

## **Supporting Information**

### **Supplementary Methods**

#### **Patient cohorts**

The aneuploid (A-) acute myeloid leukemia (AML) cohort included six cases with isolated trisomy, one case displaying trisomy plus another alteration, two *EVI1*-related, three *KMT2A*-rearranged and eight core binding factor (CBF) AML carrying additional abnormalities (including whole chromosome gain/loss) and 22 cases with complex (CK) or monosomal (MK) karyotype. E-AML cases were normal karyotype AML or carried structural chromosomal abnormalities in the absence of clonal numerical alterations. Statistical significance of patients' features was determined using the Mann-Whitney test for continuous variables and the Fisher's exact test or chi-square test for categorical variables. Linear regression analysis was performed using GraphPad Prism 6 (GraphPad Software).

#### **Sample preparation**

Leukocytes were enriched by separation on Ficoll density gradient and lysed in RLT buffer. Buccal swab samples, used as normal matching, were collected with the Oragene Discover kit (DNA Genotek). Genomic DNA, RNA and proteins were extracted by column purification (AllPrep DNA/RNA/Protein Mini Kit and QIAcube, Qiagen) and from saliva by paramagnetic particles (Maxwell® 16 LEV DNA Blood Purification Kit and Maxwell® MDx Instrument), according to the manufacturer's recommendations.

#### **Chromosome banding analysis**

Chromosome banding analysis was performed on bone marrow cells after 24/48 hours culture <sup>1</sup>. A CK was defined by  $\geq 3$  chromosomal abnormalities in the same clone. Aneuploidy is defined as gain/loss of  $\geq 1$  whole chromosomes. Chromosomal gains/structural abnormalities and loss detected in  $\geq 2$  and  $\geq 3$  metaphases, respectively, were acknowledged as clonal (International System for Human Cytogenomic Nomenclature 2016).

## Somatic variant detection

Data generated by sequencing (average coverage of 80X) were pre-processed as described in GATK best practice <sup>2</sup>. Sequencing reads were quality control checked using Fastqc tool (<http://www.bioinformatics.babraham.ac.uk/projects/fastqc>) before and after trimming to remove adapter sequences and adjust quality values. A phred value of 20 was chosen as the minimum threshold for base quality. The reads having more than 80% of low quality bases were removed or had their 3' extremity bases trimmed when the minimum threshold was not reached. The sequence reads were then mapped to the reference using BWA-MEM <sup>3</sup> to produce SAM format files which were sorted by coordinate by Picard tool (<http://broadinstitute.github.io/picard>) outputting BAM formatted files. Duplicates were marked and resulting BAM files were indexed by Picard tool. Local realignment was performed around indels to artifacts and base quality scores were recalibrated to improve the accuracy of the variant calls. Resulting BAM files were analyzed by MuTect <sup>4</sup> and VarScan 2 algorithms <sup>5</sup> in order to characterize each sample in terms of single nucleotide variants and small indels. The output was annotated by ANNOVAR tool <sup>6</sup>. Non-exonic and synonymous point mutations, variants targeting genes previously annotated as apparent false-positive findings <sup>7</sup> or located in segmental duplication regions were removed. Moreover, mutations called by VarScan 2 were subjected to somatic filtering procedure as described by *Koboldt et al.* <sup>5</sup>. Variants were filtered for SNP reported in dbSNP138 ([www.ncbi.nlm.nih.gov/projects/SNP](http://www.ncbi.nlm.nih.gov/projects/SNP)), Exome Sequencing Project (ESP, <http://evs.gs.washington.edu/EVS>), Exome Aggregation Consortium (ExAC, <http://exac.broadinstitute.org>), 1000 Genomes Project (<http://www.internationalgenome.org>) with minor allele frequency  $\geq 0.01$ . The final list of somatic variants is reported in Table S11 (for reviewers only). The impact of variants on the functional protein state was analyzed *in silico* by the prediction algorithms Sorting Intolerant From Tolerant (SIFT), Polymorphism Phenotyping (PolyPhen-2) and Mutation Assessor. Statistical significance was determined using the Student's *t* test for the number of mutations, the Fisher's exact test for the number of patients carrying mutations and one-way analysis of variance for the distribution of cases according to the mutation number.

## DNA Sanger sequencing and targeted NGS-based resequencing

Candidate non-silent somatic mutations detected by WES were validated by conventional Sanger-based resequencing of polymerase chain reaction (PCR) products obtained from tumor (n=56, variant allele frequency (VAF) higher or equal to 0.23) and paired tumor-germline (n=21) genomic DNA using primers specific for the exon encompassing the variant. A Next Generation Sequencing (NGS)-based targeted sequencing approach was used to validate variants in myeloid-related genes (n=38 validation) on tumor samples (TrueSight Myeloid Sequencing Panel and MiSeq instrument, Illumina Inc.). Library preparation and sequencing were performed according to manufacturer's instructions. Overall, a validation rate of 91.5% was obtained (Table S11). *FLT3-ITD* mutations were detected as previously described<sup>8</sup>. AML cases from the gene expression profiling (GEP) cohort were analyzed by conventional Sanger sequencing for *TP53* mutations in exon 5-9, using the following primers for DNA (5'-3'): *TP53* exon 5-6 fw: CACTTGTGCCCTGACTTTCA, rev: TTGCACATCTCATGGGGTTA; *TP53* exon 7-9 fw: CGCACTGGCCTCATCTTGG, rev: TGTCTTTGAGGCATCACTGC.

## Mutational signatures

Synonymous and non-synonymous single nucleotide variants identified as above were used for mutational signature analysis<sup>9</sup>. Briefly, for each mutation, information on the substitution class and the bases immediately 5' and 3' were integrated to obtain somatic motifs. The frequency of these motifs across multiple samples was represented as a matrix  $M_{ij}$ , where  $i$  counts over the motifs and  $j$  over the samples.  $M$  was decomposed by non-negative matrix factorization (NMF) with the constraint of positive components in  $W$  and  $H$ <sup>10</sup>. The optimal number of signature ( $r$ ) was determined according to biological knowledge, with computation of the residuals sum of squares and the explained variance between the observed  $M$  and fitted  $WH$  mutational spectrum for different numbers of signatures. Then clustering was computed by grouping by the sample dimension of the spectrum employing the Euclidean distance. Continuous variables were analyzed by one-way ANOVA.

## **Structural variant detection by high-density SNP arrays**

Genomic DNA was digested, ligated, amplified and purified according to manufacturer's instructions. Labeling, hybridization, washing, staining and scanning were performed according to manufacturer's recommendation. Data were processed by Affymetrix Genotyping Console and Chromosome Analysis Suite (ChAS, Affymetrix) to evaluate CEL files Median Absolute Pairwise Difference (MAPD) and by Nexus Copy Number software (professional version 7.5, Biodiscovery) to obtain segmentation data. The following filter settings were used: copy number variants (CNVs) larger than or equal to 1Kb covered by more than 7 probes <sup>11</sup>. Each segment was compared in terms of position and event type to the Database of Genomic Variants (DGV, <http://dgv.tcag.ca/dgv/app/home>) and to a cohort of healthy subjects (GSE59150 <sup>11</sup>). Segments previously reported in healthy subjects were filtered out. Retained segments were grouped separately by event type according to standard thresholds (1-copy gain >0.1, 2-copy gain >0.7, heterozygous loss <-0.15, homozygous loss <-1.1, Nexus Copy Number software). To increase the signal to noise ratio, median intensity value and median absolute deviation were calculated for each chromosome (including sex chromosomes) and thresholds for low and high boundaries were estimated as  $T_L = -3.5 \cdot MAD$  and  $T_H = 7 \cdot MAD$  respectively. Segments having intensity values  $\geq T_L$  and  $\leq T_H$  were retrieved to fill gaps. Genes located in the defined segments were annotated and supervised filtering according to DGV annotations was performed. Loss of heterozygosity (LOH) was defined as a region displaying LOH without a CN loss. Circos plots were obtained by Circos v0.69-4 <sup>12</sup>. Microarray data are available upon request at the following link: <https://ngs-ptl.unibo.it:5006>.

## **Enrichment analysis**

Enrichment analyses were conducted in R v3.3.2 <sup>13</sup> and Bioconductor v3.4 (BiocInstaller 1.24.0) using the following packages: "org.Hs.eg.db" v3.4.0,<sup>14</sup> "clusterProfiler" v3.2.11 <sup>15</sup>, "GO.db" v3.4.0 <sup>16</sup>. Genes affected by CNAs were annotated according to Gene Ontology Biological Processes (GO-BP) <sup>17</sup>. For enrichment on cytobands, WEB-based GENE SeT AnaLysis Toolkit was used <sup>18</sup>.

## **Network analysis**

Based on pathway enrichment analysis (GO-BP), two bipartite graphs were created, for the euploid and aneuploid cohorts, respectively, in which the nodes represented patients and pathways and the links represented significantly enriched pathways. The projection of the bipartite graph resulted in graph in which the nodes were pathways and the links between nodes represented the number of patients having both pathways enriched. We considered only links with weights  $\geq 2$ . The pathways were then ranked according to their degree and betweenness centrality in the euploid and aneuploid networks. The enrichment analysis was performed using the R/Bioconductor packages clusterProfiler. The network analyses were performed using Cytoscape and the python package Networkx.

## **Analysis of GEP data**

Raw data were processed by Expression Console software with Robust Multi-Array (RMA) normalization. Supervised data analysis was carried out with Transcriptome Analysis Console v3.0 software (Affymetrix). Non-coding genes and transcripts with a low average signals were excluded from downstream analysis. Since an extra chromosome copy was previously shown to induce a 1.3 fold change difference on average <sup>19,20</sup>, we selected transcripts up- or downregulated by a factor of at least 1.3. The False discovery rate (FDR) cut-off was set at 0.15. Functional annotation clustering was performed using David Bioinformatics Resources 6.8 (National Institute of Allergy and Infectious Diseases, NIH) <sup>21</sup>. Gene set enrichment analysis (GSEA) was performed with GSEA software (Broad Institute) <sup>22,23</sup>. Discriminating signatures were obtained by a custom Discriminant Analysis approach, based on a network obtained from all couples of transcripts. The available data underwent a 5-fold cross-validation procedure to assess unbiased signature performance. The top scoring signatures were then analyzed for biological and therapeutic significance. Microarray data are available upon request at the following link: <https://ngs-ptl.unibo.it:5006>.

### **Flow cytometry**

Bone marrow leukocytes were fixed in 70% methanol (according to manufacturer's protocol) and stained with BV421-conjugated anti-Ki-67 (clone B56) and then with peridinin chlorophyll protein cyanine 5.5-conjugated anti-CD45 (clone HI30, all BD). Data were acquired on a FACSCanto II (BD) using FACSDiva software (BD); data were analyzed using FACSDiva.

### **Western blot analysis**

Protein extracts were separated by SDS-PAGE and transferred onto nitrocellulose membranes. The following antibodies were used: rabbit anti-UBE2C, anti-UHRF1 (D6G8E), anti-RAD50, anti-CDC20 (D6C2Q), anti-PLK1 (28G4; all Cell Signaling Technologies), mouse anti-UBA3 (F-10), anti-Ub (P4D1; all Santa Cruz Biotechnology), anti- $\beta$ -actin (AC-74; Sigma-Aldrich); HRP-conjugated anti-rabbit/anti-mouse IgG (GE Healthcare). ECL Prime (GE Healthcare) and SuperSignal West Femto Maximum Sensitivity Substrate (Thermo Fisher Scientific) reagents were used for detection. Quantitative analysis was performed by ImageJ software (1.45s; National Institutes of Health), with  $\beta$ -actin serving as control.

## References

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## Supplementary Figure Legends

**Figure S1. Regression of mutations vs. patients' age.** Number of somatic mutations vs. patients' age in A-AML and E-AML from our cohort (A) and from the TCGA AML dataset (B). The linear regression coefficient shows a significant increase with age only for aneuploid patients in both cohorts: (A) A-AML, slope:  $0.50 \pm 0.20$ ,  $p=0.018$ ; E-AML, slope:  $0.014 \pm 0.11$ , not significant (ns); (B) TCGA A-AML, slope:  $0.32 \pm 0.09$ ,  $p=0.002$ ; TCGA E-AML, slope:  $0.07 \pm 0.04$ , ns.

