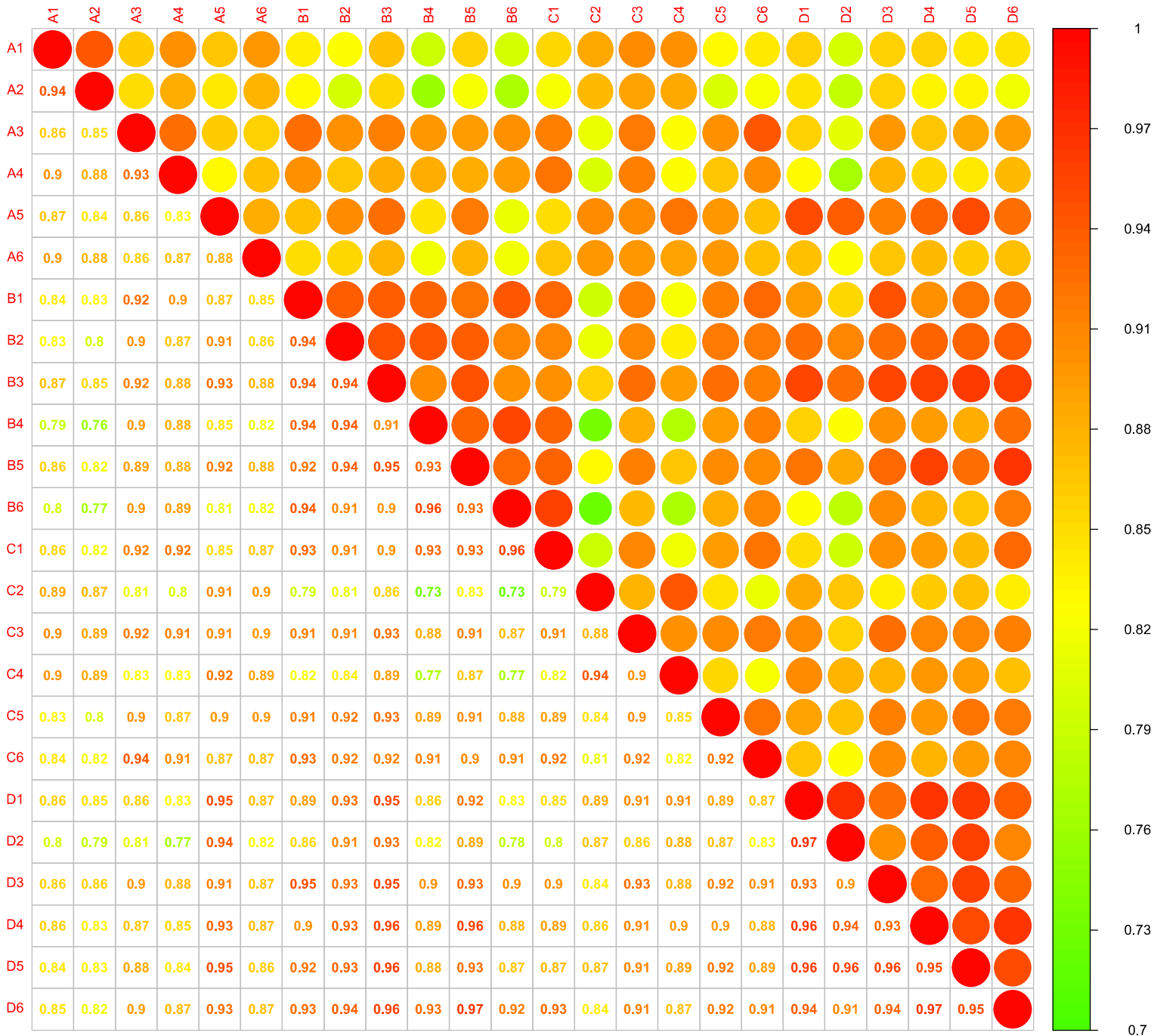


Supplement Figure 4 Distribution of DMPs according region in relation to CpG islands (CGI, shore and shelf (flanking CGIs, 2-4 kb from CGIs), open sea (non-related to CGIs)). (A, B) Differentially hypermethylated and hypomethylated probes of A vs B. (C, D) Differentially hypermethylated and hypomethylated probes of C vs D.

