

Radiation-Induced 3D Genome Structure Reorganization Regulates Gene Transcription

Supplementary File

S1. Methods and materials

S1.1. High-throughput chromosome conformation capture (Hi-C) data processing

S1.1.1. Interaction decay exponent (IDE) analysis

Hi-C data were standardized according to the bin using HiC-Pro v2.10.0 software, and the relationship between contact frequency and linear genome distance was calculated using HiCdat^[1]. The slope of the model corresponds to IDE.

S1.1.2. Three-dimensional (3D) structure simulation

The multidimensional scaling (MDS) algorithm within Pastis software was employed to simulate the 3D location of chromatin. The protein data bank files were generated based on Poisson distribution and PyMOL software to visualize the 3D structures.

S1.1.3. Compartment analysis

First, the Z scores of the contact matrices at 100 kb resolution were generated as described previously^[2], and Pearson correlation of the Z score matrices was calculated. Principal component analysis was performed at a resolution of 100 kb using HOMER^[3] with HiTC v1.24.0 software^[4]. DNA segments with positive first principal component (PC1) value were defined as compartment A, while those with negative value as compartment B. Genome-wide gene density was calculated to assign A-type and B-type compartmentalization.

S1.1.4. Topologically associating domains (TADs) and TAD boundaries

Normalized contact matrix was used to identify the TAD units as previously^[5]. Directionality index (DI) was calculated from upstream 2 Mb to downstream 2Mb along the center of each bin at 40-kb resolution. We used the same criteria of 400 kb to distinguish unorganized chromatin from topological boundaries. Boundary correlation between samples was performed as previously described^[5]. To identify the TAD boundaries, we first normalized the DI scores. We, then, merged the center positions of the boundaries in two samples and calculated the DIs; DI delta scores were calculated for each TAD boundary. Significantly different TAD boundaries were identified with false discovery rate (FDR) < 0.01, $P < 0.05$, and not all DI delta scores in both samples were greater than 200.

S1.1.5. Loop identification

Loop community detection was determined through the improved Hi-C computational unbiased peak search (HiCCUPS) method^[6,7]. The interaction patterns across all loop regions were aggregated, and the overlap of loops was removed with the methods described by Zhang *et al.*^[7] to identify the differences between samples. Original interaction values of non-overlapping loops in every sample were regarded as the input of edgeR v3.8.6^[8]. Significantly different loops were determined with FDR < 0.01, $P < 0.05$, and fold change (FC) > 2.

S1.1.6. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses

GO enrichment analysis was carried out using the cluster Profiler R software package. We used the KEGG Orthology-Based Annotation System (KOBAS)^[9] software to test the statistical enrichment of differentially expressed genes (DEGs) in KEGG pathways. We used cluster Profiler R packages to identify significantly enriched KEGG pathways compared to the entire genome background.

S1.2. Ribonucleic acid (RNA) and RNA sequencing (RNA-seq)

The same batch of cells in Hi-C experiment was used for the construction of RNA libraries. According to the manufacturer's instructions, total RNA was extracted from two control and treated cell pairs using TRIzol Reagent (Life Technologies, California, USA). Messenger RNA (mRNA) was isolated with NEBNext Poly(A) mRNA Magnetic Isolation Module (NEB, E7490). Strand-specific RNA libraries were prepared according to the manufacturer's instructions of NEBNext Ultra RNA Library Prep Kit for Illumina (NEB, E7530) and NEBNext Multiplex Oligos for Illumina (NEB, E7500). The constructed cDNA libraries were, then, sequenced on a flow cell using the Illumina HiSeq™ sequencing platform (Biomarker Technologies Corporation, Beijing, China), generating a total of ~27.34 Gb data (Tables S1 and S6).

High-quality clean reads were obtained by removing reads with > 10 nt aligned to the adaptor, or low-quality reads containing over 10% uncalled bases (Ns) or including over 50% of bases with base quality scores less than five. The

remaining clean reads were aligned to the human reference genome (GRCh38/hg38) using HISAT2^[10]. StringTie and Cufflinks were used to quantify gene expression^[11]. Only protein-coding genes with fragments per kilobase of exon per million mapped fragments (FPKM) > 0.5 in at least one of the samples were kept for subsequent analyses. The DEGs software was applied to detect DEGs based on the read count produced by HTSeq^[12]. Genes with $P < 0.001$ and Benjamini-adjusted $P < 0.05$ were identified as DEGs.

S1.3. Functional enrichment analysis

The Enrichr Web server (<http://amp.pharm.mssm.edu/Enrichr/>) was used to perform gene functional enrichment analysis of Gene Ontology and KEGG pathway categories^[13,14]. Only GO biological processes, GO molecular function, GO cellular component, and KEGG pathways with adjusted $P < 0.05$ and combined score > 10 were considered to be significant and were retained in the list.

S2. Tables and data

Table S1. Primer sequence used in this study

| Gene | 5'-3' | 3'-5' |
|----------------|-------------------------|---------------------------|
| <i>GAPDH</i> | AGGTCGGTGTGAACGGATTTG | GGGGTCGTTGATGGCAACA |
| <i>ACTB</i> | CATGTACGTTGCTATCCAGGC | CTCCTTAATGTCACGCACGAT |
| <i>HLA-DOA</i> | CCTACGGACCCGCCTTCTA | GGCCTCGCTTTTCTTCAGG |
| <i>HLA-DMA</i> | CCTGCACACAGTGTACTGC | CACCCGAGTGTTCTGGGAA |
| <i>HLA-DMB</i> | ACCTGTCTGTTGGATGATGCT | CGCAAGGGGCCATCTTATTCT |
| <i>HLA-DRA</i> | AGTCCCTGTGCTAGGATTTTTCA | ACATAAACTCGCCTGATTGGTC |
| <i>HLA-DPB</i> | TGTCCACCAACCTGATCCGTA | CCACGGTGACAGGACTATCCA |
| <i>HLA-DPA</i> | CAAGGCGGACCATGTGTCAA | GTGGTTGGAACGCTGGATCA |
| <i>CTNNA1</i> | AAATCATTGTGGACCCCTTGAG | TTGCCCATGTACTCCGAAAGC |
| <i>CCL1</i> | CTCTTAGCTTCACCAGGCTCA | GAGAAGGGTACCTGCATGCTCTT |
| <i>CCL3L1</i> | TCTGCAACCAGGTCCTCTCTG | GGCCTCTCTGGTTAGGAAGATGAC |
| <i>CCL8</i> | TCTCATGCTGAAGCTCACACC | GAATGGAAACTGAATCTGGCTG |
| <i>CCL13</i> | GCACTCAACGTCCCATCTACT | GCCCAGTTTGGTTCTGAAGATGA |
| <i>CCL14</i> | CCATCCCTTCTTCTCCTCATCAC | GCACTGGCTGTTGGTCTCATAGTAA |

Table S2. Mapping statistics and data quality of Hi-C sequencing

| Bioinformation processing | Sequencing statistics and evaluation | BLK | IR |
|----------------------------------|---|-------------|-------------|
| Sequenced reads | Sequenced total read pairs | 529,978,055 | 517,942,537 |
| | High-quality read pairs | 514,714,687 | 504,424,237 |
| | GC (%) | 48 | 47 |
| Library evaluation | Truncated reads | 273,369,756 | 274,531,436 |
| Alignment | Unique mapped reads | 416,396,869 | 405,764,414 |
| Filtering | | | |
| Valid interaction pairs | Valid interaction pairs | 390,355,225 | 381,267,371 |
| | Valid interaction pairs (%) | 94 | 94 |
| Invalid interaction pairs | Self-circle ligation | 111,132 | 101,372 |
| | Dangling ends | 7,108,534 | 6,380,564 |
| | Re-ligation | 4,108,487 | 3,716,059 |
| PCR duplicate | | 9,747,634 | 8,951,930 |
| Hi-C contacts | Cis contacts | 321,376,036 | 312,186,895 |
| | Trans contacts | 68,979,189 | 69,080,476 |