**Figure S2. Pattern of genomic lesions in A-AML and E-AML cases carrying mutations in genes involved in intracellular trafficking.** Each row denotes one or more specific gene(s); columns represent (left to right): functional categories, mutated genes/group of genes or other genomic alterations and single patients. Colors indicate functional categories.

**Figure S3. Pattern of genomic lesions in A-AML and E-AML cases carrying mutations in genes involved in protein ubiquitination.** Each row denotes one or more specific gene(s); columns represent (left to right): functional categories, mutated genes/group of genes or other genomic alterations, single patients. Colors indicate functional categories.

**Figure S4. Pattern of genomic lesions in A-AML and E-AML cases carrying mutations in genes involved in cell adhesion.** Each row denotes one or more specific gene(s); columns represent (left to right): functional categories, mutated genes/group of genes or other genomic alterations, single patients. Colors indicate functional categories.

**Figure S5. Ubiquitin level in A-AML and E-AML.** (A) Western blot of four representative cases of each cohort.. (B) Densitometry after normalization for the mean value across all E-AML cases, with  $\beta$ -actin serving as control. Statistical significance was determined by Student's *t* test (*ns* =not significant).

**Figure S6. Overview of aneuploid (A) and euploid (B) networks.** Each node is a GO-BP pathway and the links connect pathways enriched in least two patients.

**Figure S7. Signature of p53-downregulation in A-AML.** A-AML cases carrying *TP53* mutation or chromosome 17 monosomy were excluded (n=18, A-AML; n=27, E-AML).

## Supplementary Figures

Figure S1

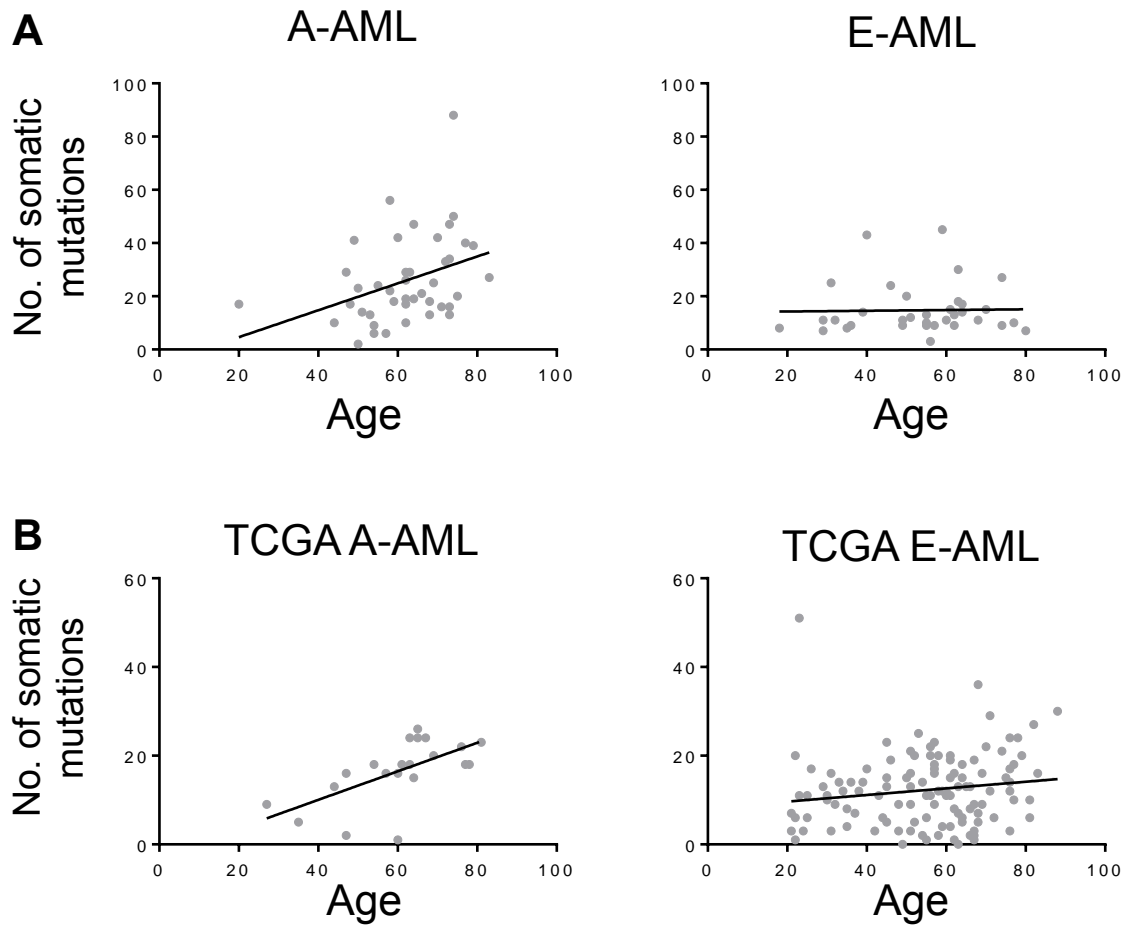


Figure S2

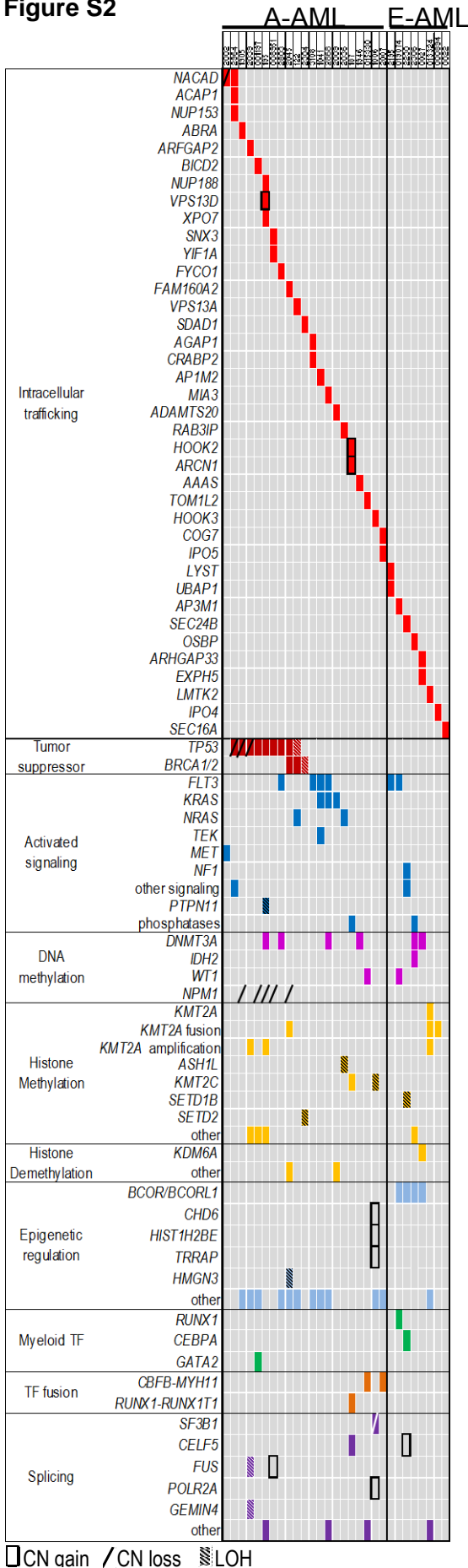
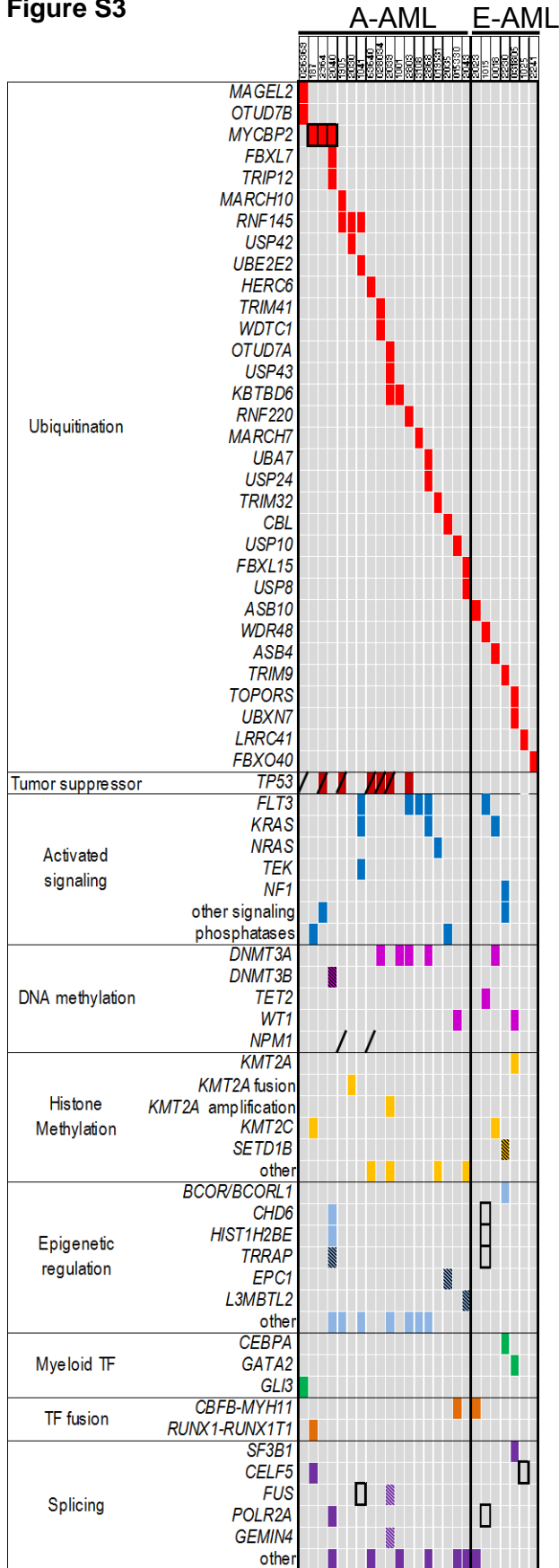