PCA

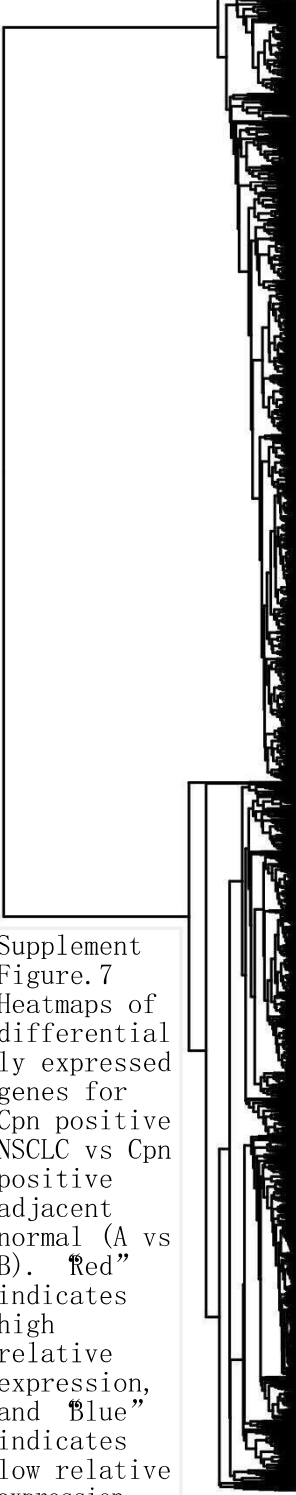
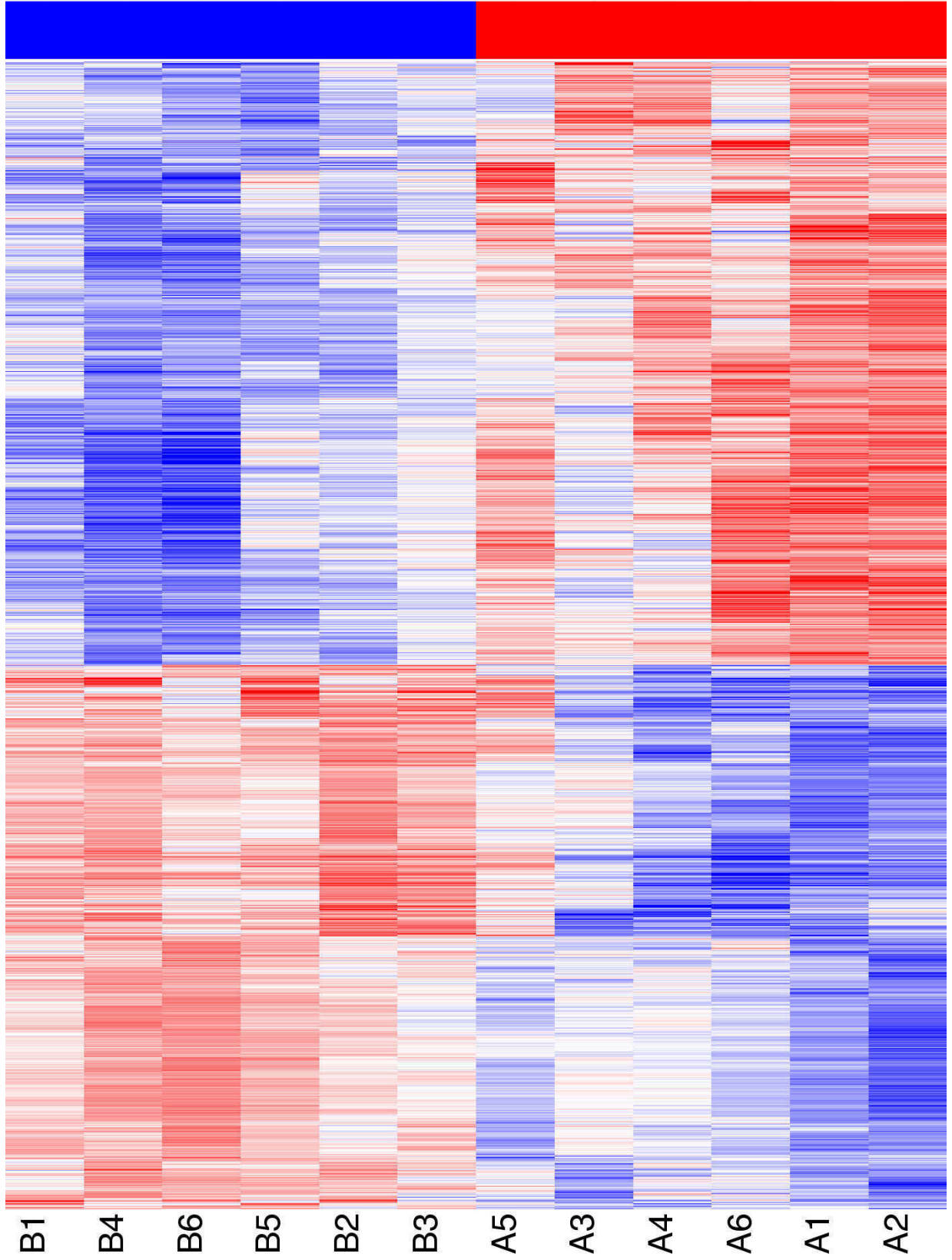
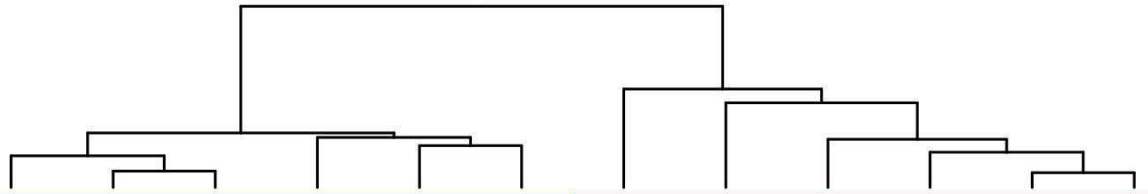
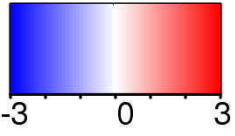


Supplement Figure.5 Principal component analysis (PCA) plots of human gene expression data (x-axis: 35.87%, and y-axis: 21.76%).