PCR: Polymerase chain reaction

Table S3. GO/KEGG analysis of gene related to compartment switched from B to A

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|------------|----------|---------------|----------|----------|---|---|
| GO_BP | GO:0060348 | Bone development | 4/286 | 21/8946 | 5.96 | 0.003982 | 0.594749 | ENSG00000120693/ ENSG00000134253/ ENSG00000145431/ ENSG00000170776 | SMAD9 TRIM45 PDGFC AKAP13 |
| GO_BP | GO:0006921 | Cellular component disassembly involved in execution phase of apoptosis | 3/286 | 12/8946 | 7.82 | 0.00574 | 0.594749 | ENSG00000102010/ ENSG00000138794/ ENSG00000163932 | BMX CASP6 PRKCD |
| GO_BP | GO:0006974 | Cellular response to DNA damage stimulus | 6/286 | 52/8946 | 3.61 | 0.005996 | 0.594749 | ENSG00000129521/ ENSG00000130985/ ENSG00000146872/ ENSG00000147133/ ENSG00000173575/ ENSG00000279765 | EGLN3 UBA1 TLK2 TAF1 CHD2 AC013394.1 |
| GO_BP | GO:0042127 | Regulation of cell proliferation | 9/286 | 107/8946 | 2.63 | 0.00714 | 0.594749 | ENSG0000004848/ ENSG0000054967/ ENSG00000102010/ ENSG00000129521/ ENSG00000130234/ ENSG00000134046/ ENSG00000139292/ ENSG00000197579/ ENSG00000285602 | ARX RELT BMX EGLN3 ACE2 MBD2 LGR5 TOPORS AC097625.1 |
| GO_BP | GO:0019229 | Regulation of vasoconstriction | 3/286 | 13/8946 | 7.22 | 0.007287 | 0.594749 | ENSG00000130234/ ENSG00000135643/ ENSG00000285602 | ACE2 KCNMB4 AC097625.1 |
| GO_BP | GO:0032508 | DNA duplex unwinding | 4/286 | 25/8946 | 5 | 0.007613 | 0.594749 | ENSG0000004700/ ENSG00000135829/ ENSG00000173575/ ENSG00000279765 | RECQL DHX9 CHD2 AC013394.1 |
| GO_BP | GO:0048247 | Lymphocyte chemotaxis | 3/286 | 14/8946 | 6.7 | 0.009058 | 0.594749 | ENSG00000275688/ ENSG00000275718/ ENSG00000276409 | CCL15- CCL14 CCL15 CCL14 |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|------------|---------|---------------|----------|----------|---|---|
| GO_BP | GO:0048666 | Neuron development | 3/286 | 14/8946 | 6.7 | 0.009058 | 0.594749 | ENSG0000058866/ ENSG00000138674/ ENSG00000171094 | DGKG SEC31A ALK |
| GO_BP | GO:0000733 | DNA strand renaturation | 3/286 | 15/8946 | 6.26 | 0.011059 | 0.601221 | ENSG0000004700/ ENSG00000186329/ ENSG00000285458 | RECQL TMEM212 AC093827.5 |
| GO_BP | GO:0006888 | ER to Golgi vesicle-mediated transport | 6/286 | 60/8946 | 3.13 | 0.011933 | 0.601221 | ENSG00000117533/ ENSG00000129083/ ENSG00000129472/ ENSG00000145362/ ENSG00000173626/ ENSG00000282218 | VAMP4 COPB1 RAB2B ANK2 TRAPPC3L AL132671.2 |
| GO_BP | GO:0006024 | Glycosaminoglycan Biosynthetic process | 3/286 | 16/8946 | 5.86 | 0.013294 | 0.601221 | ENSG00000153936/ ENSG00000179399/ ENSG00000267561 | HS2ST1 GPC5 AC093155.3 |
| GO_BP | GO:0032259 | methylation | 6/286 | 63/8946 | 2.98 | 0.014965 | 0.601221 | ENSG00000003509/ ENSG00000172943/ ENSG00000184154/ ENSG00000241644/ ENSG00000284844/ ENSG00000284922 | NDUFAF7 PHF8 LRTOMT INMT AP000812.4 AP000812.5 |
| GO_BP | GO:0034613 | Cellular protein localization | 3/286 | 17/8946 | 5.52 | 0.015767 | 0.601221 | ENSG00000138660/ ENSG00000149357/ ENSG00000177301 | APIAR LAMTOR1 KCNA2 |
| GO_BP | GO:0007166 | Cell surface receptor signaling pathway | 7/286 | 86/8946 | 2.55 | 0.019852 | 0.601221 | ENSG00000102195/ ENSG00000163930/ ENSG00000173698/ ENSG00000204577/ ENSG00000244482/ ENSG00000250349/ ENSG00000284969 | GPR50 BAP1 ADGRG2 LILRB3 LILRA6 AF241726.2 AL049629.2 |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|------------|----------|---------------|----------|----------|---|--|
| GO_BP | GO:0006468 | Protein phosphorylation | 8/286 | 106/8946 | 2.36 | 0.020011 | 0.601221 | ENSG00000038382/ ENSG00000044446/ ENSG00000058091/ ENSG00000059758/ ENSG00000073331/ ENSG00000120693/ ENSG00000147044/ ENSG00000177189 | TRIO PHKA2 CDK14 CDK17 ALPK1 SMAD9 CASK RPS6KA3 |
| GO_BP | GO:0006310 | DNA recombination | 4/286 | 34/8946 | 3.68 | 0.022314 | 0.601221 | ENSG00000147140/ ENSG00000163930/ ENSG00000278023/ ENSG00000285458 | NONO BAP1 RDM1 AC093827.5 |
| GO_BP | GO:0002548 | Monocyte chemotaxis | 3/286 | 21/8946 | 4.47 | 0.028082 | 0.601221 | ENSG00000275688/ ENSG00000275718/ ENSG00000276409 | CCL15- CCL14 CCL15 CCL14 |
| GO_BP | GO:0018105 | Peptidyl-serine phosphorylation | 5/286 | 55/8946 | 2.84 | 0.030531 | 0.601221 | ENSG00000065243/ ENSG00000146872/ ENSG00000147133/ ENSG00000163932/ ENSG00000183943 | PKN2 TLK2 TAF1 PRKCD PRKX |
| GO_BP | GO:0031397 | Negative regulation of protein ubiquitination | 3/286 | 23/8946 | 4.08 | 0.035691 | 0.601221 | ENSG00000069345/ ENSG00000147099/ ENSG00000285547 | DNAJA2 HDAC8 AL133500.1 |
| GO_BP | GO:0006198 | cAMP catabolic process | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000172572/ ENSG00000205268 | PDE3A PDE7A |
| GO_BP | GO:0010596 | Negative regulation of endothelial cell migration | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000145147/ ENSG00000173482 | SLIT2 PTPRM |
| GO_BP | GO:0019228 | Neuronal action potential | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000135643/ ENSG00000177301 | KCNMB4 KCNA2 |
| GO_BP | GO:0030177 | Positive regulation of Wnt signaling pathway | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000134046/ ENSG00000182220 | MBD2 ATP6AP2 |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|--|------------|---------|---------------|----------|----------|---|---------------------------------------|
| GO_BP | GO:0030837 | Negative regulation of actin filament polymerization | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000145147/ ENSG00000163932 | SLIT2 PRKCD |
| GO_BP | GO:0035269 | Protein O-linked mannosylation | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000120697/ ENSG00000198488 | ALG5 B3GNT6 |
| GO_BP | GO:0050707 | Regulation of cytokine secretion | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000174125/ ENSG00000174130 | TLR1 TLR6 |
| GO_BP | GO:0060088 | Auditory receptor cell stereocilium organization | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000138802/ ENSG00000187416 | SEC24B LHFPL3 |
| GO_BP | GO:0097252 | Oligodendrocyte apoptotic process | 2/286 | 10/8946 | 6.26 | 0.038688 | 0.601221 | ENSG00000186329/ ENSG00000285458 | TMEM212 AC093827.5 |
| GO_BP | GO:0042102 | Positive regulation of T cell proliferation | 4/286 | 41/8946 | 3.05 | 0.041013 | 0.601221 | ENSG00000071051/ ENSG00000131042/ ENSG00000134258/ ENSG00000284969 | NCK2 LILRB2 VTCN1 AL049629.2 |
| GO_BP | GO:0002474 | Antigen processing and presentation of peptide antigen via MHC class I | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000138674/ ENSG00000138802 | SEC31A SEC24B |
| GO_BP | GO:0006491 | N-glycan processing | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000198162/ ENSG00000205301 | MAN1A2 MGAT4D |
| GO_BP | GO:0010881 | Regulation of cardiac muscle contraction by regulation of the release of sequestered calcium ion | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000145362/ ENSG00000198363 | ANK2 ASPH |
| GO_BP | GO:0021510 | Spinal cord development | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000145147/ ENSG00000163930 | SLIT2 BAP1 |
| GO_BP | GO:0030878 | Thyroid gland development | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000042832/ ENSG00000116830 | TG TTF2 |
| GO_BP | GO:0032456 | Endocytic recycling | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000149823/ ENSG00000213047 | VPS51 DENND1B |
| GO_BP | GO:0034113 | Heterotypic cell-cell adhesion | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000131042/ ENSG00000138448 | LILRB2 ITGAV |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|--------------|------------|---|------------|----------|---------------|----------|----------|---|--|
| GO_BP | GO:0042246 | Tissue regeneration | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000213533/ ENSG00000248592 | STIMATE TMEM110- MUSTN1 |
| GO_BP | GO:0042312 | Regulation of blood vessel diameter | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000130234/ ENSG00000285602 | ACE2 AC097625.1 |
| GO_BP | GO:0060218 | Hematopoietic stem cell differentiation | 2/286 | 11/8946 | 5.69 | 0.046305 | 0.601221 | ENSG00000173575/ ENSG00000279765 | CHD2 AC013394.1 |
| GO_BP | GO:0051726 | Regulation of cell cycle | 5/286 | 62/8946 | 2.52 | 0.047541 | 0.601221 | ENSG0000058091/ ENSG0000059758/ ENSG0000133794/ ENSG0000163930/ ENSG0000189308 | CDK14 CDK17 ARNTL BAP1 LINS4 |
| KEGG_pathway | ko00360 | Phenylalanine metabolism | 4/240 | 17/7004 | 6.87 | 0.00225 | 0.497191 | ENSG0000069535/ ENSG0000125166/ ENSG0000171759/ ENSG0000189221 | MAOB GOT2 PAH MAOA |
| KEGG_pathway | ko04614 | Renin-angiotensin system | 4/240 | 25/7004 | 4.67 | 0.009647 | 0.995093 | ENSG0000130234/ ENSG0000138792/ ENSG0000182220/ ENSG00000285602 | ACE2 ENPEP ATP6AP2 AC097625.1 |
| KEGG_pathway | ko00512 | Mucin type O-glycan biosynthesis | 4/240 | 30/7004 | 3.89 | 0.018294 | 0.995093 | ENSG0000109586/ ENSG0000110328/ ENSG0000185274/ ENSG0000198488 | GALNT7 GALNT18 GALNT17 B3GNT6 |
| KEGG_pathway | ko05202 | Transcriptional misregulation in cancer | 11/240 | 175/7004 | 1.83 | 0.037634 | 0.995093 | ENSG0000005381/ ENSG0000058091/ ENSG0000109320/ ENSG0000126752/ ENSG0000135363/ ENSG0000140443/ ENSG0000147050/ ENSG0000157554/ ENSG0000164120/ ENSG0000172493/ ENSG00000250349 | MPO CDK14 NFKB1 SSX1 LMO2 IGFIR KDM6A ERG HPGD AFF1 AF241726.2 |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|-----------------|---------------|--|------------|----------|---------------|----------|----------|------------------|-------------|
| KEGG pathway | ko00220 | Arginine biosynthesis | 3/240 | 22/7004 | 3.98 | 0.037836 | 0.995093 | ENSG00000036473/ | OTC |
| | | | | | | | | ENSG00000125166/ | GOT2 |
| | | | | | | | | ENSG00000166123 | GPT2 |
| KEGG pathway | ko05205 | Proteoglycans in cancer | 12/240 | 209/7004 | 1.68 | 0.054905 | 0.995093 | ENSG00000100644/ | HIF1A |
| | | | | | | | | ENSG00000105971/ | CAV2 |
| | | | | | | | | ENSG00000109458/ | GAB1 |
| | | | | | | | | ENSG00000115414/ | FN1 |
| | | | | | | | | ENSG00000115904/ | SOS1 |
| | | | | | | | | ENSG00000124749/ | COL21A1 |
| | | | | | | | | ENSG00000138448/ | ITGAV |
| | | | | | | | | ENSG00000140443/ | IGF1R |
| | | | | | | | | ENSG00000145362/ | ANK2 |
| | | | | | | | | ENSG00000147257/ | GPC3 |
| | | | | | | | | ENSG00000156299/ | TIAM1 |
| ENSG00000197943 | PLCG2 | | | | | | | | |
| KEGG pathway | ko00534 | Glycosaminoglycan biosynthesis - heparan sulfate / heparin | 3/240 | 26/7004 | 3.37 | 0.057848 | 0.995093 | ENSG00000151348/ | EXT2 |
| | | | | | | | | ENSG00000153936/ | HS2ST1 |
| | | | | | | | | ENSG00000267561 | AC093155.3 |
| KEGG pathway | ko05100 | Bacterial invasion of epithelial cells | 6/240 | 81/7004 | 2.16 | 0.058591 | 0.995093 | ENSG00000105971/ | CAV2 |
| | | | | | | | | ENSG00000106299/ | WASL |
| | | | | | | | | ENSG00000109458/ | GAB1 |
| KEGG pathway | ko05012 | Parkinson's disease | 9/240 | 147/7004 | 1.79 | 0.065037 | 0.995093 | ENSG00000112290/ | WASF1 |
| | | | | | | | | ENSG00000115414/ | FN1 |
| | | | | | | | | ENSG00000197959 | DNM3 |
| | | | | | | | | ENSG00000130985/ | UBA1 |
| | | | | | | | | ENSG00000147123/ | NDUFB11 |
| | | | | | | | | ENSG00000151366/ | NDUFC2 |
| | | | | | | | | ENSG00000154723/ | ATP5PF |
| | | | | | | | | ENSG00000165264/ | NDUFB6 |
| | | | | | | | | ENSG00000169100/ | SLC25A6 |
| | | | | | | | | ENSG00000204370/ | SDHD |
| | | | | | | | | ENSG00000255292/ | AP002884.3 |
| ENSG00000259112 | NDUFC2-KCTD14 | | | | | | | | |