Figure S3



□ CN gain / CN loss ▨ LOH

Figure S4

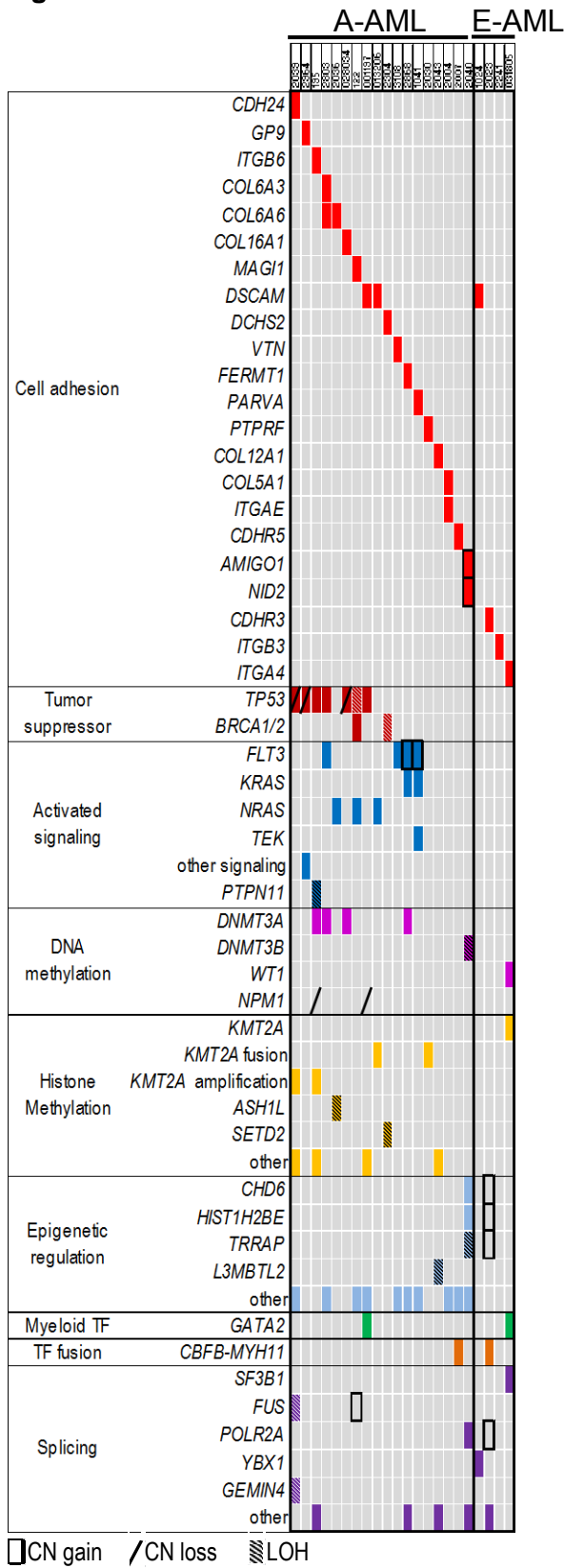


Figure S5

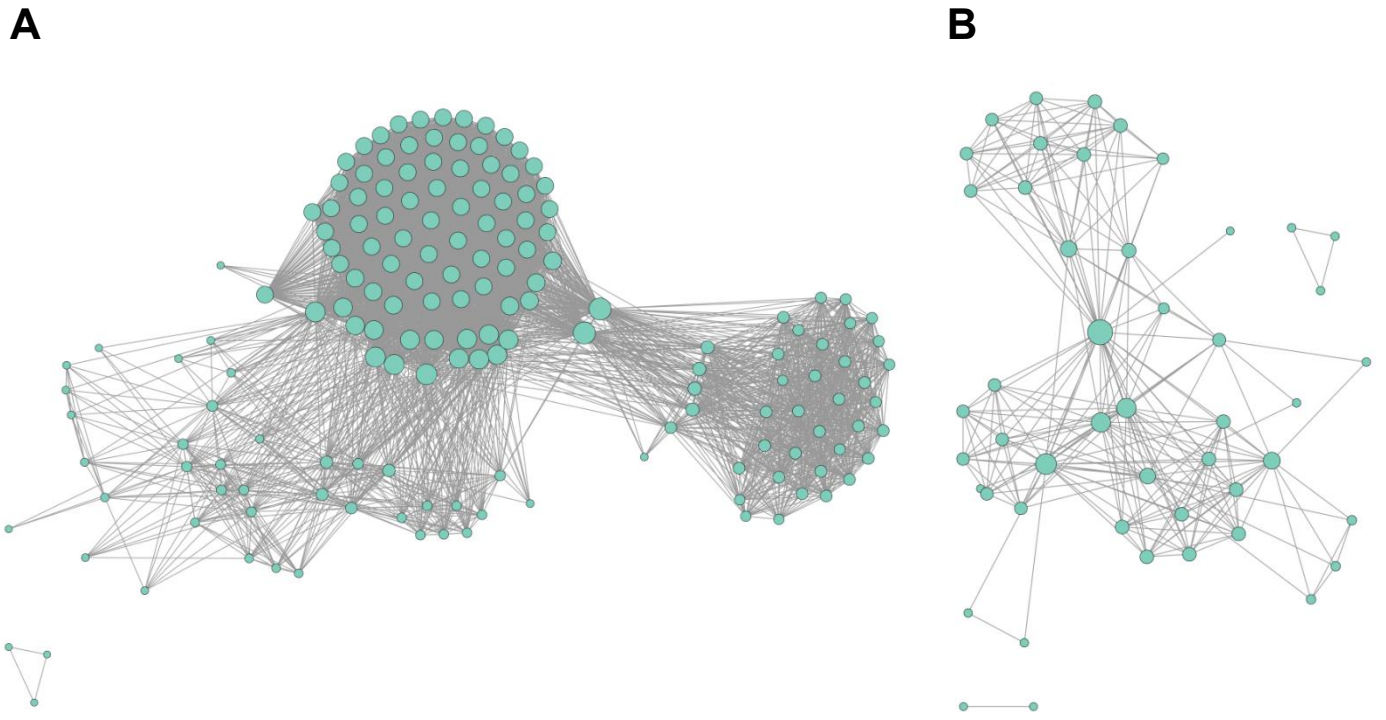


Figure S6

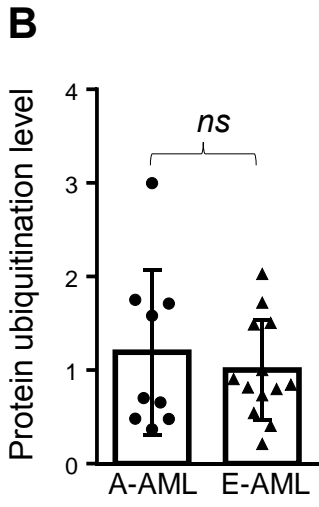
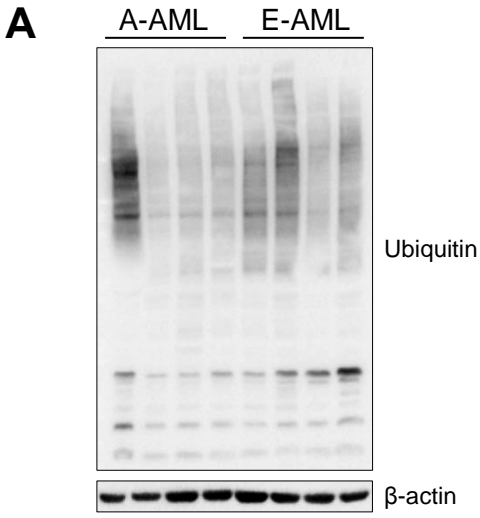
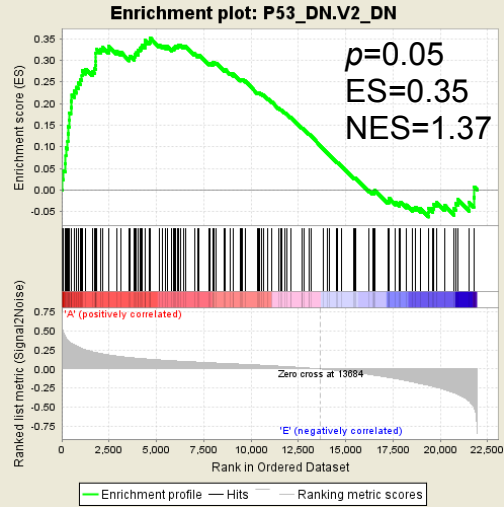




Figure S7



Supplementary Tables

Table S1. Aneuploid and Euploid AML patients' characteristics.

Patient ID	WES	SNP	GEP	Karyotype	De novo/sec-t-AML	FAB type	Diagnosis (D)/Relapse (R)	Sex	Age	Sample type (BM/PB)	WBC count (x10 <sup>9</sup> /L)	Genetic group
<b>Aneuploid AML</b>												
001197	x	x		45-48,XX, idic(5)(q11), dic(6;22)(p11;p11), +r(6), del(8)(p11), +der(8)t(6;8)(?;p11)x1-2, der(8;12)dic(8;12)(p11;p11)t(12;15)(q24;q?) [15/15]	de novo	M2	D	F	51	BM	31.0	Adverse
006187	x	x		50,XY,+4,+14,+21,+22[5/8]/46,XY[3/8]	de novo	M1	D	M	59	BM	0.9	Adverse
008951	x	x		48,XX,der(3)t(3;5)(p11;p11),del(3)(q21q26),del(5)(q11q35),+der(5)del(5)(q14q34),+8,i(9)(p10)[7/19]/48,XX,der(3)t(3;5)(p11;p11),del(3)(q21q26),del(5)(q11q35),+der(5)del(5)(q14q34),der(7)t(5;7)(?;p11),+8,i(9)(p10),der(12)t(7;12)(p11;p11)[3/19]/46,XX[9/19]	sec (MDS)	M6	D	F	73	BM	1.6	Adverse
019531	x			45,XY,t(2;3)(p21;q26),-7,der(12)ins(12;7)(p13;q22q34)[19/23]/46,XY[4/23]	de novo	M0	D	M	53	BM	na	Adverse
026369	x	x		46,XX,-5,der(7)t(5;7)(?;q11),+der(8)del(8)(p11p23),+11,der(17)t(5;17)(?;p13),-18,-20,+der(22)t(5;22)(?;q13)[3/23]/47,XX,-5,+6,der(7)t(5;7)(?;q11),+del(8)(p11p23),+11,der(17)t(5;17)(?;p13),-18,-20,+der(22)t(5;22)(?;q13)[4/23]/46,XX[16/23]	de novo	M2	D	F	73	BM	1.0	Adverse
026656	x	x		45,X,-Y,t(2;21;8)(p25;q22;q22)[16/20]/46,XY[4/20]	de novo	M1	D	M	20	BM	6.4	Favorable
028034	x	x		46,X,-X,del(5)(q13q35),+6,-7,der(11)t(7;11)(q11;p11),del(8)(q11),der(16;17)(p10;q10),+22[9/11]/47,XX,del(5)(q13q35),+6,+8,der(16;17)(p10;q10)[2/11]	de novo	M2	D	F	58	BM	3.7	Adverse
015330	x			47,XY,t(3;6;3)(p26;p24;p21),+8,inv(16)(p13q22)[18/20]/46,XY[2/20]	de novo	M1	D	M	75	BM	na	Favorable
007827	x	x		45,X,-Y,t(8;21)(q22;q22)[9/20]/46,XY[11/20]	de novo	M2	D	M	62	BM	7.1	Favorable
013206	x	x		52,XY,+6,ins(6;11)(q27;q13q23),+8,+9,+13,+19,+21[21/21]	de novo	M1	D	M	44	BM	na	Adverse
006473	x	x		46,XY,inv(16)(p13q22)[14/21]/48,XY,inv(16)(p13q22),+8,+13[1/21]/93,XXYY,inv(16)(p13q22)x2,-2,+8,+8[3/21]/46,XY[3/21]	de novo	M4eo	D	M	62	BM	na	Favorable
042101	x			48,XX,+8,+22.ish der(16)ins(16;16)(q22;p13p13)[19/22]/46,XX[3/22]	de novo	M4eo	D	F	64	BM	na	Favorable