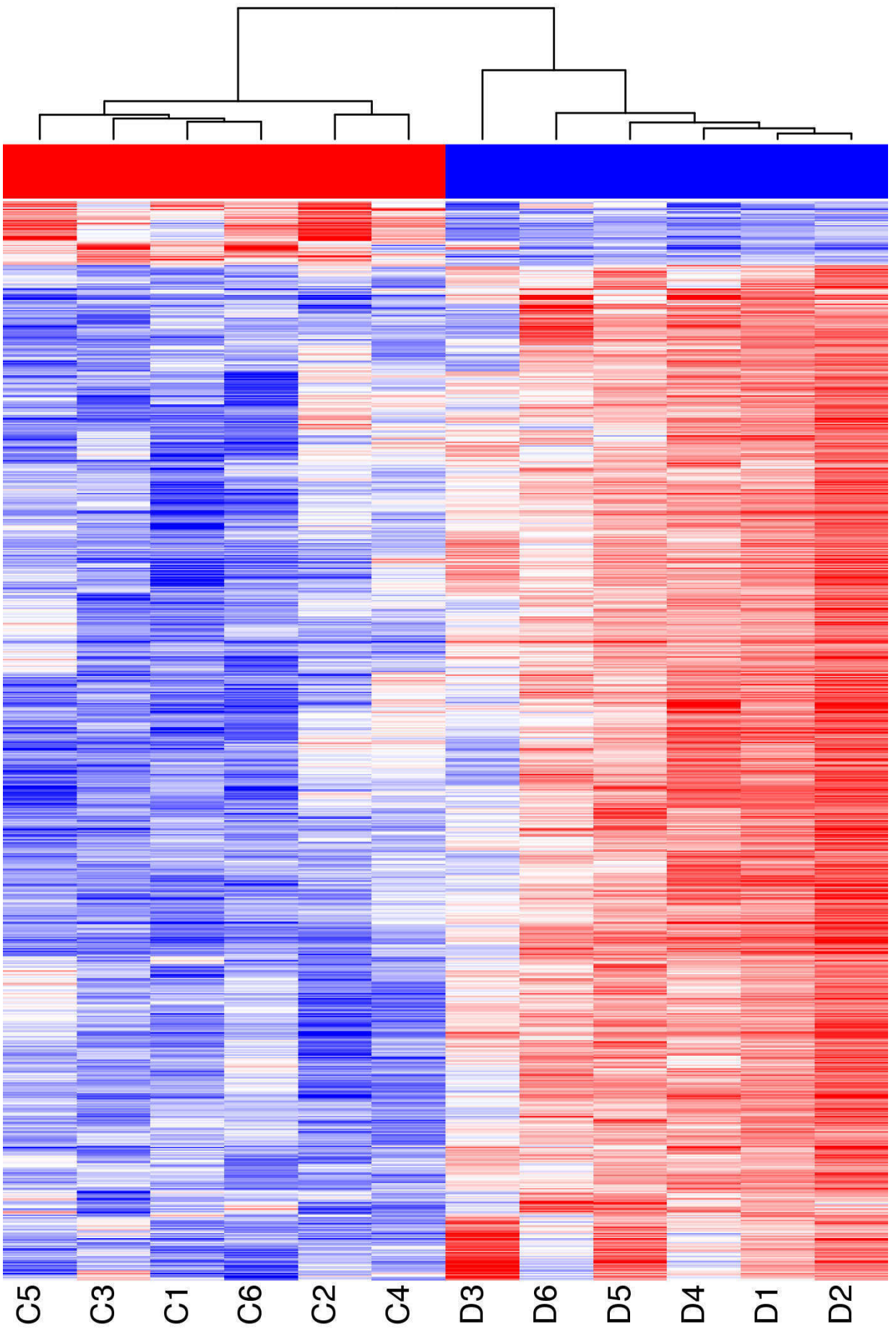
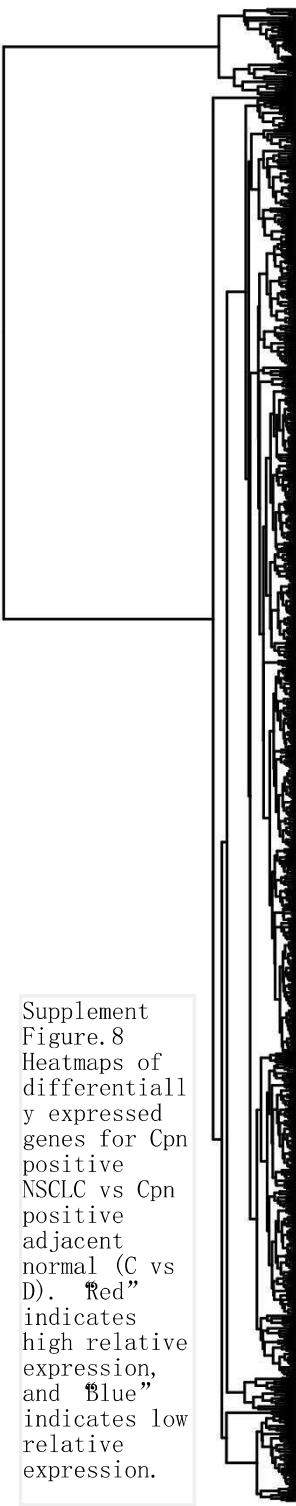
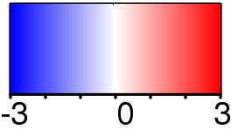
Supplement Figure.6 The relationship between gene expression profiles of all lung cancer tissues.