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Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol | | | | | | | | |
|------------------|------------|--------------------------------|------------|----------|---------------|----------|----------|------------------|-------------|-----------------------|--------|----------|------|----------|----------|------------------|--------|
| KEGG pathway | ko04514 | Cell adhesion molecules (CAMs) | 9/240 | 148/7004 | 1.77 | 0.067281 | 0.995093 | ENSG00000067141/ | NEO1 | | | | | | | | |
| | | | | | | | | ENSG00000105695/ | MAG | | | | | | | | |
| | | | | | | | | ENSG00000113946/ | CLDN16 | | | | | | | | |
| | | | | | | | | ENSG00000134258/ | VTCN1 | | | | | | | | |
| | | | | | | | | ENSG00000138448/ | ITGAV | | | | | | | | |
| | | | | | | | | ENSG00000146938/ | NLGN4X | | | | | | | | |
| | | | | | | | | ENSG00000154721/ | JAM2 | | | | | | | | |
| | | | | | | | | ENSG00000163347/ | CLDN1 | | | | | | | | |
| | | | | | | | | ENSG00000173482 | PTPRM | | | | | | | | |
| | | | | | | | | KEGG pathway | ko05016 | Huntington's disease | 11/240 | 196/7004 | 1.64 | 0.073168 | 0.995093 | ENSG00000114841/ | DNAH1 |
| ENSG00000115423/ | DNAH6 | | | | | | | | | | | | | | | | |
| ENSG00000147123/ | NDUFB11 | | | | | | | | | | | | | | | | |
| ENSG00000151366/ | NDUFC2 | | | | | | | | | | | | | | | | |
| ENSG00000154723/ | ATP5PF | | | | | | | | | | | | | | | | |
| ENSG00000165264/ | NDUFB6 | | | | | | | | | | | | | | | | |
| ENSG00000169100/ | SLC25A6 | | | | | | | | | | | | | | | | |
| ENSG00000185842/ | DNAH14 | | | | | | | | | | | | | | | | |
| ENSG00000204370/ | SDHD | | | | | | | | | | | | | | | | |
| ENSG00000255292/ | AP002884.3 | | | | | | | | | | | | | | | | |
| KEGG pathway | ko05231 | Choline metabolism in cancer | 7/240 | 108/7004 | 1.89 | 0.076766 | 0.995093 | ENSG00000058866/ | DGKG | | | | | | | | |
| | | | | | | | | ENSG00000075651/ | PLD1 | | | | | | | | |
| | | | | | | | | ENSG00000100644/ | HIF1A | | | | | | | | |
| | | | | | | | | ENSG00000106299/ | WASL | | | | | | | | |
| | | | | | | | | ENSG00000112290/ | WASF1 | | | | | | | | |
| | | | | | | | | ENSG00000115904/ | SOS1 | | | | | | | | |
| | | | | | | | | ENSG00000145431 | PDGFC | | | | | | | | |
| | | | | | | | | KEGG pathway | ko00510 | N-glycan biosynthesis | 4/240 | 49/7004 | 2.38 | 0.085967 | 0.995093 | ENSG00000120697/ | ALG5 |
| | | | | | | | | | | | | | | | | ENSG00000159063/ | ALG8 |
| | | | | | | | | | | | | | | | | ENSG00000198162/ | MAN1A2 |
| ENSG00000205301 | MGAT4D | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |

(Contd...)

Table S3. (Continued)

| Category | ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|--------------|---------|-----------------------------------|------------|----------|---------------|----------|----------|------------------|-------------|
| KEGG pathway | ko00982 | Drug metabolism - cytochrome P450 | 5/240 | 69/7004 | 2.11 | 0.086941 | 0.995093 | ENSG00000007933/ | FMO3 |
| | | | | | | | | ENSG00000065621/ | GSTO2 |
| | | | | | | | | ENSG00000069535/ | MAOB |
| | | | | | | | | ENSG00000094963/ | FMO2 |
| | | | | | | | | ENSG00000189221 | MAOA |
| KEGG pathway | ko00230 | Purine metabolism | 10/240 | 179/7004 | 1.63 | 0.08704 | 0.995093 | ENSG00000061918/ | GUCY1B1 |
| | | | | | | | | ENSG00000101868/ | POLAI |
| | | | | | | | | ENSG00000113448/ | PDE4D |
| | | | | | | | | ENSG00000138363/ | ATIC |
| | | | | | | | | ENSG00000162433/ | AK4 |
| | | | | | | | | ENSG00000164116/ | GUCY1A1 |
| | | | | | | | | ENSG00000170502/ | NUDT9 |
| | | | | | | | | ENSG00000171408/ | PDE7B |
| | | | | | | | | ENSG00000172572/ | PDE3A |
| | | | | | | | | ENSG00000205268 | PDE7A |