2803	x	x		47,XY,del(5)(q11q33),der(8)t(5;8)(q33;q24),+der(8)t(5;8)(q33;q24)[18/20]/46,XY[2/20]	sec (MDS)	M4	D	M	73	PBL	56.9	Adverse
2030	x	x	x	47,XX,+8,t(9;11)(p22;q23)[16/20]/48,XX,+8,+8,t(9;11)(p22;q23)[1/20]/50,XX,+8,+8,t(9;11)(p22;q23),+13,+19[3/20]	de novo	M5	D	F	62	BM	23.1	Adverse
37			x	45,X,-Y,t(8;21)(q22;q22)[11/20]/46,X,-Y,t(8;21),+mar(3/20)/46,XY[6/20]	de novo	M2	D	M	39	BM	na	Favorable
3108	x	x		46,XX[19/21]/47,XX,+4[2/21]	de novo	M5	D	F	69	BM	129.0	Intermediate
2004	x			48-50,XX,+2,-5,+6,der(8),del(9)(q22),der(11)t(8;11;17)(q12;q13;p13),+13,+der(13)del(13)(q14q32),+1~2 mar[18/19]/46,XX[1/19]	de novo	M2	D	F	55	BM	0.8	Adverse
63640	x	x		41-45,XX,t(1;2;?)(q21;q12;?),-3,t(5;11)(q13;p13),-7,add(8)(q24),-16,-17,-22,3~4mar[13/21]; 46,XX[8/21]	de novo	na	D	F	70	BM	1.0	Adverse
2002	x	x	x	45,XY,t(3;3)(q21;q26),-7[20/20]	t-AML	M0	D	M	68	PBL	5.2	Adverse
2007	x	x		47,XY,+8,inv(16)(p13q22)[9/20]/46,XY,t(9;17)(q34;q21),inv(16)(p13q22)[8/20]/46,XY,add(8)(q24),inv(16)(p13q22)[3/20]	t-AML	M2-M4	D	M	68	BM	14.0	Favorable
1014	x	x		47,XX,+4[3/20]/46,XX[17/20]	de novo	M4	D	F	48	PBL	4.7	Intermediate
69			x	47,XX,+X,i(17)(q10)[14/20]/46,XX[6/20]	de novo	M2	D	F	72	BM	35.1	Intermediate
2035	x	x		46,XY,t(3;12)(p22;q24),+4,-15,+mar[19/20]/46,XY[1/20]	de novo	na	R	M	62	BM	na	Adverse
2868	x	x		47,XX,del(5)(q13q33),+8[20/20]	de novo	na	D	F	72	BM	8.9	Adverse
187	x	x		74,XXX,t(8;21)(q22;q22)X2,-7,+8,+9,+13,+16,+17,+19[9/10]/46,XX[1/10]	de novo	na	D	F	74	BM	1.7	Favorable
70			x	45,X,-Y,t(8;21)(q22;q22)[19/20]/46,XY[1/20]	de novo	M4	D	M	31	BM	5.1	Favorable
2964	x	x		44,XX,+der(3)t(3;20)(p12;p11),del(5)(q13q33),-7,-13,t(13;20)(q12;p11),-17,der(21)t(17;21)(q11;q22),+mar[14/20]/45,XX,t(1;16)(q12;q11),del(5)(q13q33),del(6)(q21q25),-7,add(22)(q13)[6/20]	sec (MDS)	sec (MDS)	D	F	60	BM	1.5	Adverse
2009	x	x		45,XX,t(3;14;16)(q21;q22;q22),add(7)(q34),-7,del(14)(q23q32),add(16)(q22),-21,+mar[16/20]/46,XY,t(3;14;16)(q21;q22;q22),add(7)(q34),der(7),del(14)(q23q32),add(16)(q22),-21,+mar[4/20]	de novo	M2	D	M	50	PBL	14.5	Adverse
5			x	45,XY,t(1;3;13)(p34;q26;q14),-7[18/20]/45,XY,t(1;3;13)(p34;q26;q14),-7,der(21)t(7;21)(q10;p10)[1/20]/46,XX[1/20]	de novo	na	D	F	68	BM	8.6	Adverse
54			x	47,XY,del(7)(q32q36),t(16;16)(p13;q22),+22[15/20]/48,XY,del(7)(q32q36),t(16;16)(p13;q22),+21,+22[2/20]/46,XY[3/20]	de novo	M4	D	M	61	BM	7.4	Favorable
21			x	48,XX,+4,+8[30/30]	de novo	M4	D	F	70	BM	na	Intermediate

13		x		44,XX,t(3;17)(p21;p13),del(5)(q13q33),-12,del(13)(q14),der(14)t(12;14)(p11p11),-18,add(21)(q13)[24/25]/46,XX [1/25]	na	M4	D	F	69	BM	na	Adverse
1006	x	x	x	47,XX,+4[13/20]/46,XX[7/20]	t-AML	M1	D	F	62	BM	13.4	Intermediate
1			x	47,XX,+21[16/20]/46,XX[4/20]	de novo	M0-M1	D	F	54	BM	38.9	Intermediate
122	x	x		51,XX,+X,t(1;3)(p36;p21),del(5)(q13q33),-7,+8,+9,add(10)(p15),+13,+20,+22[20/20]	de novo	na	D	F	83	BM	1.8	Adverse
24			x	43,XY,-7,hsr(11)(q13q23),-13,-17,del(20)(q11q13),-21,-der(22)add(22)(p13),+mar,1~3dmin[19/23]/44,XY,-7,hsr(11)(q13q23),-13,-17,del(20)(q11q13),-21,-der(22)add(22)(p13),+2mar,1~3dmin[4/23]	t-AML	M5	D	M	69	BM	238	Adverse
2304	x	x		52,XY,inv(3)(q21q26),+8,+10,+13,+15,+21,+22[18/20]/45,XY,inv(3)(q21q26),-7[2/20]	de novo	M1	D	M	47	BM	1.0	Adverse
2033	x	x		47,XX,del(11)(p11p15);t(15;17)(q24;q25)*,inv(16)(p13q22),+8[20/20]	de novo	M1	D	F	57	BM	48.3	Favorable
1001	x	x		47,XY,+13[20/20]	de novo	na	D	M	54	BM	66.0	Intermediate
71			x	44-47,XX,t(4;17)(p15;q21),del(5)(q13q33),-7,-18,der(X),1~3mar[9/20]/46,XX[11/20]	de novo	M2	D	M	67	BM	3.6	Adverse
1946	x	x		46,XY,+8,add(11)(p15),-13,+mar[7/19]/46,XY,+8,add(11)(p15)x2,-13,+mar[5/19]/46,XY,+8,add(11)(p15)[5/19]/46,XY,+8,add(11)(p15)x2[2/19]	de novo	M5	D	F	49	BM	3.0	Adverse
2045	x	x		44,XX,-3,del(4)(q21q31),-5,del(7)(q22q36),der(8)t(3;8)(q25;p21),del(10)(q22q24),inv(11)(q13q23),der(12),add(13)(q34),del(15)(q11q24),del(16)(q22),add(17)(p13),-18,+r[15/20]/46,XX[5/20]	de novo	M0	D	F	64	BM	3.1	Adverse
56			x	45,XX,t(3;21)(q26;q22),der(5)(q?),-7,del(12)(p11p13)[15/18]/45,XX,t(3;21)(q26;q22),der(5)(q?),-7,del(11)(p13p15),del(12)(p11p13)[3/18]	t-AML	na	D	F	62	BM	77	Adverse
2043	x	x		46,XY,del(12)(p11p13)(7/20)/47,XY,del(12)(p11p13)+13[2/20]/48,XY,del(12)(p11p13),+13,+14[3/20]/49,XY,del(12)(p11;p13),+der(12)(p11;p13),+13,+14[3/20]/46,XY[5/20]	de novo	M1	R	M	63	BM	na	Adverse
195	x	x		44,XY,t(Y;1;5)(p11;p32;q33),-7,del(12)(p12;p13)(5/19)/44,XY,t(Y;1;5)(p11;p32;q33),-7,add(11)(q23),del(12)(p12;p13),-18[3/19]/44,XY,t(Y;1;5)(p11;p32;q33),der(2),-7,del(12)(p12;p13),t(12?;19)(q13?;p13),-18,del(X)(p21)[9/19]/46,XY[2/19]	sec (MDS)	sec (MDS)	D	M	58	BM	20.3	Adverse
1905	x	x		42,XY,-4,del(5)(q13q33),-7,-12,der(16),add(17)(p13),der(19)t(4;19)(q31;p13),-20,-21,-22,+mar[9/21]/42,XY,-4,-5,del(7)(q11q36),der(16),add(17)(p13),der(19)t(4;19)(q31;p13),-20,-21,+mar[2/21]/69-72,XXY,id[10/21]	de novo	na	D	M	79	BM	3.0	Adverse
2005	x	x		45,XX,-7[9/17]/46,XX[8/17]	de novo	M1	D	F	50	BM	1.6	Adverse
58			x	47,XY,+8[11/20]/46,X,-Y,+8[9/20]	de novo	M5	D	M	42	BM	66.9	Intermediate

2040	x	x	x	92-104,XXXX,+5,+8,+8,+9,+13,+13,+13,+20,+20,+21,+22,+22[20/20]	t-AML	M5	D	F	74	BM	2.8	Adverse
23			x	48,XY,+1,+13[16/27]/46,XY[11/27]	de novo	na	D	M	82	BM	na	Intermediate
1028	x	x		47,XX,+21[6/8]/46,XX[2/8]	de novo	M1	D	F	54	BM	1.2	Intermediate
2039	x	x		45 XY del(5)(q13;q33),dup(11)(q13;q25),t(12;16)(p13;p13),-13,-17,+r[20/20]	de novo	na	D	M	73	BM	25.0	Adverse
12			x	46,XX[11/20]/47,XX,+der(13)i(13)(q10)[8/20]/47,XX,+13[1/20]	t-AML	na	D	F	76	BM	na	Intermediate
68			x	48,XX,+14,inv(16)(p13q22),+21[18/20]/46,XX,inv(16)(p13q22)[2/20]	t-AML	M4	D	F	57	BM	10.5	Favorable
213	x	x		42-48,XX,del(5)(q13q33),i(21)(q10),+der(21)i(21)(q10)x2[18/20]/42-48,XX,del(5q),del(11)(p13p15),-17,i(21q),+der(21)i(21)(q10)x2[2/20]	de novo	na	D	F	71	BM	2.5	Adverse
2036	x	x	x	49,XY,+3r[17/20]/46,XY[3/20]	de novo	M4	D	M	66	BM	115.0	Adverse
25			x	43,XY,del(2)(q?),+der(3)del(3)(q?)-5,-7,i(8)(q10),-13,-14,der(16),-17,add(22)(p13),+r[16/20]/43,XY,del(2)(q?)+der(3)del(3)(q?)-5,-7,der(8)t(8q?;11q?)-11,der(16),-17[3/20]/46,XY[1/20]	de novo	M0	D	M	62	BM	1.5	Adverse
55			x	47,XX,+8[20/20]	de novo	M4	D	F	71	BM	90	Intermediate
1041	x	x		47,XY,+8[14/20]/46,XY[6/20]	de novo	M5	D	M	77	BM	12.6	Intermediate
<b>Euploid AML</b>												
025288	x	x		46,XX,t(6;11)(q27;q23)[20/21]/46,XX[1/21]	de novo	M4	D	F	49	BM	76.0	Adverse
007340	x			46,XX,del(7)(q34),inv(16)(p13q22)[13/20]/46,XX[7/20]	de novo	M4e o	D	F	35	BM	na	Favorable
009796	x	x		46,XX,ins(8;21)(q22;q22q22),del(9)(q12q34)[12/15]/46,XX[3/15]	de novo	M2	D	F	29	BM	6.1	Favorable
019074	x	x		46,XX,der(7)t(3;7)(q26;q11.2)[20/20]	t-AML	M2	D	F	50	BM	20.4	Intermediate
000894	x	x		46,XY,t(11;19)(q23;p13)[20/20]	t-AML	na	D	M	29	BM	na	Intermediate
013324	x	x		46,XY,der(19)t(17;19)(q21;p13).ish der(10)ins(10;11)(p12;q23q23)[15/20]/46,XY[5/20]	de novo	M1	D	M	49	BM	115.0	Adverse
031805	x	x		46,XY,t(3;3)(q21;q26)[12/12]	de novo	na	D	M	31	BM	1.1	Adverse
2973	x	x		46,XX,t(16;16)(p13;q22)[20/20]	t-AML	M4	D	F	46	BM	95.0	Favorable
6			x	46,XY[20/20]	de novo	M4	D	M	57	BM	2.9	Intermediate
18			x	46,XX[20/20]	na	na	D	F	42	BM	14.5	Intermediate

1024	x	x		46,XY,dup(1)(p22p36)[20/20]	sec (MDS)	sec (MDS)	D	M	74	BM	1.5	Intermediate
1026	x	x		46,XX,del(9)(q12q34)[20/20]	sec (MDS)	sec (MDS)	D	F	63	BM	21.8	Intermediate
48			x	46,XX[20/20]	de novo	M1	D	F	60	BM	3.2	Intermediate
2306	x			46XX,del(7)(q22q32)[15/20]/46,XX[5/20]	de novo	M1	D	F	40	BM	1.1	Intermediate
0027	x	x		46,XX[13/15]/46,XX,del(5)(q31q33)[2/15]	de novo	M0-M1	D	F	70	BM	3.8	Adverse
47			x	46,XX[20/20]	de novo	M1-M2	D	F	66	BM	35.9	Intermediate
66			x	46,XY[20/20]	de novo	na	D	M	70	BM	234	Intermediate
2195	x	x	x	46,XX[10/10]	de novo	M2	D	F	63	BM	44.3	Intermediate
14			x	46,XX[20/20]	de novo	M0	D	F	51	BM	3.8	Intermediate
2241	x	x		46,XY[20/20]	de novo	M5	D	M	62	BM	50.0	Intermediate
64			x	46,XX[20/20]	sec (MDS)	sec (MDS)	D	F	66	BM	na	Intermediate
41			x	46,XX[20/20]	de novo	na	D	F	60	BM	68.5	Intermediate
40			x	46,XX[20/20]	na	na	D	F	76	BM	na	Intermediate
50			x	46,XX[20/20]	de novo	M1	D	F	34	BM	102	Intermediate
59			x	46,XY[20/20]	de novo	M1	D	M	64	BM	1.9	Intermediate
0017	x	x		46, XY[20/20]	de novo	M0-M1	D	M	57	BM	3.1	Intermediate
49			x	46,XX[20/20]	de novo	na	D	F	72	BM	26.1	Intermediate
85			x	46,XX[20/20]	de novo	M2-M4	D	F	67	BM	46.7	Intermediate
2798	x	x		46,XY[20/20]	de novo	na	R	M	60	BM	37.6	Intermediate
65			x	46,XY[28/28]	de novo	M1	D	M	64	BM	65.1	Intermediate