Color Key



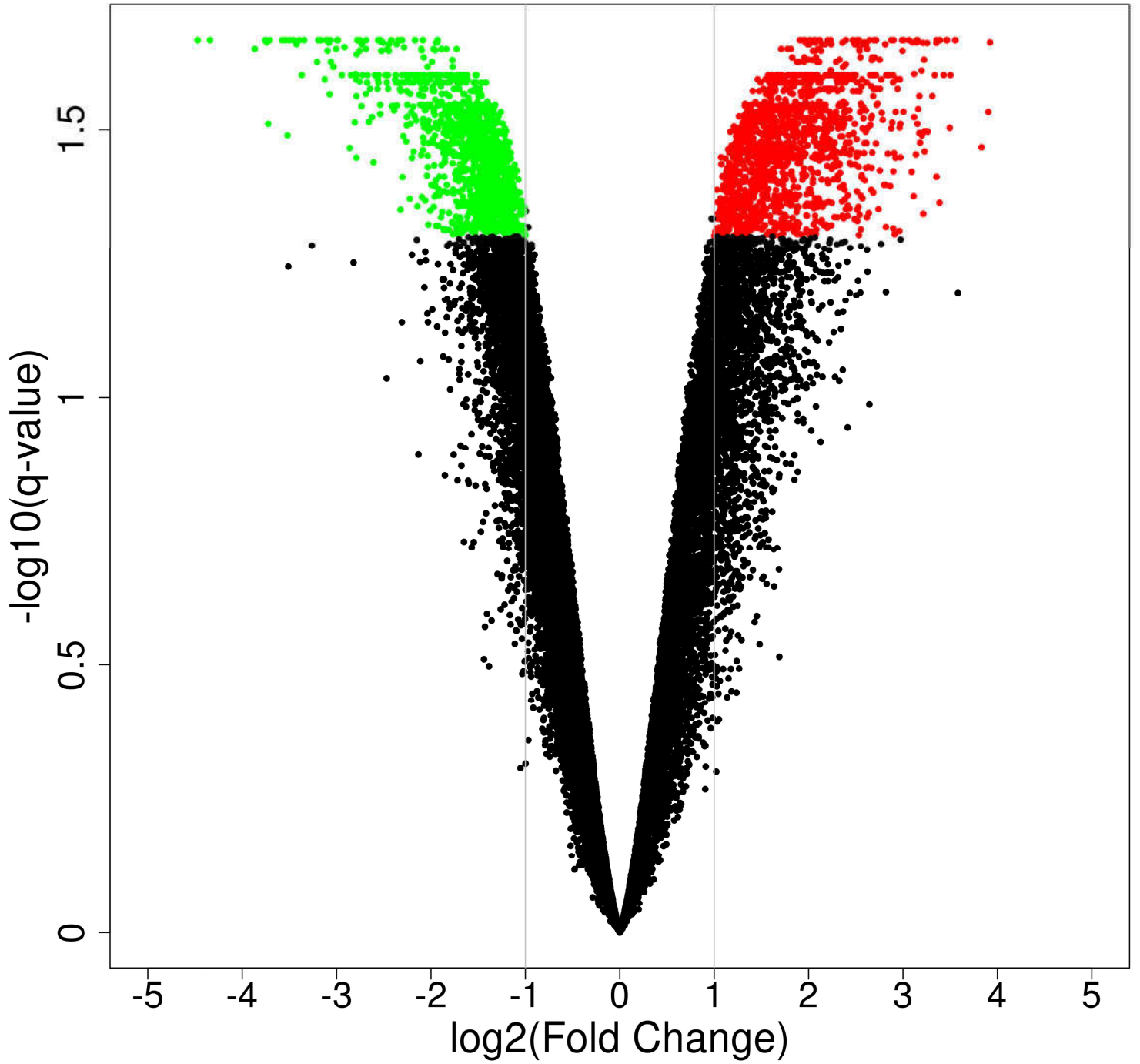
Supplement Figure. 7
Heatmaps of differentially expressed genes for Cpn positive NSCLC vs Cpn positive adjacent normal (A vs B). "Red" indicates high relative expression, and "Blue" indicates low relative expression.

Color Key



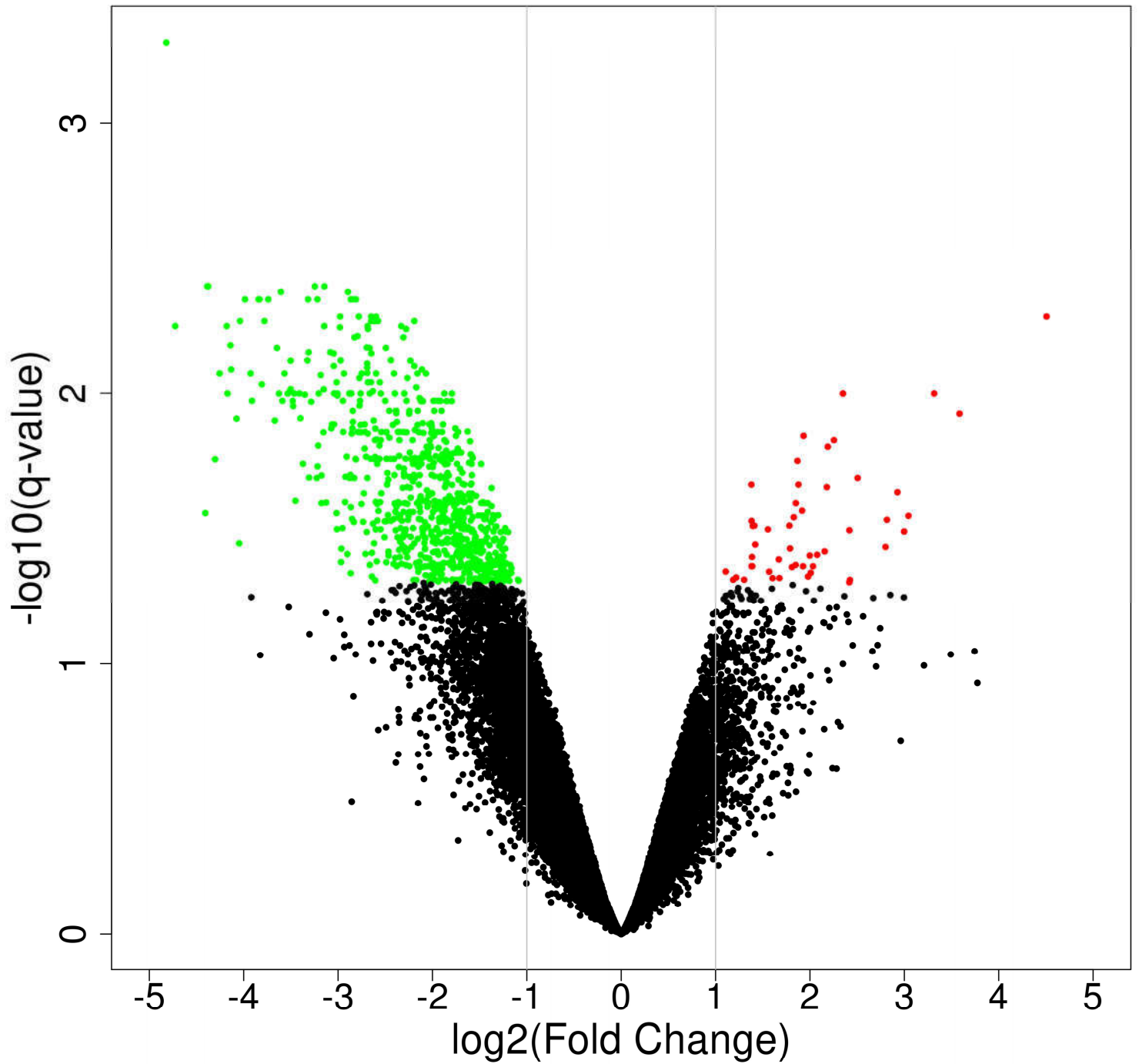
Supplement Figure. 8
Heatmaps of differentially expressed genes for Cpn positive NSCLC vs Cpn positive adjacent normal (C vs D). "Red" indicates high relative expression, and "Blue" indicates low relative expression.