Table S4. GO/KEGG analysis of gene in dynamic TAD boundaries

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|------------|--------------------|------------|---------|---------------|----------|----------|------------------|-------------|
| GO:0015671 | Oxygen transport | 6/423 | 11/8946 | 11.54 | 4.07E-06 | 0.003043 | ENSG00000213931/ | HBE1 |
| | | | | | | | ENSG00000213934/ | HBG1 |
| | | | | | | | ENSG00000223609/ | HBD |
| | | | | | | | ENSG00000239920/ | AC104389.4 |
| GO:0001895 | Retina homeostasis | 6/423 | 29/8946 | 4.38 | 0.002025 | 0.458744 | ENSG00000244734/ | HBB |
| | | | | | | | ENSG00000284931 | AC104389.5 |
| | | | | | | | ENSG00000101441/ | CST4 |
| | | | | | | | ENSG00000134987/ | WDR36 |
| | | | | | | | ENSG00000170369/ | CST2 |
| | | | | | | | ENSG00000170373/ | CST1 |
| | | | | | | | ENSG00000198062/ | POTEH |
| | | | | | | | ENSG00000230031 | POTEB2 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|------------|---|------------|---------|---------------|----------|----------|---|---|
| GO:0071347 | Cellular response to interleukin-1 | 7/423 | 40/8946 | 3.7 | 0.002417 | 0.458744 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000112578/ ENSG00000181374/ ENSG00000240065 | CCL7 CCL2 CCL8 CCL1 BYSL CCL13 PSMB9 |
| GO:0019886 | Antigen processing and presentation of exogenous peptide antigen via MHC class II | 8/423 | 51/8946 | 3.32 | 0.002485 | 0.458744 | ENSG00000187240/ ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993 | DYNC2H1 HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 |
| GO:0006464 | Cellular protein modification process | 4/423 | 15/8946 | 5.64 | 0.004436 | 0.458744 | ENSG00000175806/ ENSG00000182768/ ENSG00000213471/ ENSG00000261147 | MSRA NGRN TLL13P AC091167.2 |
| GO:0033572 | Transferrin transport | 4/423 | 15/8946 | 5.64 | 0.004436 | 0.458744 | ENSG00000047249/ ENSG00000072274/ ENSG00000103769/ ENSG00000117410 | ATP6V1H TFRC RAB11A ATP6V0B |
| GO:0090307 | Mitotic spindle assembly | 4/423 | 15/8946 | 5.64 | 0.004436 | 0.458744 | ENSG00000103769/ ENSG00000183765/ ENSG00000283239/ ENSG00000285943 | RAB11A CHEK2 KBTBD11-OT1 AC112128.1 |
| GO:0050729 | Positive regulation of inflammatory response | 6/423 | 35/8946 | 3.63 | 0.005447 | 0.458744 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000181374/ ENSG00000204305 | CCL7 CCL2 CCL8 CCL1 CCL13 AGER |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|------------|---|------------|---------|---------------|----------|----------|--|--|
| GO:0050790 | Regulation of catalytic activity | 5/423 | 25/8946 | 4.23 | 0.005593 | 0.458744 | ENSG000000047249/ ENSG00000173281/ ENSG00000204227/ ENSG00000213654/ ENSG00000285526 | ATP6V1H PPP1R3B RING1 GPSM3 AC020907.6 |
| GO:0071346 | Cellular response to interferon-gamma | 5/423 | 27/8946 | 3.92 | 0.007865 | 0.458744 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000181374 | CCL7 CCL2 CCL8 CCL1 CCL13 |
| GO:0010942 | Positive regulation of cell death | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000134323/ ENSG00000223609/ ENSG00000244734 | MYCN HBD HBB |
| GO:0034314 | Arp2/3 complex-mediated actin nucleation | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000214021/ ENSG00000241553/ ENSG00000250151 | TTL3 ARPC4 ARPC4-TTLL3 |
| GO:0035269 | Protein O-linked mannosylation | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000132581/ ENSG00000133424/ ENSG00000198488 | SDF2 LARGE1 B3GNT6 |
| GO:0046827 | Positive regulation of protein export from nucleus | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000072062/ ENSG00000132953/ ENSG00000134072 | PRKACA XPO4 CAMK1 |
| GO:0048712 | Negative regulation of astrocyte differentiation | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000134323/ ENSG00000141644/ ENSG00000173406 | MYCN MBD1 DAB1 |
| GO:2000649 | Regulation of sodium ion transmembrane transporter activity | 3/423 | 10/8946 | 6.34 | 0.009821 | 0.458744 | ENSG00000150201/ ENSG00000266964/ ENSG00000285526 | FXYD4 FXYD1 AC020907.6 |
| GO:0071377 | Cellular response to glucagon stimulus | 4/423 | 19/8946 | 4.45 | 0.010846 | 0.464861 | ENSG00000072062/ ENSG00000162104/ ENSG00000162188/ ENSG00000174021 | PRKACA ADCY9 GNG3 GNG5 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|------------|--|------------|---------|---------------|----------|----------|---|--|
| GO:0071356 | Cellular response to tumor necrosis factor | 7/423 | 53/8946 | 2.79 | 0.011811 | 0.464861 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000133110/ ENSG00000181374/ ENSG00000185043 | CCL7 CCL2 CCL8 CCL1 POSTN CCL13 CIB1 |
| GO:0006694 | Steroid biosynthetic process | 3/423 | 11/8946 | 5.77 | 0.013036 | 0.464861 | ENSG00000182827/ ENSG00000204228/ ENSG00000277893 | ACBD3 HSD17B8 SRD5A2 |
| GO:0007026 | Negative regulation of microtubule depolymerization | 3/423 | 11/8946 | 5.77 | 0.013036 | 0.464861 | ENSG00000129682/ ENSG00000138100/ ENSG00000185043 | FGF13 TRIM54 CIB1 |
| GO:0050766 | Positive regulation of phagocytosis | 4/423 | 20/8946 | 4.23 | 0.013062 | 0.464861 | ENSG00000041353/ ENSG00000134516/ ENSG00000183049/ ENSG00000186716 | RAB27B DOCK2 CAMK1D BCR |
| GO:0030593 | Neutrophil chemotaxis | 5/423 | 31/8946 | 3.41 | 0.014184 | 0.481849 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000181374 | CCL7 CCL2 CCL8 CCL1 CCL13 |
| GO:0006368 | Transcription elongation from RNA polymerase II promoter | 6/423 | 43/8946 | 2.95 | 0.014904 | 0.482376 | ENSG00000168002/ ENSG00000181555/ ENSG00000187735/ ENSG00000206181/ ENSG00000275553/ ENSG00000278674 | POLR2G SETD2 TCEA1 ELOA2 ELOA3C ELOA3B |
| GO:0002548 | Monocyte chemotaxis | 4/423 | 21/8946 | 4.03 | 0.015546 | 0.482376 | ENSG00000108688/ ENSG00000108700/ ENSG00000108702/ ENSG00000181374 | CCL7 CCL8 CCL1 CCL13 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|------------|--|------------|---------|---------------|----------|----------|---|--|
| GO:1903779 | Regulation of cardiac conduction | 5/423 | 32/8946 | 3.3 | 0.016176 | 0.482376 | ENSG00000072062/ ENSG00000150201/ ENSG00000221946/ ENSG00000266964/ ENSG00000285526 | PRKACA FXVD4 FXVD7 FXVD1 AC020907.6 |
| GO:0050860 | Negative regulation of T cell receptor signaling pathway | 3/423 | 12/8946 | 5.29 | 0.016781 | 0.482376 | ENSG00000149177/ ENSG00000175354/ ENSG00000204290 | PTPRJ PTPN2 BTNL2 |
| GO:0007166 | Cell Surface receptor signaling pathway | 9/423 | 86/8946 | 2.21 | 0.019908 | 0.507357 | ENSG00000072071/ ENSG00000117114/ ENSG00000130538/ ENSG00000130561/ ENSG00000150455/ ENSG00000153294/ ENSG00000160801/ ENSG00000204305/ ENSG00000250349 | ADGRL1 ADGRL2 OR11H1 SAG TIRAP ADGRF4 PTHR1 AGER AF241726.2 |
| GO:0070098 | Chemokine-mediated signaling pathway | 5/423 | 34/8946 | 3.11 | 0.020699 | 0.507357 | ENSG00000108688/ ENSG00000108691/ ENSG00000108700/ ENSG00000108702/ ENSG00000181374 | CCL7 CCL2 CCL8 CCL1 CCL13 |
| GO:0009813 | Flavonoid biosynthetic process | 3/423 | 13/8946 | 4.88 | 0.021064 | 0.507357 | ENSG00000241119/ ENSG00000242366/ ENSG00000242515 | UGT1A9 UGT1A8 UGT1A10 |
| ko05310 | Asthma | 9/314 | 32/7004 | 6.27 | 7.34E-06 | 0.0018 | ENSG00000172156/ ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993/ ENSG00000270472 | CCL11 HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 IGHV3OR16-9 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol | | | | | | | |
|------------------|--------------------------|------------|---------|---------------|----------|----------|------------------|---------------------------|-------|---------|------|----------|----------|------------------|----------|
| ko05330 | Allograft rejection | 9/314 | 39/7004 | 5.15 | 4.20E-05 | 0.003468 | ENSG00000180644/ | PRF1 | | | | | | | |
| | | | | | | | ENSG00000204252/ | HLA-DOA | | | | | | | |
| | | | | | | | ENSG00000204257/ | HLA-DMA | | | | | | | |
| | | | | | | | ENSG00000204287/ | HLA-DRA | | | | | | | |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 | | | | | | | |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 | | | | | | | |
| | | | | | | | ENSG00000242574/ | HLA-DMB | | | | | | | |
| | | | | | | | ENSG00000248993/ | AL645941.2 | | | | | | | |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 | | | | | | | |
| ko05416 | Viral myocarditis | 11/314 | 58/7004 | 4.23 | 4.24E-05 | 0.003468 | ENSG00000164305/ | CASP3 | | | | | | | |
| | | | | | | | ENSG00000180644/ | PRF1 | | | | | | | |
| | | | | | | | ENSG00000198947/ | DMD | | | | | | | |
| | | | | | | | ENSG00000204252/ | HLA-DOA | | | | | | | |
| | | | | | | | ENSG00000204257/ | HLA-DMA | | | | | | | |
| | | | | | | | ENSG00000204287/ | HLA-DRA | | | | | | | |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 | | | | | | | |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 | | | | | | | |
| | | | | | | | ENSG00000242574/ | HLA-DMB | | | | | | | |
| | | | | | | | ENSG00000248993/ | AL645941.2 | | | | | | | |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 | | | | | | | |
| | | | | | | | ko05332 | Graft-versus-host disease | 8/314 | 39/7004 | 4.58 | 0.000272 | 0.016652 | ENSG00000180644/ | PRF1 |
| | | | | | | | | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | | | | | | | | ENSG00000204287/ | HLA-DRA |
| ENSG00000223865/ | HLA-DPB1 | | | | | | | | | | | | | | |
| ENSG00000231389/ | HLA-DPA1 | | | | | | | | | | | | | | |
| ENSG00000242574/ | HLA-DMB | | | | | | | | | | | | | | |
| ENSG00000248993 | AL645941.2 | | | | | | | | | | | | | | |
| ko04940 | Type I diabetes mellitus | 8/314 | 43/7004 | 4.15 | 0.000547 | 0.023813 | | | | | | | | ENSG00000180644/ | PRF1 |
| | | | | | | | | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993 | AL645941.2 | | | | | | | |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 | | | | | | | |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|---------|--|------------|---------|---------------|----------|----------|---|---|
| ko05320 | Autoimmune thyroid disease | 9/314 | 54/7004 | 3.72 | 0.000583 | 0.023813 | ENSG00000180644/ ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993/ ENSG00000270472 | PRF1 HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 IGHV3OR16-9 |
| ko04612 | Antigen processing and presentation | 10/314 | 73/7004 | 3.06 | 0.001429 | 0.047309 | ENSG00000100600/ ENSG00000109971/ ENSG00000168394/ ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993 | LGMN HSPA8 TAP1 HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 |
| ko04672 | Intestinal immune network for IgA production | 8/314 | 50/7004 | 3.57 | 0.001543 | 0.047309 | ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993 | HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol | | | | | | | |
|------------------|----------------------|------------|---------|---------------|----------|----------|------------------|--------------------|--------|---------|------|----------|----------|------------------|--------|
| ko05323 | Rheumatoid arthritis | 11/314 | 91/7004 | 2.7 | 0.002359 | 0.060009 | ENSG00000047249/ | ATP6V1H | | | | | | | |
| | | | | | | | ENSG00000108691/ | CCL2 | | | | | | | |
| | | | | | | | ENSG00000117410/ | ATP6V0B | | | | | | | |
| | | | | | | | ENSG00000204252/ | HLA-DOA | | | | | | | |
| | | | | | | | ENSG00000204257/ | HLA-DMA | | | | | | | |
| | | | | | | | ENSG00000204287/ | HLA-DRA | | | | | | | |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 | | | | | | | |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 | | | | | | | |
| | | | | | | | ENSG00000242574/ | HLA-DMB | | | | | | | |
| | | | | | | | ENSG00000248993/ | AL645941.2 | | | | | | | |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 | | | | | | | |
| | | | | | | | ko05032 | Morphine addiction | 11/314 | 92/7004 | 2.67 | 0.002575 | 0.060009 | ENSG00000072062/ | PRKACA |
| | | | | | | | | | | | | | | ENSG00000111886/ | GABRR2 |
| | | | | | | | | | | | | | | ENSG00000113231/ | PDE8B |
| ENSG00000113448/ | PDE4D | | | | | | | | | | | | | | |
| ENSG00000128655/ | PDE11A | | | | | | | | | | | | | | |
| ENSG00000154678/ | PDE1C | | | | | | | | | | | | | | |
| ENSG00000162104/ | ADCY9 | | | | | | | | | | | | | | |
| ENSG00000162188/ | GNG3 | | | | | | | | | | | | | | |
| ENSG00000174021/ | GNG5 | | | | | | | | | | | | | | |
| ENSG00000284741/ | PDE11A | | | | | | | | | | | | | | |
| ENSG00000284762 | AC022414.1 | | | | | | | | | | | | | | |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|---------|---------------------------------|------------|----------|---------------|----------|----------|---|--|
| ko04145 | Phagosome | 16/314 | 164/7004 | 2.18 | 0.002691 | 0.060009 | ENSG00000047249/ ENSG00000065665/ ENSG00000072274/ ENSG00000117410/ ENSG00000144566/ ENSG00000165168/ ENSG00000168394/ ENSG00000187240/ ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993/ ENSG00000270472 | ATP6V1H SEC61A2 TFRC ATP6V0B RAB5A CYBB TAPI DYNC2H1 HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 IGHV3OR16-9 |
| ko05150 | Staphylococcus aureus infection | 8/314 | 62/7004 | 2.88 | 0.006104 | 0.120622 | ENSG00000204252/ ENSG00000204257/ ENSG00000204287/ ENSG00000223865/ ENSG00000231389/ ENSG00000242574/ ENSG00000248993/ ENSG00000270472 | HLA-DOA HLA-DMA HLA-DRA HLA-DPB1 HLA-DPA1 HLA-DMB AL645941.2 IGHV3OR16-9 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|---------|----------------------------------|------------|----------|---------------|----------|----------|-------------------|-------------|
| ko04514 | Cell adhesion molecules (CAMs) | 14/314 | 148/7004 | 2.11 | 0.006393 | 0.120622 | ENSG000000112124/ | CD22 |
| | | | | | | | ENSG00000013297/ | CLDN11 |
| | | | | | | | ENSG00000105695/ | MAG |
| | | | | | | | ENSG00000172260/ | NEGR1 |
| | | | | | | | ENSG00000177300/ | CLDN22 |
| | | | | | | | ENSG00000185758/ | CLDN24 |
| | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993/ | AL645941.2 |
| | | | | | | | ENSG00000285218 | AC026316.5 |
| ko05321 | Inflammatory bowel disease (IBD) | 8/314 | 66/7004 | 2.7 | 0.008887 | 0.155698 | ENSG00000175387/ | SMAD2 |
| | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993 | AL645941.2 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | geneID | Gene_symbol |
|---------|--------------------------|------------|----------|---------------|----------|----------|------------------|-------------|
| ko05168 | Herpes simplex infection | 16/314 | 192/7004 | 1.86 | 0.012125 | 0.198261 | ENSG00000005339/ | CREBBP |
| | | | | | | | ENSG00000100650/ | SRSF5 |
| | | | | | | | ENSG00000107643/ | MAPK8 |
| | | | | | | | ENSG00000108691/ | CCL2 |
| | | | | | | | ENSG00000115875/ | SRSF7 |
| | | | | | | | ENSG00000162227/ | TAF6L |
| | | | | | | | ENSG00000162231/ | NXF1 |
| | | | | | | | ENSG00000164305/ | CASP3 |
| | | | | | | | ENSG00000168394/ | TAP1 |
| | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993 | AL645941.2 |
| ko05152 | Tuberculosis | 15/314 | 183/7004 | 1.83 | 0.017097 | 0.257724 | ENSG00000005339/ | CREBBP |
| | | | | | | | ENSG00000047249/ | ATP6V1H |
| | | | | | | | ENSG00000107643/ | MAPK8 |
| | | | | | | | ENSG00000117410/ | ATP6V0B |
| | | | | | | | ENSG00000144566/ | RAB5A |
| | | | | | | | ENSG00000150455/ | TIRAP |
| | | | | | | | ENSG00000164305/ | CASP3 |
| | | | | | | | ENSG00000204252/ | HLA-DOA |
| | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993/ | AL645941.2 |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 |