2008	x	x		46,XY,der(1)r(1p),t(5;13)(q22;q32),t(9;20)(q13;q11),der(19)t(1;19)(q21;q13),HSR[17/20]/46,XY[3/20]	sec (MDS)	sec (MDS)	D	M	55	BM	2.6	Adverse
45			x	46,XY[20/20]	de novo	na	D	M	42	BM	163.9	Intermediate
83			x	46,XY[20/20]	de novo	na	D	M	73	BM	2	Intermediate
2031	x	x		46,XX,del(13)(q14q22)[10/20]/46,XX,del(8)(p21),del(13)(q14q22)[3/20]/46,XX[7/20]	t-AML	M1	D	F	64	BM	13.0	Intermediate
1858	x	x		46,XX[20/20]	de novo	M1	D	F	36	BM	5.6	Intermediate
0018	x	x		46,XX[20/20]	sec (MDS)	M2	D	F	51	PBL	61.6	Intermediate
3154	x	x		46,XX[20/20]	de novo	M5	D	F	62	BM	10.7	Intermediate
3010	x	x		46,XX[20/20]	de novo	M1	D	F	56	BM	84.3	Intermediate
15			x	46,XX[20/20]	de novo	M2	D	F	47	BM	89.4	Intermediate
46			x	46,XY[20/20]	de novo	M5	D	M	45	BM	88	Intermediate
16			x	46,XY[30/30]	de novo	M4	D	M	67	BM	9.7	Intermediate
0037	x	x	x	46,XX[20/20]	de novo	M2	D	F	59	BM	1.6	Intermediate
0022	x	x	x	46,XY[20/20]	de novo	M2	D	M	77	BM	6.9	Intermediate
2240	x	x		46,XY,inv(16)(p13q22)[19/20]/46,XY[1/20]	de novo	M4	D	M	55	BM	10.0	Favorable
39			x	46,XX[20/20]	de novo	M5	D	F	50	BM	77.7	Intermediate
2230	x	x		46,XY[20/20]	sec (MDS)	na	D	M	74	BM	1.8	Favorable
3213	x	x		46,XX[20/20]	de novo	M4	D	F	32	BM	15.6	Favorable
51			x	46,XX[20/20]	de novo	M1	D	F	38	BM	37.2	Intermediate
20			x	46,XY[20/20]	sec (MDS)	na	D	M	71	BM	2.3	Intermediate
3062	x	x		46XY,t(6;11)(q27;q23)[19/20]/46XY[1/20]	de novo	M2	D	M	18	BM	127.0	Adverse
1015	x	x		46,XX,t(2;14)(q21;q32),t(11;12)(p15;q22)[17/20]/46,XX[3/20]	de novo	M0-M1	D	F	39	BM	50.0	Intermediate
1010	x	x		46,XY,t(6;17)(p21;q11)[20/20]	sec (MDS)	M2	D	M	64	BM	30.5	Intermediate

26		x		46,XX[20/20]	de novo	M0	D	F	67	BM	108.6	Intermediate
44		x		46,XY[20/20]	de novo	M4	D	M	66	BM	18.9	Intermediate
2138	x	x		46,XX[20/20]	sec (MDS)	M2	D	F	68	BM	5.2	Intermediate
1025	x	x		46,XX[14/28]/46,XX,der(9)t(1;9)(q11;q34)[14/28]	de novo	M4	D	F	55	BM	13.7	Intermediate
1905a	x	x		46,XY[20/20]	sec (MDS)	sec (MDS)	D	M	80	BM	3.9	Intermediate
2023	x			46,XX,del(7)(q22;q32),inv(16)(p13q22)[15/20]/47,XX,del(7)(q22;q32),inv(16)(p13;q22),+9[1/20]/46,XX[4/20]	t-AML	na	D	F	62	BM	1.2	Favorable
1034	x	x		46,XX,inv(3)(q21q26)[8/20]/46,XX[12/20]	de novo	M7	D	F	61	BM	12.7	Adverse

FAB=French-American-British; idic=isodicentric chromosome; i=isochromosome; dic=dicentric chromosome; dmin=double minute; der=derivative chromosome; ish=in situ hybridization ; r=ring chromosome; mar=marker chromosome; \* not involving PML-RARA.



**Table S2. Number and type of mutations detected by WES.**

	No. mutations	Missense	Frameshift deletion	Frameshift insertion	In-frame deletion	In-frame insertion	Stop-gain	Stop-loss
<b>Aneuploid AML</b>								
2005	2	2						
1001	6	5	1					
2033	6	6						
1028	9	9						
013206	10	9		1				
006473	10	9					1	
026369	13	12					1	
019531	13	12					1	
001197	14	13	1					
2002	13	13						
213	16	15					1	
008951	16	14					2	
2030	17	17						
1014	17	17						
006187	18	15			1	1	1	
2007	18	16					2	
1006	19	17					2	
026656	17	12		2	1		2	
042101	19	18			1			
015330	20	15	1	1			3	
2036	21	20					1	
028034	22	19			2		1	
2009	23	22	1					
2004	24	23			1			
007827	26	22			1		3	
122	27	26					1	
2043	29	28					1	
2035	29	27					2	
2304	29	27	1				1	
3108	25	22			1		2	
2868	33	33						
2803	34	31	1	1			1	
1905	39	36	1				2	
1041	40	36			1	2	1	
63640	42	37				1	4	
1946	41	40					1	
2964	42	39		1			2	
2039	47	46		1				
2045	47	44	1		1		1	
187	50	44	1		1		4	
195	56	48					8	
2040	88	83					5	

Euploid AML				
3010	3	3		
1905a	7	7		
000894	7	7		
3062	8	7	1	
007340	8	7		1
1024	9	8		1
2241	9	7	1	1
2008	9	8	1	
1858	9	9		
025288	9	8	1	
3154	9	9		
0017	9	9		
0022	10	8		2
2240	10	10		
2798	11	8	1	2
3213	11	9	1	1
013324	11	11		
009796	11	9	2	
2138	11	10	1	
0018	12	11		1
2023	13	12	1	
1015	14	13		1
1010	14	10		4
1025	13	12		1
0027	15	13		2
1034	15	15		
2031	17	15	1	1
1026	18	17	1	
019074	20	15	3	2
2973	24	23		1
031805	25	23	2	
2230	27	19	3	5
2195	30	29		1
2306	43	39	1	3
0037	45	44		1

**Table S3. List of mutations in the functional categories associated with the aneuploid phenotype.**

Functional category	Genes mutated in A-AML	Genes mutated in E-AML
<b>Transcription</b>	AR; ARNTL; BDP1; CDX4; EVX2; FOXP3; GABPB2; HOXA1; HOXC10; HOXC9; ICE1; JAZF1; LIMD1; MAZ; MED11; MED20; MED23; MGA; MLLT10; MSC; MYBL1; NCOA6; NFATC2IP; NFATC4; NFE2L1; NFKB2; NPAS1; NPAS2; NR2C2; NR4A1; NRIP2; PARP14; POLR2B; POLR2H; POLR3A; POLR3B; POLR3E; RAI1; RORB; SALL3; SATB2; SERTAD3; SOX13; SOX30; SPEN; SPI1; TAF4B; TCF20; TLE2; TSHZ3; VGLL3; ZBTB38; ZEB2; ZHX1; ZHX2; ZKSCAN5; ZMYM2; ZNF107; ZNF205; ZNF227; ZNF28; ZNF282; ZNF383; ZNF407; ZNF423; ZNF57; ZNF626; ZNF653; ZNF696; ZNF845; ZNF91; ZSCAN26; ZXDC	AFF1; ARNT2; BTAF1; CAMTA1; DNNTIP2; HIC1; HNF1B; HOXD13; MED10; MGA; NOTCH3; PATZ1; PITX1; PLAG1; POLR1A; RAI1; TEAD2; TRERF1; UBTF; ZFP82; ZKSCAN7; ZNF148; ZNF229; ZNF333; ZNF407; ZNF460; ZNF483; ZNF491; ZNF558; ZNF572; ZNF595; ZNF718; ZNF621; ZNF628; ZNF891
<b>Metabolism</b>	AASDHPPT; ACOT11; ACSL3; ADCY8; AGXT2; AKR7A3; ALOXE3; APOB; CES2; CHST9; COL4A3BP; CPOX; CPT2; CTH; CTNNA1; CUBN; CYP3A43; DAOA; ENPP3; ENTPD4; EXT2; FAR2; FLAD1; FOXRED2; GALNT8; GCNT3; GLA; GPD1L; GPR119; HK3; IDO2; IMPDH2; LDHD; LSR; MACROD2; MORC2; NAAA; NADSYN1; NAGS; NCF2; NNT; NT5E; NUDT18; P4HB; PANK2; PASK; PCK1; PDE12; PENK; PHKB; PIBF1; PIGQ; PIP5K1C; PLA2G4E; POMGNT2; PPAPDC2; PTGS1; RNF219; RRP8; SDSL; SOD2; SSTR4; UGT3A1; VNN3; VSTM4	AASDHPPT; AASS; ACOT11; ACOX1; ACPT; ACSL3; ADCK3; ADCY8; AGXT2; AK9; AKR7A3; ALG9; ALOXE3; APOB; ATP8A2; CES2; CHDH; CHST5; CHST9; CIDEA; COL4A3BP; CPOX; CPT2; CTH; CTNNA1; CUBN; CYP1A1; CYP1B1; CYP3A43; DAOA; ENPP3; ENTPD4; EXT2; FAR2; FLAD1; FOXRED2; GALNT8; GCNT3; GLA; GLP1R; GPD1L; GPR119; GYG2; H6PD; HK3; HMGCR; IDO2; IMPDH2; LDHD; LSR; MACROD2; MAN2C1; MBOAT1; MORC2; MTCH2; NAAA; NADSYN1; NAGS; NAT2; NCF2; NDST1; NDST4; NDUFS1; NNT; NPC1L1; NT5E; NUDT18; OSBPL7; P4HB; PANK2; PASK; PC; PCK1; PDE12; PENK; PGAP2; PGM2; PHKB; PIBF1; PIGQ; PIGT; PIGZ; PIP5K1C; PKM; PLA2G4E; POMGNT2; PPAPDC2; PTGS1; PYGM; RNF219; RRP8; SDSL; SMPD3; SOD2; SSTR4; TYSND1; UGT3A1; VNN3; VSTM4; XDH
<b>Cell cycle</b>	AHCTF1; AKAP9; BUB1B; C10orf90; CASP8AP2; CDK10; CDK20; CDK5RAP2; CDKN1C; CENPJ; CEP152; CEP70; CHAF1A; CLTC; DDIAS; ESPL1; FAM64A; FHL1; FOXM1; HAUS4; INCENP; MCM6; MCM7; MELK; MIS18A; NASP; NCAPD2; NDC1; NSUN2; NUSAP1; ODF2; PCM1; PKHD1; POLA1; PPM1D; PRIMPOL; RBM38; RBMS1; RSF1; SMC1A; STOX1; TAF1; TICRR; TOP3A; TRIOBP; URGCP; USP44; YY1AP1	CDC20B; CENPO; CEP250; CEP295; CEP85; CHFR; CNTRL; MNAT1; MTUS2; NINL; NUP37; SFI1; SMC1A; TUBGCP2; WRN
<b>Signal transduction</b>	ADCYAP1R1; AGER; AKAP12; AKAP6; ALPK2; AMER3; APLP2; ARHGAP31; ARHGEF11; ARHGEF37; ARHGEF40; ARHGEF6; CALCRL; CARD10; CSK; DACT2; DDR1; DENND5A; DENND6A; DLK1; EDN2; EPHA10; EPHA5; ERRF1; ESR1; ESRRB; EVI2A; FRS3; FZD2; GAREML; GPC6; GPR153; GPRC5C; IL22RA1; INSRR; ITPR3; MAGI3; MAST3; MCF2L2; MERTK; MFNG; MPP6; NLRC3; NRK; OSMR; PAK6; PIK3R1; PLA2R1; PLCD1; PLD1; PLEKHG4; PLEKHG5; PRKCE; PRKRIR; PTK7; PYGO1; RASGEF1A; RASGRP3; RGS22; RHOBTB1; RHOQ; RPTOR; SBF1; SGK1; SIPA1; SIPA1L2; SMEK2; SOCS4; ST5; SULF1; TBC1D9; TIFAB; TNFRSF1A; TRAF2; TRAF4; TRIP6; TSC1; VRK3; WWC2	APLP2; ARHGEF12; ARHGEF33; CALCOCO1; CALCRL; CGN; CSNK2A1; DAPK2; DIRAS2; DKK1; EGFR; EPHA3; EPHA7; GNB1; GPR34; GRAP2; GRK6; IBTK; INPPL1; INSR; IQSEC1; ITPR2; KCTD16; LPAR5; MAST1; NLRC5; PDE5A; PLA2R1; PPP2R1A; PYGO1; RALGDS; RAP1B; RASAL2; RASD2; RGS3; RIPK2; RIT1; SIK1; STK11IP; WDR24; ZFYVE1
<b>Cytoskeleton</b>	ACTBL2; ACTR3B; ALMS1; ARHGAP26; BAIAP2L2; CAPZA2; CDC42EP1; COBL; DIAPH2; DST; ELMO1; ELMO2; EPB41L4B; FLNA; KANK3; KIF1B; KLC4; LAMA2; LAMA4; LAMB1; LMNB2; MICALL2; MTSS1; MYLK;	CTTN; EPB41L1; GAS2L2; KIF1A; KIF21A; KLC2; LAMC3; LMNA; MARK2; MICAL3; MYH14; MYH4; MYO1H; OBSL1; RICTOR; RLTPR; SDC3; SHROOM1; SNTB2; SORBS3; UBXN11