A vs B



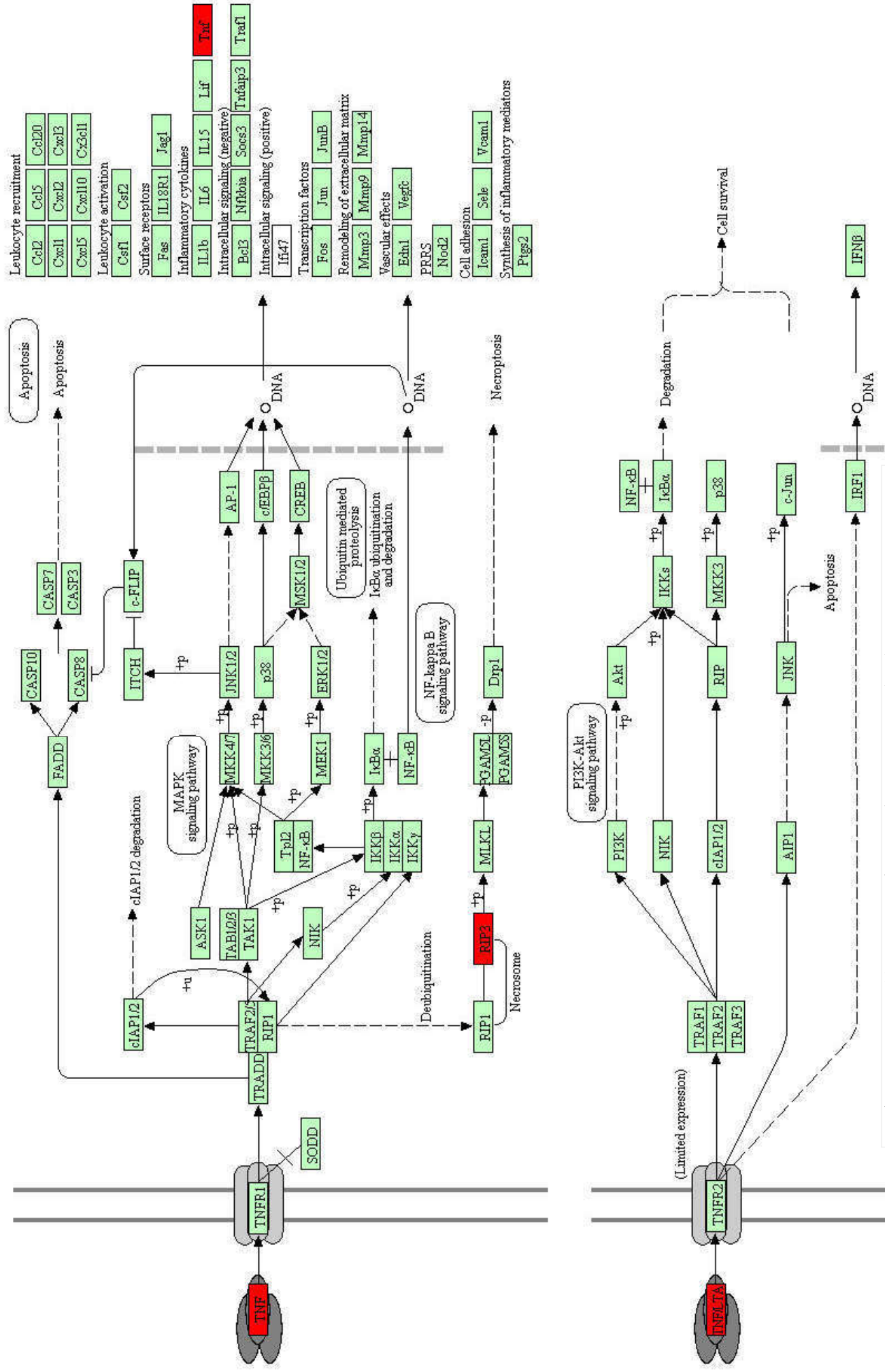
Supplement Figure.9 Volcano plots of gene expression differences in A vs B.