(Contd...)

Table S4. (Continued)

| ID | Description | Gene Ratio | BgRatio | Enrich_factor | P-value | Q-value | genelD | Gene_symbol |
|------------------|----------------------------------|------------|---------|---------------|----------|----------|-------------------|-------------------------------------|
| ko04977 | Vitamin digestion and absorption | 4/314 | 23/7004 | 3.88 | 0.017864 | 0.257724 | ENSG00000084674/ | APOB |
| | | | | | | | ENSG00000107611/ | CUBN |
| | | | | | | | ENSG00000138074/ | SLC5A6 |
| | | | | | | | ENSG00000147160 | AWAT2 |
| ko05140 | Leishmaniasis | 8/314 | 76/7004 | 2.35 | 0.019878 | 0.270854 | ENSG000000204252/ | HLA-DOA |
| | | | | | | | ENSG00000204257/ | HLA-DMA |
| | | | | | | | ENSG00000204287/ | HLA-DRA |
| | | | | | | | ENSG00000223865/ | HLA-DPB1 |
| | | | | | | | ENSG00000231389/ | HLA-DPA1 |
| | | | | | | | ENSG00000242574/ | HLA-DMB |
| | | | | | | | ENSG00000248993/ | AL645941.2 |
| | | | | | | | ENSG00000270472 | IGHV3OR16-9 |
| | | | | | | | ko04925 | Aldosterone synthesis and secretion |
| ENSG00000134072/ | CAMK1 | | | | | | | |
| ENSG00000152495/ | CAMK4 | | | | | | | |
| ENSG00000162104/ | ADCY9 | | | | | | | |
| ENSG00000183049/ | CAMK1D | | | | | | | |
| ENSG00000184304/ | PRKDI | | | | | | | |
| ENSG00000213676/ | ATF6B | | | | | | | |
| ENSG00000231852 | CYP21A2 | | | | | | | |