	MYO1A; PPP1R18; QRIC1; RAC2; SPTA1; SPTB; SVIL; SYNE2; SYNPO2L; TBCB; TNS3; TUBA8; VCL; VILL	
<b>Homeostasis</b>	ANO8; ASPH; ATP13A2; BEST2; CACNA1C; CACNA2D2; CACNB4; CFTR; CHRN2; DPP6; HEPH; HTR3B; KCNA5; KCNA6; KCNC1; KCNH4; KCNJ3; KCNK5; KCNQ1; KCNT1; KCNV1; KCNV2; LRRC8A; MCOLN2; ORAI1; PDZD2; PIEZO2; SARAF; SLC12A8; SLC34A1; SLC38A10; SLC38A6; SLC4A10; TPCN2	ANO3; CACNA1H; CACNA2D3; CLCA2; KCNG4; KCNK13; PIEZO2; SLC34A1; SLC4A4; SLC9A7; SLC9A9
<b>Intracellular trafficking</b>	AAAS; ABRA; ACAP1; ADAMTS20; AGAP1; AP1M2; ARCN1; ARFGAP2; BICD2; COG7; CRABP2; FAM160A2; FYCO1; HOOK2; HOOK3; IPO5; MIA3; NACAD; NUP153; NUP188; RAB3IP; SDAD1; SNX3; TOM1L2; VPS13A; VPS13D; XPO7; YIF1A	AP3M1; ARHGAP33; EXPH5; IPO4; LMTK2; LYST; OSBP; SEC16A; SEC24B; UBAP1
<b>Activated signaling</b>	DUSP10; FLT3; KIT; KRAS; MAP3K4; MAPK14; MET; NRAS; PPP2R2A; PRKCA; PTPN11; PTPN5; PTPRM; RET; STAT5A; TEK	FLT3; KRAS; MET; NF1; NRAS; PHLPP1; PTPN11; PTPN3; STAT3
<b>Ubiquitination</b>	CBL; FBXL15; FBXL7; HERC6; KBTBD6; MAGEL2; MARCH10; MARCH7; MYCBP2; OTUD7A; OTUD7B; RNF145; RNF220; TRIM32; TRIM41; TRIP12; UBA7; UBE2E2; USP10; USP24; USP42; USP43; USP8; WDTC1	ASB4; ASB10; FBXO40; LRRC41; TOPORS; TRIM9; UBXN7; WDR48
<b>Cell adhesion</b>	AMIGO1; CDH24; CDHR5; COL12A1; COL16A1; COL5A1; COL6A3; COL6A6; DCHS2; DSCAM; DSCAM; FERMT1; GP9; ITGAE; ITGB6; MAGI1; NID2; PARVA; PTPRF; VTN	CDHR3; DSCAM; ITGA4; ITGB3
<b>Epigenetic regulation</b>	ARID1A; ARID5A; ASXL2; BAZ1B; C11orf30; C17orf49; CCDC101; CECR2; CHD1; CHD4; CHD6; EPC1; HIST1H2BA; HIST1H2BE; HIST1H2BF; HMGN3; KAT6B; L3MBTL2; MSL2; MTA1; PAF1; PHC1; RTF1; TRRAP	ASXL1; ASXL2; BCOR; BCORL1; BPTF; KANSL1; MEN1
<b>Post-translational modification</b>	ADAMTSL1; ART1; ART5; B3GALT5; B3GALTL; CPN2; FNTB; FUT2; GXYL1; HHAT; HYOU1; IBA57; METAP1; MIPEP; NAA25; PADI3; PPIG; RPN1; SDF2; SIAE; TMX1; TPST1; UGGT2	COLGALT1; DAD1; MTMR8; NOTUM; PFDN5; TGM1; ZDHHC4; ZDHHC8
<b>RNA metabolism</b>	ADARB2; AGO1; ATXN1; DDX1; DIS3L; DNAJB11; ELAC1; FTSJ3; IMP3; INTS1; LCMT2; MEX3B; MPHOSPH10; NOP2; PUS1; PXDNL; QARS; RC3H1; RNASEK; RNH1; SMG7; WIBG; YBX3; ZC3H13; ZCCHC11; ZCCHC6	AGO1; BICD1; CNOT1; DCP2; HNRNPL; MATR3; RNMTL1; RPU5D2; SAMD4A
<b>Immune response</b>	BPI; CD1D; CD84; CD96; CNR2; DMBT1; F8; F9; FCRL3; IL10RA; IL16; IL2RB; IRF5; MAVS; NLRP14; NLRX1; PRB3; SERPINA3; SIGLEC5; TLR10	CLEC4M; DEFB134; DMBT1; EPX; HAVCR1; HHLA2; IFI44L; LRRC32; MARCO; MMRN1; MND4; SERPINA5; XPNPEP2
<b>Cell proliferation/survival</b>	ADNP2; BAG3; CSF3R; DOCK1; ENDOG; FGF1; FGF6; FGFR1; LGALS1; LIX1L; LTBP3; MACC1; MTUS1; PACRG; RPS6; TACSTD2; TGFB2; ZFP36L1; ZNF217	ADNP2; AHI1; C1orf56; CASP5; DOCK4; MCC; PDGFA; PEG3; PLAGL1; REL; SETBP1; VWCE
<b>Histone methylation</b>	ASH1L; KMT2C; KMT2D; MLL amplification; MLL fusion; PRDM14; PRMT6; SETD2; SETD4; SETD5; SMYD1	EZH2; KMT2C; MLL; MLL amplification; MLL fusion; SETD1B
<b>Splicing</b>	CELF5; CLASRP; DDX50; EIF4A3; FUS; GEMIN4; LUC7L2; POLR2A; PRPF40B; PTBP2; SF3B1; SNRNP200; SRRM2; ZNF326	DDX41; PABPC1; QKI; SF3B1; SRSF2; YBX1; YTHDC2

<b>Protein degradation</b>	ADAMTS12; ADAMTS15; ADAMTS5; CTBS; DDI1; DDI2; HGFAC; KLK12; PSMB6; PSMC2; RCE1; WFDC13; ZFAND2B	A2ML1; ADAMTS16; ADAMTS17; CPA5; KLK8; PSME4
<b>Tumor suppressor</b>	BRCA1; BRCA2; TP53	TP53
<b>DNA Methylation</b>	DNMT3A; DNMT3B; IDH2; WT1	DNMT3A; IDH2; NPM1; TET2; WT1
<b>Transport</b>	ABCA13; ABCA2; ABCC1; ATP6V1G1; MFI2; SLC28A3; SLC2A9; SLC38A5; SLC45A3; SLC5A3; SLC6A14; SLCO2B1; STRA6	ABCA12; ABCA13; ABCC1; SLCO1C1; STEAP3
<b>Translation</b>	DDX31; EEF1D; EIF2S3; EIF3D; EPRS; GTPBP2; METTL17; MRPL14; MTRF1; RPL19; RPL22L1; RPL6; SARS	EIF5; HARS; MARS2; MRPS2; NARS
<b>DNA damage and repair</b>	ANKLE1; APTX; CHEK2; ERCC6L2; FANCE; HERC2; MLH3; NEIL3; RIF1; SPIDR; XAB2; ZRANB3	ATM; CDK12; CHEK2; HIPK2; LIG3; MSH5; NEIL3; PARP1; REV3L; RNF169; RTEL1; SLX4; SPRTN
<b>Cell differentiation</b>	ANXA13; DMXL1; EDRF1; GLIPR1; MFHAS1; NBEAL2; NFE2; WNT8A; ZBTB7A; ZNF3	AHR; DLL3; MFHAS1; MYADM
<b>Cell migration</b>	FAT1; LIMS2; LRRC16A; PLXNB1; PLXND1; PPIA; S1PR1	FAT1; FLT1; PEAK1; SPATA13
<b>Endocytosis</b>	ANKRD13B; CD163; CHODL; EEA1; RILP; STAB2	MRC2
<b>Apoptosis</b>	PIDD1; RTN3; TM7SF3; UNC5D; ZNF420	UNC5D
<b>Autophagy</b>	ATG2B; WDFY3; SOGA1; WDFY3; ATG2B	
<b>Myeloid transcription factor</b>	GATA2; GLI3; MYC; RUNX1	CEBPA; GATA2; RUNX1
<b>Histone DeMethylation</b>	KDM6A; KDM6B; KDM7A	KDM5C; KDM6A; PHF8