C vs D



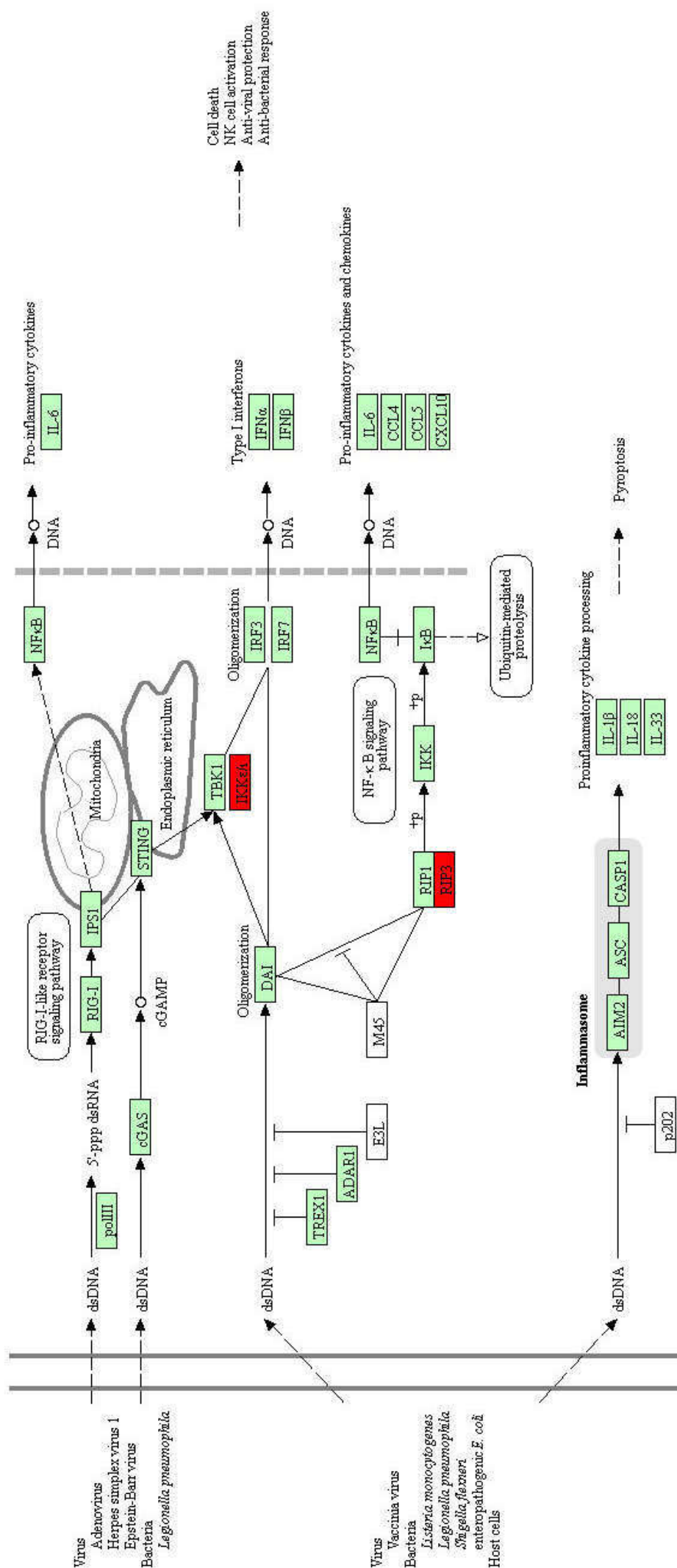
Supplement Figure.10 Volcano plots of gene expression differences in C vs D.

TNF SIGNALING PATHWAY



Supplement Figure.11 TNF signaling pathway in KEGG database.

CYTOSOLIC DNA-SENSING PATHWAY

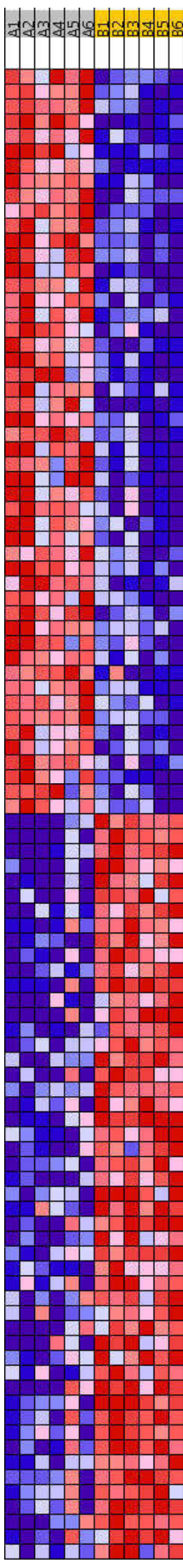


Supplement Figure. 12 Cytosolic DNA-sensing pathway in KEGG database.



Supplement Figure.13 The Heat map and gene list correlation profile in the dataset for the comparison of A vs B by GSEA.