Table S5. GO/KEGG analysis of genes related to compartment switched from A to B

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|-----------|---------|---------------|----------|----------|------------------|-------------|
| GO_BP | GO:0002227 | Innate immune response in mucosa | 6/333 | 19/8946 | 8.48 | 4.57E-05 | 0.032255 | ENSG00000184678/ | HIST2H2BE |
| | | | | | | | | ENSG00000203814/ | HIST2H2BF |
| | | | | | | | | ENSG00000206047/ | DEFA1 |
| | | | | | | | | ENSG00000234289/ | H2BFS |
| | | | | | | | | ENSG00000239839/ | DEFA3 |
| | | | | | | | | ENSG00000240247 | DEFA1B |
| GO_BP | GO:0098609 | Cell-cell adhesion | 5/333 | 18/8946 | 7.46 | 0.000398 | 0.140364 | ENSG00000062598/ | ELMO2 |
| | | | | | | | | ENSG00000183598/ | HIST2H3D |
| | | | | | | | | ENSG00000203811/ | HIST2H3C |
| | | | | | | | | ENSG00000203852/ | HIST2H3A |
| | | | | | | | | ENSG00000204628 | RACK1 |
| | | | | | | | | ENSG00000184678/ | HIST2H2BE |
| GO_BP | GO:0019731 | Antibacterial humoral response | 6/333 | 31/8946 | 5.2 | 0.000851 | 0.199964 | ENSG00000203814/ | HIST2H2BF |
| | | | | | | | | ENSG00000206047/ | DEFA1 |
| | | | | | | | | ENSG00000234289/ | H2BFS |
| | | | | | | | | ENSG00000239839/ | DEFA3 |
| | | | | | | | | ENSG00000240247 | DEFA1B |
| | | | | | | | | ENSG00000004700/ | RECQL |
| GO_BP | GO:0000724 | Double-strand break repair via homologous recombination | 7/333 | 46/8946 | 4.09 | 0.001423 | 0.230449 | ENSG00000072121/ | ZFYVE26 |
| | | | | | | | | ENSG00000173559/ | NABP1 |
| | | | | | | | | ENSG00000184260/ | HIST2H2AC |
| | | | | | | | | ENSG00000184270/ | HIST2H2AB |
| | | | | | | | | ENSG00000203812/ | HIST2H2AA3 |
| | | | | | | | | ENSG00000214941 | ZSWIM7 |
| GO_BP | GO:0051290 | Protein heterotetramerization | 5/333 | 26/8946 | 5.17 | 0.002392 | 0.230449 | ENSG00000183598/ | HIST2H3D |
| | | | | | | | | ENSG00000203811/ | HIST2H3C |
| | | | | | | | | ENSG00000203852/ | HIST2H3A |
| | | | | | | | | ENSG00000270276/ | HIST2H4B |
| | | | | | | | | ENSG00000270882 | HIST2H4A |
| | | | | | | | | | |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|-----------|----------|---------------|----------|----------|---|--|
| GO_BP | GO:0044267 | Cellular protein metabolic process | 7/333 | 51/8946 | 3.69 | 0.002627 | 0.230449 | ENSG00000131183/ ENSG00000182752/ ENSG00000183598/ ENSG00000203811/ ENSG00000203852/ ENSG00000270276/ ENSG00000270882 | SLC34A1 PAPPA HIST2H3D HIST2H3C HIST2H3A HIST2H4B HIST2H4A |
| GO_BP | GO:0000183 | Chromatin silencing at rDNA | 5/333 | 27/8946 | 4.97 | 0.002848 | 0.230449 | ENSG00000183598/ ENSG00000203811/ ENSG00000203852/ ENSG00000270276/ ENSG00000270882 | HIST2H3D HIST2H3C HIST2H3A HIST2H4B HIST2H4A |
| GO_BP | GO:0006335 | DNA replication-dependent nucleosome assembly | 5/333 | 27/8946 | 4.97 | 0.002848 | 0.230449 | ENSG00000183598/ ENSG00000203811/ ENSG00000203852/ ENSG00000270276/ ENSG00000270882 | HIST2H3D HIST2H3C HIST2H3A HIST2H4B HIST2H4A |
| GO_BP | GO:0050830 | Defense response to Gram-positive bacterium | 7/333 | 52/8946 | 3.62 | 0.002941 | 0.230449 | ENSG00000184678/ ENSG00000203814/ ENSG00000206047/ ENSG00000213809/ ENSG00000234289/ ENSG00000239839/ ENSG00000240247 | HIST2H2BE HIST2H2BF DEFA1 KLRK1 H2BFS DEFA3 DEFA1B |
| GO_BP | GO:0006468 | Protein phosphorylation | 10/333 | 106/8946 | 2.53 | 0.005984 | 0.324945 | ENSG00000004799/ ENSG0000058091/ ENSG0000073331/ ENSG0000102225/ ENSG0000145675/ ENSG0000170209/ ENSG0000170390/ ENSG0000183049/ ENSG0000185900/ ENSG00000205111 | PDK4 CDK14 ALPK1 CDK16 PIK3R1 ANKK1 DCLK2 CAMK1D POMK CDKL4 |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|--|-----------|---------|---------------|----------|----------|--|---|
| GO_BP | GO:0050832 | Defense response to fungus | 3/333 | 11/8946 | 7.33 | 0.00675 | 0.324945 | ENSG00000206047/ ENSG00000239839/ ENSG00000240247 | DEFA1 DEFA3 DEFA1B |
| GO_BP | GO:0060968 | Regulation of gene silencing | 3/333 | 11/8946 | 7.33 | 0.00675 | 0.324945 | ENSG00000183598/ ENSG00000203811/ ENSG00000203852 | HIST2H3D HIST2H3C HIST2H3A |
| GO_BP | GO:0017158 | Regulation of calcium ion-dependent exocytosis | 4/333 | 21/8946 | 5.12 | 0.006829 | 0.324945 | ENSG00000134207/ ENSG00000141837/ ENSG00000147041/ ENSG00000229674 | SYT6 CACNA1A SYTL5 AL121578.2 |
| GO_BP | GO:0098792 | Xenophagy | 7/333 | 62/8946 | 3.03 | 0.007882 | 0.324945 | ENSG00000004799/ ENSG0000073331/ ENSG00000124786/ ENSG00000177675/ ENSG00000183598/ ENSG00000203811/ ENSG00000203852 | PDK4 ALPK1 SLC35B3 CDI63L1 HIST2H3D HIST2H3C HIST2H3A |
| GO_BP | GO:0000077 | DNA damage checkpoint | 4/333 | 22/8946 | 4.88 | 0.008106 | 0.324945 | ENSG00000184260/ ENSG00000184270/ ENSG00000203812/ ENSG00000229674 | HIST2H2AC HIST2H2AB HIST2H2AA3 AL121578.2 |
| GO_BP | GO:0006342 | Chromatin silencing | 4/333 | 22/8946 | 4.88 | 0.008106 | 0.324945 | ENSG00000184260/ ENSG00000184270/ ENSG00000187516/ ENSG00000203812 | HIST2H2AC HIST2H2AB HYPM HIST2H2AA3 |
| GO_BP | GO:0001657 | Ureteric bud development | 3/333 | 12/8946 | 6.72 | 0.008754 | 0.324945 | ENSG00000145147/ ENSG00000170365/ ENSG00000176692 | SLIT2 SMAD1 FOXC2 |
| GO_BP | GO:0032200 | Telomere organization | 3/333 | 12/8946 | 6.72 | 0.008754 | 0.324945 | ENSG00000183598/ ENSG00000203811/ ENSG00000203852 | HIST2H3D HIST2H3C HIST2H3A |
| GO_BP | GO:0034605 | Cellular response to heat | 3/333 | 12/8946 | 6.72 | 0.008754 | 0.324945 | ENSG00000162129/ ENSG00000172995/ ENSG00000249915 | CLPB ARPP21 PDCD6 |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|---|-----------|---------|---------------|----------|----------|---|---|
| GO_BP | GO:0045815 | Positive regulation of gene expression, epigenetic | 5/333 | 36/8946 | 3.73 | 0.010123 | 0.35697 | ENSG00000183598/ ENSG00000203811/ ENSG00000203852/ ENSG00000270276/ ENSG00000270882 | HIST2H3D HIST2H3C HIST2H3A HIST2H4B HIST2H4A |
| GO_BP | GO:0001580 | Detection of chemical stimulus involved in sensory perception of bitter taste | 4/333 | 24/8946 | 4.48 | 0.011108 | 0.373048 | ENSG00000121314/ ENSG00000121318/ ENSG00000121377/ ENSG00000121381 | TAS2R8 TAS2R10 TAS2R7 TAS2R9 |
| GO_BP | GO:0048791 | Calcium ion-regulated exocytosis of neurotransmitter | 4/333 | 25/8946 | 4.3 | 0.012844 | 0.383119 | ENSG00000134207/ ENSG00000141837/ ENSG00000147041/ ENSG00000229674 | SYT6 CACNA1A SYTL5 AL121578.2 |
| GO_BP | GO:0002230 | Positive regulation of defense response to virus by host | 7/333 | 68/8946 | 2.77 | 0.012866 | 0.383119 | ENSG00000004799/ ENSG00000073331/ ENSG00000124786/ ENSG00000177675/ ENSG00000183598/ ENSG00000203811/ ENSG00000203852 | PDK4 ALPK1 SLC35B3 CDI63L1 HIST2H3D HIST2H3C HIST2H3A |
| GO_BP | GO:0006352 | DNA-templated transcription, initiation | 3/333 | 14/8946 | 5.76 | 0.013707 | 0.383119 | ENSG00000182521/ ENSG00000270276/ ENSG00000270882 | TBPL2 HIST2H4B HIST2H4A |
| GO_BP | GO:0007163 | Establishment or maintenance of cell polarity | 3/333 | 14/8946 | 5.76 | 0.013707 | 0.383119 | ENSG00000133627/ ENSG00000135525/ ENSG00000197702 | ACTR3B MAP7 PARVA |
| GO_BP | GO:0035725 | Sodium ion transmembrane transport | 5/333 | 39/8946 | 3.44 | 0.014124 | 0.383119 | ENSG00000065923/ ENSG00000066230/ ENSG00000131183/ ENSG00000146950/ ENSG00000180251 | SLC9A7 SLC9A3 SLC34A1 SHROOM2 SLC9A4 |
| GO_BP | GO:0006464 | Cellular protein modification process | 3/333 | 15/8946 | 5.37 | 0.01667 | 0.435426 | ENSG00000102174/ ENSG00000166532/ ENSG00000175806 | PHEX RIMKLB MSRA |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|----------|------------|--|-----------|---------|---------------|----------|----------|---|--|
| GO_BP | GO:0031047 | Gene silencing by RNA | 6/333 | 60/8946 | 2.69 | 0.023533 | 0.59275 | ENSG00000146707/ ENSG00000183598/ ENSG00000203811/ ENSG00000203852/ ENSG00000270276/ ENSG00000270882 | POMZP3 HIST2H3D HIST2H3C HIST2H3A HIST2H4B HIST2H4A |
| GO_BP | GO:1902600 | Hydrogen ion transmembrane transport | 4/333 | 31/8946 | 3.47 | 0.026851 | 0.647408 | ENSG00000065923/ ENSG0000066230/ ENSG00000131174/ ENSG00000180251 | SLC9A7 SLC9A3 COX7B SLC9A4 |