**Table S4. Summary of GO-BP pathways enriched in A-AML according to CNAs.**

Pathway ID	Pathway name	Logistic regression coefficient *	p value (adj) †	% A-AML cases ‡	%E-AML cases ‡	Genes and frequency in A-AML §	Genes and frequency in E-AML §
<b>CELL CYCLE</b>							
GO:1901989	positive regulation of cell cycle phase transition	-5.015	0.012	7.89	0	ZNF16 (7.89)	
GO:1901992	positive regulation of mitotic cell cycle phase transition	-4.931	0.012	7.89	0	TMOD3 (7.89)	
GO:1901991	negative regulation of mitotic cell cycle phase transition	-3.744	0.013	21.05	3.12	RGCC (18.42); TPRA1 (5.26); ZFP36L1 (10.53)	RGCC (3.12)
GO:0000082	G1/S transition of mitotic cell cycle	-4.291	0.012	76.32	65.62	ACVR1 (10.53); ACVR1B (7.89); AKT1 (10.53); CCND1 (10.53); CCNE1 (7.89); CCNE2 (39.47); CDC6 (5.26); CDC7 (5.26); CDK2 (5.26); CDK3 (10.53); CDK4 (7.89); CDK6 (7.89); CDK7 (15.79); CDKN1A (13.16); CDKN1B (5.26); CDKN2A (18.42); CDKN2C (7.89); CDKN2D (7.89); CRLF3 (5.26); CUL3 (7.89); EIF4EBP1 (5.26); HINFP (10.53); INHBA (5.26); IQGAP3 (5.26); ITGB1 (7.89); LATS1 (18.42); LATS2 (2.63); MARK4 (7.89); MAX (10.53); MCM10 (7.89); MCM2 (5.26); MCM4 (50); MCM5 (18.42); MCM6 (7.89); MCM7 (2.63); MCM8 (10.53); MYC (52.63); ORC1 (7.89); ORC2 (7.89); ORC3 (18.42); ORC4 (10.53); PLK2 (7.89); PLK3 (7.89); POLE (7.89); POLE3 (13.16); PPP6C (10.53); PRIM1 (2.63); RANBP2 (5.26); RANBP3 (7.89); RANBP3L (2.63); RB1 (57.89); RBBP8 (5.26); RPA1 (5.26); RPA2 (10.53); SPDYA (5.26); TFDP3 (7.89); USP37 (5.26); WEE1 (7.89)	CDK3 (3.12); CDK6 (6.25); CDK7 (3.12); CDKN2A (3.12); CDKN2C (6.25); LATS1 (3.12); LATS2 (3.12); MARK4 (3.12); ORC1 (3.12); PHF8 (6.25); PLK3 (3.12); RB1 (59.38)
GO:1902806	regulation of cell cycle G1/S phase transition	-4.041	0.012	55.26	0	C8orf4 (47.37); FBXW7 (13.16); TAF1 (7.89)	
GO:2000045	regulation of G1/S transition of mitotic cell cycle	-4.083	0.011	26.32	3.12	CCND1 (10.53); E2F1 (10.53); ECD (5.26); ID2 (5.26); INO80 (7.89); KIF14 (5.26); PSME1 (10.53); PSME2 (10.53); SENP2 (5.26); TCF3 (7.89)	SENP2 (3.12)
GO:1902807	negative regulation of cell cycle G1/S phase transition	-3.781	0.012	10.53	0	CDKN2D (7.89); MEN1 (7.89)	
GO:2000134	negative regulation of G1/S transition of mitotic cell cycle	-3.763	0.012	65.79	65.62	BCL2 (5.26); BRD7 (7.89); CDC73 (5.26); CDK2AP2 (7.89); CDKN1A (13.16); CTDSP1 (5.26); DACT1 (10.53); DCUN1D3 (5.26); E2F7	FBXO7 (3.12); PTEN (9.38); RB1 (59.38)

GO:0000083	regulation of transcription involved in G1/S transition of mitotic cell cycle	-8.165	0.011	68.42	59.38	(7.89); EZH2 (2.63); FBXO7 (21.05); FHL1 (10.53); GPNMB (5.26); MYO16 (5.26); PRMT2 (2.63); PTEN (10.53); RB1 (57.89); SMARCA4 (7.89); ZNF655 (2.63) BACH1 (23.68); BRD4 (7.89); CCNA1 (18.42); CCNE1 (7.89); CDC6 (5.26); E2F1 (10.53); HINFP (10.53); NPAT (7.89); ORC1 (7.89); PCNA (10.53); RB1 (57.89); RRM2 (5.26); TFDP1 (23.68) AURKB (7.89); BUB1B (7.89); BUB3 (7.89); CDC20 (10.53); CDCA8 (7.89); CENPA (7.89); CENPC (15.79); CENPH (15.79); CENPI (7.89); CENPK (10.53); CENPM (13.16); CENPO (7.89); CENPP (13.16); CENPU (13.16); CKAP5 (7.89); CLIP1 (7.89); DSN1 (7.89); ERCC6L (7.89); ESCO1 (5.26); FBXW7 (13.16); HDAC8 (7.89); KIF22 (5.26); KIF2B (5.26); KIF2C (7.89); KNTC1 (2.63); MAD2L1 (13.16); MCMBP (7.89); MIS12 (5.26); NDEL1 (7.89); NSL1 (5.26); NUF2 (5.26); NUP133 (7.89); NUP37 (7.89); NUP43 (18.42); NUP85 (10.53); NUP98 (7.89); PDS5B (2.63); PHB2 (13.16); PLK1 (5.26); PPP1CC (7.89); RAD21 (47.37); RAD21L1 (2.63); RANBP2 (5.26); REC8 (10.53); RPS27 (5.26); SEC13 (5.26); SMC1A (7.89); SMC5 (2.63); SPC24 (5.26); SPDL1 (7.89); STAG1 (5.26); STAG2 (13.16); WAPL (5.26); XPO1 (5.26); ZW10 (10.53); ZWILCH (10.53) CDC20 (3.12); ORC1 (3.12); RB1 (59.38); TFDP1 (3.12)
GO:0007062	sister chromatid cohesion	-5.659	0.011	65.79	28.12	CDC20 (3.12); CDCA8 (6.25); CENPH (3.12); CENPK (3.12); CLIP1 (3.12); KIF2B (3.12); KIF2C (3.12); NUP43 (3.12); NUP85 (3.12); SMC1A (3.12); STAG2 (12.5)
GO:0007064	mitotic sister chromatid cohesion	-4.666	0.013	26.32	12.5	CDC20 (10.53); CHTF8 (7.89); DSCC1 (7.89); GSG2 (5.26); MAU2 (7.89); NIPBL (15.79); PDS5B (2.63); SMC1A (7.89); WAPL (5.26) CDC20 (3.12); NIPBL (6.25); SMC1A (3.12)

### PROTEIN POST-TRANSLATIONAL MODIFICATION

GO:0043254	regulation of protein complex assembly	-6.775	0.009	47.37	40.62	BBS10 (2.63); DAB2IP (2.63); GFAP (5.26); HJURP (5.26); HRG (5.26); HSP90AA1 (10.53); HSPA8 (10.53); INSM1 (13.16); IRGM (5.26); LATS1 (18.42); NCLN (7.89); PTPN11 (23.68) HJURP (3.12); HRG (3.12); LATS1 (3.12); PTPN11 (34.38)
GO:0031334	positive regulation of protein complex assembly	-7.783	0.009	34.21	9.38	AJUBA (10.53); FAF1 (7.89); FNIP1 (5.26); ICE1 (10.53); IFNG (10.53); SLF1 (7.89); SLF2 (5.26); SUMO1 (7.89); TAL1 (7.89); TNF (10.53); VCP (18.42); WARS (10.53) FAF1 (9.38); ICE1 (3.12); TAL1 (3.12); VCP (3.12)

GO:0006513	protein monoubiquitination	-9.532	0.020	57.89	28.12	PEX12 (5.26); RYBP (7.89); LEO1 (7.89); KLHL12 (5.26); UBE2E1 (5.26); UBB (7.89); CUL4B (7.89); CUL3 (7.89); SKP1 (5.26); DTX3L (5.26); WDR48 (5.26); PCGF1 (7.89); UHRF1 (7.89); CTR9 (7.89); WAC (5.26); BIRC2 (10.53); KDM2B (7.89); CBL (10.53); DDB2 (7.89); UBE2W (44.74); BCOR (13.16); RING1 (15.79); HUWE1 (13.16); RBX1 (13.16); UBE2T (5.26); DTL (5.26); CDC73 (5.26)	CUL4B (6.25); BCOR (28.12); HUWE1 (15.62)
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**STEM CELL REGULATING PATHWAYS**

GO:0007224	smoothened signaling pathway	-3.497	0.013	60.53	31.25	ARL13B (5.26); ARL3 (5.26); BBS7 (13.16); BMP4 (10.53); CENPJ (21.05); DHH (7.89); DISP1 (5.26); DYRK2 (7.89); DZIP1 (18.42); EVC2 (13.16); FKBP8 (7.89); GLI1 (7.89); GLI2 (5.26); GLI3 (15.79); HHIP (13.16); HIPK1 (7.89); HSPB11 (7.89); IFT27 (18.42); IFT46 (13.16); IFT52 (2.63); IFT57 (7.89); KIAA0586 (10.53); KIF3A (5.26); NDST1 (5.26); PDX1 (23.68); PKD2L1 (5.26); PTCH1 (13.16); SEPT2 (5.26); SHH (2.63); SMO (2.63); STIL (7.89); TCTN2 (2.63); TGFBR2 (7.89); TMEM17 (5.26); TROVE2 (5.26); WDR19 (13.16)	ARL13B (3.12); CENPJ (3.12); DISP1 (3.12); DZIP1 (3.12); GLI3 (15.62); HSPB11 (3.12); IFT57 (3.12); PDX1 (3.12); PTCH1 (3.12); STIL (3.12); TGFBR2 (3.12)
GO:0008589	regulation of smoothened signaling pathway	-4.021	0.012	36.84	3.12	CREBBP (7.89); FGF10 (2.63); FGFR2 (10.53); GAS1 (13.16); GLI1 (7.89); GLI2 (5.26); INTU (13.16); OTX2 (10.53); PTCH1 (13.16); RPGRIPL1 (7.89); TCTN1 (7.89); TULP3 (13.16)	PTCH1 (3.12)
GO:0045879	negative regulation of smoothened signaling pathway	-4.610	0.013	81.58	84.38	CD3E (13.16); GLI3 (15.79); GPC3 (50); GPR37L1 (5.26); HHIP (13.16); KCTD11 (5.26); KIF7 (10.53); PTCH1 (13.16); PTCH2 (7.89); RB1 (57.89); RUNX2 (31.58); SERPINE2 (7.89); SUFU (5.26); TULP3 (13.16); ULK3 (7.89)	GLI3 (15.62); GPC3 (65.62); PTCH1 (3.12); PTCH2 (3.12); RB1 (59.38); RUNX2 (12.5)

**METABOLISM**

GO:0009116	nucleoside metabolic process	-5.870	0.010	31.58	46.88	ATIC (5.26); FPGS (10.53); HPRT1 (28.95); NME5 (5.26); NT5C1A (7.89); PRPS1 (10.53); UMPS (5.26)	HPRT1 (40.62); NT5C1A (6.25); PRPS1 (3.12)
GO:0009163	nucleoside biosynthetic process	-6.447	0.012	52.63	46.88	TXNDC9 (5.26); PDCL2 (15.79); UMPS (5.26); NT5E (18.42); TK2 (5.26); UCK1 (2.63); NME5 (5.26); PDCL (2.63); PUDP (18.42); CMPK1 (7.89); ADAL (7.89); GMPS (5.26); ADA (7.89); CAD (7.89); DCK (13.16); NME1 (5.26); NME2	PUDP (15.62); CMPK1 (3.12); HPRT1 (40.62); CTPS1 (6.25)



						(5.26); HPRT1 (28.95); CTPS1 (7.89); IMPDH2 (5.26)	
GO:0042278	purine nucleoside metabolic process	-6.337	0.010	7.89	0	MACROD1 (7.89)	
GO:0042451	purine nucleoside biosynthetic process	-7.442	0.012	42.11	40.62	NT5E (18.42); NME5 (5.26); ADAL (7.89); GMPS (5.26); ADA (7.89); NME1 (5.26); NME2 (5.26); HPRT1 (28.95); IMPDH2 (5.26) NDUFAB1 (5.26); NDUFB11 (7.89); SDHAF2 (7.89); COX7A2L (7.89); SDHD (10.53); ENTPD8 (10.53); GMPR2 (10.53); SLC25A23 (7.89); TPI1 (13.16); NUDT9 (13.16); ATP5G3 (10.53); RFK (10.53); PPIF (7.89); UQCC2 (15.79); CARD11 (2.63); COX15 (5.26); PFKFB1 (7.89); HKDC1 (7.89); COX8C (10.53); VCP (18.42); NMNAT1 (10.53); AMPD1 (5.26); ATP5B (2.63); CLPX (10.53); CCNB1 (15.79); UMPS (5.26); HSPA8 (10.53); P2RX7 (2.63); MSH2 (7.89); NT5E (18.42); NDUFAF7 (5.26); CDK1 (7.89); HTR2A (18.42); BAD (7.89); MYH3 (7.89); SURF1 (10.53); ATP6V1B2 (5.26); NDUFA8 (2.63); NDUFB9 (5.0); UQCC3 (7.89); DLG3 (21.05); SDHA (10.53); UQCRB (47.37); TK2 (5.26); PGAM1 (7.89); UCK1 (2.63); ATP5J (21.05); DUT (7.89); ALDOC (5.26); PGM1 (7.89); DNM1L (7.89); PGAM4 (7.89); SDHC (5.26); PARK7 (10.53); ATIC (5.26); ATP6V1A (5.26); GPI (5.26); GPD1 (7.89); COX6B1 (7.89); RHOA (5.26); GADD45GIP1 (5.26); NDUFA11 (7.89); MECP2 (2.63); ATP1A2 (5.26); NDUFA6 (13.16); EIF6 (10.53); MPP3 (5.26); FIGNL1 (2.63); COX6C (44.74); DLD (2.63); SLC25A25 (2.63); AMPD2 (5.26); NDUFV2 (5.26); OLA1 (10.53); AK2 (7.89); ALDOB (13.16); ENO2 (13.16); HK1 (7.89); ACTN3 (7.89); PRKAA1 (2.63); NUDT4 (7.89); COX7B (10.53); TEFM (5.26); NDUFV3 (2.63); PFAS (7.89); CMPK1 (7.89); DLG4 (5.26); NT5C1A (7.89); ATP5F1 (5.26); ATP5E (7.89); OGT (7.89); GMPS (5.26); NT5C2 (7.89); LEXM (7.89); ECD (5.26); NDUFB1 (10.53); ATP5EP2 (2.63); ARNT (5.26); NDUFS6 (13.16); NCOR1 (7.89); ADA (7.89); COQ9 (5.26); OGDHL (5.26); NDUFS5 (7.89); HIF1A (10.53); BPGM (2.63); ADSL (15.79); TIGAR (15.79); HSPA1B (15.79); UQCRHL (7.89); AK4 (7.89); NDUFAF1 (7.89); COX8A	HPRT1 (40.62)
GO:0009123	nucleoside monophosphate metabolic process	-4.625	0.011	81.58	62.5	VCP (3.12); NMNAT1 (3.12); CCNB1 (3.12); HTR2A (6.25); DLG3 (31.25); SDHA (3.12); PGM1 (3.12); PARK7 (3.12); MECP2 (9.38); AK2 (3.12); COX7B (3.12); CMPK1 (3.12); NT5C1A (6.25); LEXM (3.12); ATP5EP2 (3.12); NDUFS6 (3.12); NDUFS5 (6.25); ADSL (3.12); AK4 (3.12); NDUFB5 (3.12); NDUFA3 (3.12); STOML2 (3.12); HPRT1 (40.62); ATP5H (3.12); ATP7A (12.5); ATP5L (3.12); ENPP1 (3.12); PRPS1 (3.12)	