| SampleName | Gene | Description |
|--------------|-----------|---|
| TUBB3 | TUBB3 | tubulin, beta 3 |
| SPP1 | SPP1 | secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1) |
| NKX2-4 | NKX2-4 | NK2 transcription factor related, locus 4 (Drosophila) |
| UBE2U | UBE2U | ubiquitin-conjugating enzyme E2U (putative) |
| MND1 | MND1 | meiotic nuclear divisions 1 homolog (S. cerevisiae) |
| ARNTL2 | ARNTL2 | aryl hydrocarbon receptor nuclear translocator-like 2 |
| HCN1 | HCN1 | hyperpolarization activated cyclic nucleotide-gated potassium channel 1 |
| ANLN | ANLN | anillin, actin binding protein |
| OR11H6 | OR11H6 | olfactory receptor, family 11, subfamily H, member 6 |
| SCG5 | SCG5 | secretogranin V (7B2 protein) |
| FAP | FAP | fibroblast activation protein, alpha |
| KIF14 | KIF14 | kinesin family member 14 |
| LOC100131654 | | |
| PITX1 | PITX1 | paired-like homeodomain transcription factor 1 |
| COL1A1 | COL1A1 | collagen, type I, alpha 1 |
| TTK | TTK | TTK protein kinase |
| TIFAB | TIFAB | - |
| FAM83B | FAM83B | family with sequence similarity 83, member B |
| MELK | MELK | maternal embryonic leucine zipper kinase |
| FGF11 | FGF11 | fibroblast growth factor 11 |
| DDX53 | DDX53 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 53 |
| CTLP | CTLP | cartilage intermediate layer protein, nucleotide pyrophosphohydrolase |
| TCN1 | TCN1 | transcobalamin I (vitamin B12 binding protein, R binder family) |
| CEP55 | CEP55 | centrosomal protein 55kDa |
| LHX5 | LHX5 | LIM homeobox 5 |
| ZNF404 | ZNF404 | zinc finger protein 404 |
| TRIM59 | TRIM59 | tripartite motif-containing 59 |
| KIF20A | KIF20A | kinesin family member 20A |
| LTNC01521 | | |
| LOC283028 | LOC283028 | - |
| MEX3A | | |
| BUB1 | BUB1 | BUB1 budding uninhibited by benzimidazoles 1 homolog (yeast) |
| CLSPN | CLSPN | claspin homolog (Xenopus laevis) |
| SGOL2 | SGOL2 | shugoshin-like 2 (S. pombe) |
| RAB26 | RAB26 | RAB26, member RAS oncogene family |
| LOC100996813 | | |
| BRIP1 | BRIP1 | BRC1 interacting protein C-terminal helicase 1 |
| SEMA7A | SEMA7A | semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group) |
| GTSE1 | GTSE1 | G-2 and S-phase expressed 1 |
| CTHRC1 | CTHRC1 | collagen triple helix repeat containing 1 |
| LRRN1 | LRRN1 | leucine rich repeat neuronal 1 |
| FAM150A | | |
| CDH3 | CDH3 | cadherin 3, type 1, P-cadherin (placental) |
| MC2R | MC2R | melanocortin 2 receptor (adrenocorticotrophic hormone) |
| LY6D | LY6D | lymphocyte antigen 6 complex, locus D |
| LOC100128529 | | |
| TMEM158 | TMEM158 | transmembrane protein 158 |
| LOC100129516 | | |
| CENPM | CENPM | centromere protein M |
| CXCL14 | CXCL14 | chemokine (C-X-C motif) ligand 14 |
| C20RF40 | C20RF40 | chromosome 2 open reading frame 40 |
| ADAMTS8 | ADAMTS8 | ADAM metalloproteinase with thrombospondin type 1 motif, 8 |
| ETGF | ETGF | c-fos induced growth factor (vascular endothelial growth factor D) |
| CSE3 | CSE3 | colony stimulating factor 3 (granulocyte) |
| SLC7A2 | SLC7A2 | solute carrier family 7 (cationic amino acid transporter, y+ system), member 2 |
| SYNM | | |
| FAM13C | | |
| ITLN2 | ITLN2 | intelectin 2 |
| WASF3 | WASF3 | WAS protein family, member 3 |
| GRIA1 | GRIA1 | glutamate receptor, ionotropic, AMPA 1 |
| ANKRD1 | ANKRD1 | ankyrin repeat domain 1 (cardiac muscle) |
| ADRB1 | ADRB1 | adrenergic, beta-1-, receptor |
| AKAP6 | AKAP6 | A kinase (PRKA) anchor protein 6 |
| RSP04 | RSP04 | R-spondin family, member 4 |
| PDE8B | PDE8B | phosphodiesterase 8B |
| ITIH5 | ITIH5 | inter-alpha (globulin) inhibitor H5 |
| MYCT1 | MYCT1 | myc target 1 |
| BMP2 | BMP2 | bone morphogenetic protein 2 |
| ATP1A2 | ATP1A2 | ATPase, Na+/K+ transporting, alpha 2 (+) polypeptide |
| HSPB7 | HSPB7 | heat shock 27kDa protein family, member 7 (cardiovascular) |
| IL20RA | IL20RA | interleukin 20 receptor, alpha |
| SLC39A8 | SLC39A8 | solute carrier family 39 (zinc transporter), member 8 |
| SIK3 | | |
| PIP5K1B | PIP5K1B | phosphatidylinositol-4-phosphate 5-kinase, type I, beta |
| RAMP2 | RAMP2 | receptor (calcitonin) activity modifying protein 2 |
| SLC6A1 | SLC6A1 | solute carrier family 6 (neurotransmitter transporter, GABA), member 1 |
| LONRF1 | LONRF1 | LON peptidase N-terminal domain and ring finger 1 |
| PTH1R | | |
| ADH1B | ADH1B | alcohol dehydrogenase 1B (class I), beta polypeptide |
| RECK | RECK | reversion-inducing-cysteine-rich protein with kazal motifs |
| ANKRD29 | ANKRD29 | ankyrin repeat domain 29 |
| TGFBR3 | TGFBR3 | transforming growth factor, beta receptor III (betaglycan, 300kDa) |
| TCF21 | TCF21 | transcription factor 21 |
| MAMDC2 | MAMDC2 | MAM domain containing 2 |
| IL1RL1 | IL1RL1 | interleukin 1 receptor-like 1 |
| HBEGF | HBEGF | heparin-binding EGF-like growth factor |
| CCDC68 | CCDC68 | coiled-coil domain containing 68 |
| CLEC3B | CLEC3B | C-type lectin domain family 3, member B |
| PRELP | PRELP | proline/arginine-rich end leucine-rich repeat protein |
| MS4A8 | | |
| WFDC1 | WFDC1 | WAP four-disulfide core domain 1 |
| RASIP1 | RASIP1 | Ras interacting protein 1 |
| CLSTN2 | CLSTN2 | calsyntenin 2 |
| SYT11 | SYT11 | synaptotagmin XI |
| ETIBIN | | |
| FHL1 | FHL1 | four and a half LIM domains 1 |
| S1PR1 | | |
| LPL | LPL | lipoprotein lipase |
| GPRASP2 | GPRASP2 | G protein-coupled receptor associated sorting protein 2 |
| AOC3 | AOC3 | amine oxidase, copper containing 3 (vascular adhesion protein 1) |



Supplement Figure.14 The Heat map and gene list correlation profile in the dataset for the comparison of C vs D by GSEA.