| GO_BP | GO:0007059 | Chromosome segregation | 3/333 | 18/8946 | 4.48 | 0.027539 | 0.647408 | ENSG00000146872/ ENSG00000184661/ ENSG00000215301 | TLK2 CDCA2 DDX3X |
| GO_BP | GO:0071407 | Cellular response to organic cyclic compound | 4/333 | 32/8946 | 3.36 | 0.029815 | 0.678302 | ENSG00000074047/ ENSG00000103241/ ENSG00000170430/ ENSG00000276085 | GLI2 FOXF1 MGMT CCL3L1 |
| GO_BP | GO:0000186 | Activation of MAPKK activity | 3/333 | 20/8946 | 4.03 | 0.036435 | 0.755763 | ENSG00000102755/ ENSG00000138798/ ENSG00000197442 | FLT1 EGF MAP3K5 |
| GO_BP | GO:0048704 | Embryonic skeletal system morphogenesis | 3/333 | 20/8946 | 4.03 | 0.036435 | 0.755763 | ENSG00000108511/ ENSG00000173917/ ENSG00000182742 | HOXB6 HOXB2 HOXB4 |
| GO_BP | GO:0060048 | Cardiac muscle contraction | 3/333 | 20/8946 | 4.03 | 0.036435 | 0.755763 | ENSG00000129170/ ENSG00000170365/ ENSG00000266086 | CSRP3 SMAD1 AC015813.2 |
| GO_BP | GO:0001503 | Ossification | 4/333 | 35/8946 | 3.07 | 0.039827 | 0.769357 | ENSG00000131183/ ENSG00000134996/ ENSG00000159216/ ENSG00000176692 | SLC34A1 OSTF1 RUNX1 FOXC2 |
| GO_BP | GO:0007623 | Circadian rhythm | 3/333 | 22/8946 | 3.66 | 0.046621 | 0.769357 | ENSG00000066230/ ENSG00000165819/ ENSG00000181092 | SLC9A3 METTL3 ADIPOQ |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|--------------|------------|---|-----------|----------|---------------|----------|----------|---|--|
| GO_BP | GO:0010596 | Negative regulation of endothelial cell migration | 2/333 | 10/8946 | 5.37 | 0.051021 | 0.769357 | ENSG00000145147/ ENSG00000173482 | SLIT2 PTPRM |
| GO_BP | GO:0019079 | Viral genome replication | 2/333 | 10/8946 | 5.37 | 0.051021 | 0.769357 | ENSG00000102241/ ENSG00000175029 | HTATSF1 CTBP2 |
| GO_BP | GO:0051568 | Histone H3-K4 methylation | 2/333 | 10/8946 | 5.37 | 0.051021 | 0.769357 | ENSG00000133665/ ENSG00000170788 | DYDC2 DYDC1 |
| GO_BP | GO:0061001 | Regulation of dendritic spine morphogenesis | 2/333 | 10/8946 | 5.37 | 0.051021 | 0.769357 | ENSG00000158528/ ENSG00000197555 | PPP1R9A SIPAIL1 |
| KEGG_pathway | ko05034 | Alcoholism | 14/232 | 161/7004 | 2.63 | 0.00086 | 0.208187 | ENSG00000078061/ ENSG00000127928/ ENSG00000146592/ ENSG00000165646/ ENSG00000170425/ ENSG00000184260/ ENSG00000184270/ ENSG00000184678/ ENSG00000203811/ ENSG00000203812/ ENSG00000203814/ ENSG00000203852/ ENSG00000229674/ ENSG00000272196 | ARAF GNGT1 CREB5 SLC18A2 ADORA2B HIST2H2AC HIST2H2AB HIST2H2BE HIST2H3C HIST2H2AA3 HIST2H2BF HIST2H3A AL121578.2 HIST2H2AA4 |
| KEGG_pathway | ko05322 | Systemic lupus erythematosus | 10/232 | 123/7004 | 2.45 | 0.007442 | 0.844221 | ENSG00000102245/ ENSG00000184260/ ENSG00000184270/ ENSG00000184678/ ENSG00000203811/ ENSG00000203812/ ENSG00000203814/ ENSG00000203852/ ENSG00000229674/ ENSG00000272196 | CD40LG HIST2H2AC HIST2H2AB HIST2H2BE HIST2H3C HIST2H2AA3 HIST2H2BF HIST2H3A AL121578.2 HIST2H2AA4 |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_ factor | P-value | Q-value | GeneID | Gene_symbol | | | | | | | | |
|------------------|------------|-------------------------------|-----------|----------|----------------|----------|----------|------------------|-------------|---------|-------|---------|------|----------|----------|------------------|--------|
| KEGG_ pathway | ko04726 | Serotonergic synapse | 9/232 | 110/7004 | 2.47 | 0.010466 | 0.844221 | ENSG00000078061/ | ARAF | | | | | | | | |
| | | | | | | | | ENSG00000127928/ | GNGT1 | | | | | | | | |
| | | | | | | | | ENSG00000134716/ | CYP2J2 | | | | | | | | |
| | | | | | | | | ENSG00000141837/ | CACNA1A | | | | | | | | |
| | | | | | | | | ENSG00000147246/ | HTR2C | | | | | | | | |
| | | | | | | | | ENSG00000148408/ | CACNA1B | | | | | | | | |
| | | | | | | | | ENSG00000149305/ | HTR3B | | | | | | | | |
| | | | | | | | | ENSG00000165646/ | SLC18A2 | | | | | | | | |
| | | | | | | | | ENSG00000166736 | HTR3A | | | | | | | | |
| KEGG_ pathway | ko04742 | Taste transduction | 7/232 | 83/7004 | 2.55 | 0.019646 | 0.979066 | ENSG00000121314/ | TAS2R8 | | | | | | | | |
| | | | | | | | | ENSG00000121318/ | TAS2R10 | | | | | | | | |
| | | | | | | | | ENSG00000121377/ | TAS2R7 | | | | | | | | |
| | | | | | | | | ENSG00000121381/ | TAS2R9 | | | | | | | | |
| | | | | | | | | ENSG00000141837/ | CACNA1A | | | | | | | | |
| | | | | | | | | ENSG00000149305/ | HTR3B | | | | | | | | |
| | | | | | | | | ENSG00000166736 | HTR3A | | | | | | | | |
| | | | | | | | | KEGG_ pathway | ko05144 | Malaria | 5/232 | 51/7004 | 2.96 | 0.026021 | 0.979066 | ENSG00000102245/ | CD40LG |
| | | | | | | | | | | | | | | | | ENSG00000113296/ | THBS4 |
| ENSG00000137462/ | TLR2 | | | | | | | | | | | | | | | | |
| ENSG00000213809/ | KLRK1 | | | | | | | | | | | | | | | | |
| ENSG00000255819 | KLRC4- | | | | | | | | | | | | | | | | |
| | KLRK1 | | | | | | | | | | | | | | | | |
| | IDS | | | | | | | | | | | | | | | | |
| ENSG00000165102/ | HGSNAT | | | | | | | | | | | | | | | | |
| ENSG00000241489 | AC244197.3 | | | | | | | | | | | | | | | | |
| KEGG_ pathway | ko00531 | Glycosaminoglycan degradation | 3/232 | 20/7004 | 4.53 | 0.026971 | 0.979066 | ENSG00000078061/ | ARAF | | | | | | | | |
| | | | | | | | | ENSG00000105810/ | CDK6 | | | | | | | | |
| | | | | | | | | ENSG00000129675/ | ARHGGEF6 | | | | | | | | |
| | | | | | | | | ENSG00000138798/ | EGF | | | | | | | | |
| | | | | | | | | ENSG00000145675 | PIK3R1 | | | | | | | | |
| | | | | | | | | | RALBP1 | | | | | | | | |
| | | | | | | | | | IDS | | | | | | | | |
| | | | | | | | | | HGSNAT | | | | | | | | |
| | | | | | | | | | AC244197.3 | | | | | | | | |
| KEGG_ pathway | ko05212 | Pancreatic cancer | 6/232 | 72/7004 | 2.52 | 0.03142 | 0.979066 | ENSG00000078061/ | ARAF | | | | | | | | |
| | | | | | | | | ENSG00000105810/ | CDK6 | | | | | | | | |
| | | | | | | | | ENSG00000129675/ | ARHGGEF6 | | | | | | | | |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_factor | P-value | Q-value | GeneID | Gene_symbol |
|------------------|------------|---|-----------|----------|---------------|----------|----------|------------------|-------------|
| KEGG pathway | ko05032 | Morphine addiction | 7/232 | 92/7004 | 2.3 | 0.032366 | 0.979066 | ENSG00000113448/ | PDE4D |
| | | | | | | | | ENSG00000127928/ | GNGT1 |
| | | | | | | | | ENSG00000141837/ | CACNA1A |
| | | | | | | | | ENSG00000148408/ | CACNA1B |
| | | | | | | | | ENSG00000152270/ | PDE3B |
| | | | | | | | | ENSG00000171408/ | PDE7B |
| | | | | | | | | ENSG00000205268 | PDE7A |
| KEGG pathway | ko01200 | Carbon metabolism | 8/232 | 117/7004 | 2.06 | 0.039868 | 0.990493 | ENSG00000073578/ | SDHA |
| | | | | | | | | ENSG00000092621/ | PHGDH |
| | | | | | | | | ENSG00000101911/ | PRPS2 |
| | | | | | | | | ENSG00000102144/ | PGK1 |
| | | | | | | | | ENSG00000121691/ | CAT |
| | | | | | | | | ENSG00000136143/ | SUCLA2 |
| | | | | | | | | ENSG00000151005/ | TKTL2 |
| ENSG00000226784 | PGAM4 | | | | | | | | |
| KEGG pathway | ko05100 | Bacterial invasion of epithelial cells | 6/232 | 81/7004 | 2.24 | 0.051247 | 0.990493 | ENSG00000062598/ | ELMO2 |
| | | | | | | | | ENSG00000105971/ | CAV2 |
| | | | | | | | | ENSG00000109458/ | GAB1 |
| | | | | | | | | ENSG00000145675/ | PIK3R1 |
| | | | | | | | | ENSG00000150760/ | DOCK1 |
| | | | | | | | | ENSG00000175416 | CLTB |
| | | | | | | | | ENSG00000058091/ | CDK14 |
| KEGG pathway | ko05202 | Transcriptional misregulation in cancer | 10/232 | 175/7004 | 1.73 | 0.064842 | 0.990493 | ENSG00000102755/ | FLT1 |
| | | | | | | | | ENSG00000122025/ | FLT3 |
| | | | | | | | | ENSG00000159216/ | RUNX1 |
| | | | | | | | | ENSG00000170365/ | SMAD1 |
| | | | | | | | | ENSG00000171843/ | MLLT3 |
| | | | | | | | | ENSG00000203811/ | HIST2H3C |
| | | | | | | | | ENSG00000203852/ | HIST2H3A |
| ENSG00000239839/ | DEFA3 | | | | | | | | |
| ENSG00000250349 | AF241726.2 | | | | | | | | |