| SampleName | Gene | Description |
|------------|--------------|--|
| | SPAG5 | sperm associated antigen 5 |
| | GTSE1 | G-2 and S-phase expressed 1 |
| | PPP2R3B | protein phosphatase 2 (formerly 2A), regulatory subunit B'', beta |
| | KTAA1755 | |
| | IGF2BP1 | insulin-like growth factor 2 mRNA binding protein 1 |
| | KRTAP9-4 | keratin associated protein 9-4 |
| | NHLRC1 | NHL repeat containing 1 |
| | MYO7A | myosin VIIA |
| | CLSPN | claspin homolog (Xenopus laevis) |
| | CDH3 | cadherin 3, type 1, P-cadherin (placental) |
| | ACTL10 | |
| | DPEP1 | dipeptidase 1 (renal) |
| | CTF18 | CTF18, chromosome transmission fidelity factor 18 homolog (S. cerevisiae) |
| | E4F1 | E4F transcription factor 1 |
| | FBXO27 | F-box protein 27 |
| | BCAS4 | breast carcinoma amplified sequence 4 |
| | B4GALNT3 | beta-1,4-N-acetyl-galactosaminyl transferase 3 |
| | GEER | growth factor, augmenter of liver regeneration (ERV1 homolog, S. cerevisiae) |
| | FGF8 | fibroblast growth factor 8 (androgen-induced) |
| | SPPL2C | |
| | LOC400965 | LOC400965 - |
| | C16ORF46 | chromosome 16 open reading frame 46 |
| | CD79B | CD79b molecule, immunoglobulin-associated beta |
| | SHIM1 | |
| | COL8A2 | collagen, type VIII, alpha 2 |
| | ANKRD23 | ankyrin repeat domain 23 |
| | IKBKE | inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon |
| | DMBX1 | diencephalon/mesencephalon homeobox 1 |
| | FAAH | fatty acid amide hydrolase |
| | TMEM198 | |
| | NHS | Nance-Horan syndrome (congenital cataracts and dental anomalies) |
| | DNASE1L2 | deoxyribonuclease I-like 2 |
| | B4GALNT4 | beta-1,4-N-acetyl-galactosaminyl transferase 4 |
| | SNORA76C | |
| | EBI3 | Epstein-Barr virus induced gene 3 |
| | PRR22 | |
| | INCENP | inner centromere protein antigens 135/155kDa |
| | GALE | UDP-galactose-4-epimerase |
| | KLK4 | kallikrein 4 (protease, enamel matrix, prostate) |
| | P2RY6 | pyrimidinergic receptor P2Y, G-protein coupled, 6 |
| | FAM19A5 | family with sequence similarity 19 (chemokine (C-C motif)-like), member A5 |
| | CHAF1A | chromatin assembly factor 1, subunit A (p150) |
| | ZNF750 | zinc finger protein 750 |
| | LTBR | lymphotoxin beta receptor (TNFR superfamily, member 3) |
| | LOC100132363 | |
| | LOC155060 | |
| | GP1BA | glycoprotein Ib (platelet), alpha polypeptide |
| | IGKV1D-13 | immunoglobulin kappa variable 1D-13 |
| | CACNG1 | calcium channel, voltage-dependent, gamma subunit 1 |
| | TNFRSF18 | tumor necrosis factor receptor superfamily, member 18 |
| | CST11 | cystatin 11 |
| | DHRS4-AS1 | |
| | COX18 | COX18 cytochrome c oxidase assembly homolog (S. cerevisiae) |
| | PNPLA4 | patatin-like phospholipase domain containing 4 |
| | LOC100128571 | |
| | C20RF40 | chromosome 2 open reading frame 40 |
| | LGALS13 | lectin, galactoside-binding, soluble, 13 (galectin 13) |
| | ANKRD29 | ankyrin repeat domain 29 |
| | SPATA8 | spermatogenesis associated 8 |
| | CYB5R1 | cytochrome b5 reductase 1 |
| | LOC100131032 | |
| | CLDN18 | claudin 18 |
| | OR8B4 | olfactory receptor, family 8, subfamily B, member 4 |
| | LOC100131822 | |
| | TAC3 | tachykinin 3 (neuromedin K, neurokinin beta) |
| | TAGLN3 | transgelin 3 |
| | FABP4 | fatty acid binding protein 4, adipocyte |
| | ADAMTS8 | ADAM metalloproteinase with thrombospondin type 1 motif, 8 |
| | MAGEA9 | melanoma antigen family A, 9 |
| | MT1M | metallothionein 1M |
| | MPP7 | membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7) |
| | EDDM3A | |
| | LEUTX | |
| | HBB | hemoglobin, beta |
| | LOC101929412 | |
| | ADH1B | alcohol dehydrogenase 1B (class I), beta polypeptide |
| | KIR3DX1 | killer cell immunoglobulin-like receptor, three domains, X1 |
| | PAQR5 | progesterin and adipoQ receptor family member V |
| | ZNF536 | zinc finger protein 536 |
| | SMYD1 | SET and MYND domain containing 1 |
| | RSP01 | R-spondin homolog (Xenopus laevis) |
| | FIGF | c-fos induced growth factor (vascular endothelial growth factor D) |
| | BANF2 | |
| | FANCD20S | |
| | FLJ45743 | FLJ45743 - |
| | IP6K3 | |
| | HS3ST4 | heparan sulfate (glucosamine) 3-O-sulfotransferase 4 |
| | LOC102723456 | |
| | ZNF177 | zinc finger protein 177 |
| | ADH1A | alcohol dehydrogenase 1A (class I), alpha polypeptide |
| | GKN2 | |
| | DPYSL2 | dihydropyrimidinase-like 2 |
| | PLLP | plasma membrane proteolipid (plasmalipin) |
| | CDH20 | cadherin 20, type 2 |
| | TIMP3 | TIMP metalloproteinase inhibitor 3 (Sorsby fundus dystrophy, pseudoinflammatory) |
| | GRIA1 | glutamate receptor, ionotropic, AMPA 1 |
| | PKNOX2 | PBX/knotted 1 homeobox 2 |
| | MROH3P | |
| | BMP2 | bone morphogenetic protein 2 |
| | PRR5L | |