(Contd...)

Table S5. (Continued)

| Category | ID | Description | GeneRatio | BgRatio | Enrich_ factor | P-value | Q-value | GeneID | Gene_symbol | | | |
|------------------|---------|---------------------------|------------------|----------|----------------|------------------|----------|------------------|-------------|----------|------------------|------|
| KEGG pathway | ko04014 | Ras signaling pathway | 12/232 | 235/7004 | 1.54 | 0.089753 | 0.990493 | ENSG00000017797/ | RALBP1 | | | |
| | | | ENSG00000077264/ | PAK3 | | | | | | | | |
| | | | ENSG00000102755/ | FLT1 | | | | | | | | |
| | | | ENSG00000108061/ | SHOC2 | | | | | | | | |
| | | | ENSG00000109458/ | GAB1 | | | | | | | | |
| | | | ENSG00000127472/ | PLA2G5 | | | | | | | | |
| | | | ENSG00000127928/ | GNGT1 | | | | | | | | |
| | | | ENSG00000138798/ | EGF | | | | | | | | |
| | | | ENSG00000145675/ | PIK3R1 | | | | | | | | |
| | | | ENSG00000156427/ | FGF18 | | | | | | | | |
| KEGG pathway | ko04930 | Type II diabetes mellitus | 4/232 | 52/7004 | 2.32 | 0.092534 | 0.990493 | ENSG00000141837/ | CACNA1A | | | |
| | | | ENSG00000145675/ | PIK3R1 | | | | | | | | |
| | | | ENSG00000148408/ | CACNA1B | | | | | | | | |
| | | | ENSG00000181092 | ADIPOQ | | | | | | | | |
| | | | ENSG00000078061/ | ARAF | | | | | | | | |
| | | | ENSG00000105810/ | CDK6 | | | | | | | | |
| | | | ENSG00000138798/ | EGF | | | | | | | | |
| | | | ENSG00000145675/ | PIK3R1 | | | | | | | | |
| | | | ENSG00000156427 | FGF18 | | | | | | | | |
| | | | KEGG pathway | ko05218 | Melanoma | 5/232 | 76/7004 | 1.99 | 0.106652 | 0.990493 | ENSG00000078061/ | ARAF |
| ENSG00000105810/ | CDK6 | | | | | | | | | | | |
| ENSG00000145675/ | PIK3R1 | | | | | | | | | | | |
| ENSG00000159216/ | RUNX1 | | | | | | | | | | | |
| ENSG00000175029 | CTBP2 | | | | | | | | | | | |
| KEGG pathway | ko05220 | Chronic myeloid leukemia | | | | 5/232 | 76/7004 | 1.99 | 0.106652 | 0.990493 | ENSG00000078061/ | ARAF |
| | | | | | | ENSG00000105810/ | CDK6 | | | | | |
| | | | | | | ENSG00000145675/ | PIK3R1 | | | | | |
| | | | | | | ENSG00000159216/ | RUNX1 | | | | | |
| | | | | | | ENSG00000175029 | CTBP2 | | | | | |

Table S6. RNA-seq data description

| Sample name | BLK1 | BLK2 | IR1 | IR2 |
|--|-------|----------|-------|-------|
| Total raw data (Gb) | | 27.34 Gb | | |
| Mean raw data (Gb) | | ≥5.81 Gb | | |
| Error ratio (%) | 0.04 | 0.04 | 0.04 | 0.04 |
| Q30 (%) | 93.91 | 93.99 | 93.46 | 93.03 |
| GC (%) | 46.93 | 46.88 | 47.10 | 46.45 |
| High-quality data (Gb) | 22.08 | 23.65 | 19.41 | 26.18 |
| Mapped data (Gb) | 20.88 | 22.35 | 18.33 | 24.68 |
| Mapping ratio (%) | 92.37 | 92.36 | 92.33 | 92.17 |
| Genes with FPKM > 0.5 (at least in one sample) | 23907 | 23907 | 23907 | 23907 |

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