						(7.89); DNPH1 (18.42); PAICS (15.79); NDUFB7 (7.89); COA6 (5.26); AK1 (2.63); PGK1 (7.89); CAD (7.89); DCK (13.16); PGK2 (18.42); NDUFB5 (5.26); NDUFA2 (5.26); ATP5A1 (5.26); NDUFA7 (7.89); NDUFB4 (5.26); NDUFA3 (13.16); NUDT5 (7.89); COX6A1 (7.89); STOML2 (18.42); SLC25A13 (2.63); STAT3 (5.26); GART (21.05); NDUFC1 (13.16); NDUFB3 (7.89); HPRT1 (28.95); DCTD (15.79); NDUFA12 (5.26); NUDT3 (15.79); COX4I2 (2.63); DGUOK (7.89); PFKL (2.63); ATP5H (10.53); IMPDH2 (5.26); MLXIPL (2.63); SIRT6 (7.89); CYC1 (7.89); NDUFA13 (7.89); COX6A2 (7.89); OGDH (2.63); ATP5G2 (2.63); NUDT10 (7.89); COX5A (7.89); DDIT4 (5.26); FLCN (7.89); ATP7A (15.79); ATP5L (13.16); TJP2 (2.63); ATP6V0A2 (7.89); CBFA2T3 (7.89); ENPP1 (18.42); ATP6V1B1 (7.89); IGF1 (2.63); ENO4 (7.89); PRPS1 (10.53); SCRIB (42.11); MYOG (5.26); ATP5J2 (2.63); UQCRQ (5.26)	
GO:0009124	nucleoside monophosphate biosynthetic process	-6.730	0.015	10.53	0	ENTPD8 (10.53)	
						ENTPD8 (10.53); TPI1 (13.16); NUDT9 (13.16); CARD11 (2.63); PFKFB1 (7.89); HKDC1 (7.89); P2RX7 (2.63); HTR2A (18.42); BAD (7.89); DLG3 (21.05); PGAM1 (7.89); ALDOC (5.26); PGM1 (7.89); PGAM4 (7.89); GPI (5.26); GPD1 (7.89); NME5 (5.26); EIF6 (10.53); MPP3 (5.26); AK2 (7.89); ALDOB (13.16); ENO2 (13.16); HK1 (7.89); ACTN3 (7.89); PRKAA1 (2.63); CMPK1 (7.89); DLG4 (5.26); NUDT18 (5.26); OGT (7.89); AK8 (10.53); ECD (5.26); ARNT (5.26); NCOR1 (7.89); OGDHL (5.26); HIF1A (10.53); BPGM (2.63); TIGAR (15.79); AK4 (7.89); AK1 (2.63); PGK1 (7.89); PGK2 (18.42); NME1 (5.26); NME2 (5.26); NUDT5 (7.89); ENTPD4 (5.26); STAT3 (5.26); PFKL (2.63); MLXIPL (2.63); SIRT6 (7.89); OGDH (2.63); ENTPD3 (5.26); ENTPD2 (2.63); DDIT4 (5.26); TJP2 (2.63); CBFA2T3 (7.89); IGF1 (2.63); ENO4 (7.89); SCRIB (42.11); CMPK2 (5.26); MYOG (5.26)	
GO:0009132	nucleoside diphosphate metabolic process	-5.954	0.011	71.05	40.62	GNAI3 (5.26); GUCY1A3 (15.79); ATP5G3 (10.53); LPAR1 (2.63); CRH (47.37); DRD3 (5.26); RFK (10.53); PANK3 (7.89); EDNRA	HTR2A (6.25); DLG3 (31.25); PGM1 (3.12); AK2 (3.12); CMPK1 (3.12); AK4 (3.12)
GO:0046390	ribose phosphate biosynthetic process	-6.351	0.012	84.21	59.38		VCP (3.12); AKAP9 (6.25); PTGIR (3.12); NF1 (34.38); NPPB (3.12); RXFP2 (12.5); GPR65 (9.38); VIP (3.12); NPPA (3.12); PPCS (6.25);

(13.16); PANK2 (2.63); VCP (18.42); AMPD1 (5.26); ATP5B (2.63); WFS1 (10.53); MC3R (7.89); HRH3 (5.26); AKAP9 (2.63); GUCA1A (18.42); PTGIR (7.89); UMPS (5.26); NF1 (21.05); NPPB (10.53); HTR1B (18.42); SURF1 (10.53); DCAKD (5.26); RXFP2 (31.58); GPR65 (15.79); UQCC3 (7.89); GNAI2 (5.26); APLP1 (10.53); AVP (2.63); UCK1 (2.63); ATP5J (21.05); TSHR (10.53); GUCY2F (7.89); ADCY7 (7.89); CCR2 (5.26); GHRH (7.89); VIP (18.42); PTH (7.89); DRD1 (5.26); CALCA (7.89); ATIC (5.26); NPPA (10.53); OPRL1 (2.63); PDZD3 (10.53); PPCS (7.89); PANK1 (7.89); MRAP (2.63); GUCY2C (5.26); RCVRN (2.63); NME5 (5.26); RLN2 (18.42); AMPD2 (5.26); AK2 (7.89); COASY (5.26); GUCA1B (18.42); GALR3 (15.79); APOE (7.89); ADCY10 (5.26); PFAS (7.89); CMPK1 (7.89); ADCY1 (2.63); ACAT1 (7.89); ATP5F1 (5.26); EDNRB (21.05); RAF1 (5.26); ATP5E (7.89); TAAR1 (18.42); GUCA2A (7.89); NOS1 (7.89); GMPS (5.26); GIPR (5.26); NPR3 (15.79); ATP5EP2 (2.63); MC4R (5.26); AKAP5 (10.53); NPY2R (13.16); ADRB2 (5.26); TMIGD3 (5.26); ADORA3 (5.26); ADNP (10.53); GUCA2B (7.89); ADCY3 (7.89); ADSL (15.79); RUNDC3A (5.26); PAICS (15.79); CAD (7.89); NME1 (5.26); ATP5A1 (5.26); GRM2 (5.26); NME2 (5.26); STOML2 (18.42); SLC25A13 (2.63); GABBR1 (2.63); PAPSS2 (5.26); SLC26A1 (13.16); HPCA (7.89); STAT3 (5.26); GART (21.05); GALR2 (7.89); HPRT1 (28.95); ADORA2B (7.89); LTB4R2 (10.53); ATP5H (10.53); CTPS1 (7.89); IMPDH2 (5.26); ADRB1 (7.89); CYC1 (7.89); GPER1 (2.63); GUCY1B2 (2.63); ATP5G2 (2.63); ADCY4 (10.53); FLCN (7.89); ATP5L (13.16); PAPSS1 (13.16); NPR2 (15.79); ADGRD1 (7.89); ATP6V0A2 (7.89); P2RY11 (7.89); GPR161 (5.26); AKAP12 (21.05); PTK2B (39.47); GUCY2D (7.89); ADGRG6 (18.42); PRPS1 (10.53); RAMP2 (5.26); ATP5J2 (2.63); ADRB3 (5.26); TXNDC9 (5.26); GMPR2 (10.53); GNAI3 (5.26); AHCY (13.16); CARD11 (2.63); PDCL2 (15.79); UMPS (5.26); NT5E (18.42); DLG3 (21.05); UCK1 (2.63); RHOA (5.26); NME5 (5.26);

RLN2 (3.12); AK2 (3.12); APOE (3.12); CMPK1 (3.12); EDNRB (3.12); TAAR1 (3.12); GUCA2A (6.25); GIPR (3.12); NPR3 (3.12); ATP5EP2 (3.12); GUCA2B (6.25); ADSL (3.12); STOML2 (3.12); SLC26A1 (18.75); HPCA (3.12); GALR2 (3.12); HPRT1 (40.62); ATP5H (3.12); CTPS1 (6.25); ATP5L (3.12); AKAP12 (3.12); ADGRG6 (3.12); PRPS1 (3.12)

DLG3 (31.25); CMPK1 (3.12); NT5C1A (6.25); AK4 (3.12); HPRT1 (40.62); CTPS1 (6.25)

GO:0009119 ribonucleoside metabolic process -6.410 0.009 73.68 50

GO:0042454	ribonucleoside catabolic process	-9.301	0.014	47.37	40.62	PDCL (2.63); MPP3 (5.26); CMPK1 (7.89); DLG4 (5.26); ADAL (7.89); NUDT18 (5.26); NT5C1A (7.89); APOBEC3C (13.16); GMPS (5.26); NT5C2 (7.89); NFS1 (2.63); MOCOS (5.26); ADA (7.89); RAB23 (13.16); ENPP4 (18.42); AK4 (7.89); CAD (7.89); NME1 (5.26); NME2 (5.26); AHCYL1 (5.26); PEMT (7.89); APOBEC2 (15.79); ENTPD4 (5.26); MOCS3 (10.53); HPRT1 (28.95); DGUOK (7.89); CTPS1 (7.89); IMPDH2 (5.26); MOCS1 (15.79); TJP2 (2.63); GPHN (10.53); SCRIB (42.11) AHCY (13.16); ADAL (7.89); NUDT18 (5.26); APOBEC3C (13.16); ADA (7.89); ENPP4 (18.42); APOBEC2 (15.79); ENTPD4 (5.26); HPRT1 (28.95)	HPRT1 (40.62)
GO:0046128	purine ribonucleoside metabolic process	-6.301	0.010	68.42	50	GMPS (5.26); NT5C2 (7.89); NFS1 (2.63); MOCOS (5.26); ADA (7.89); RAB23 (13.16); ENPP4 (18.42); AK4 (7.89); NME1 (5.26); NME2 (5.26); AHCYL1 (5.26); PEMT (7.89); MOCS3 (10.53); HPRT1 (28.95); DGUOK (7.89); IMPDH2 (5.26); MOCS1 (15.79); TJP2 (2.63); GPHN (10.53); SCRIB (42.11)	DLG3 (31.25); NT5C1A (6.25); AK4 (3.12); HPRT1 (40.62)
GO:0046129	purine ribonucleoside biosynthetic process	-7.442	0.012	42.11	40.62	NT5E (18.42); NME5 (5.26); ADAL (7.89); GMPS (5.26); ADA (7.89); NME1 (5.26); NME2 (5.26); HPRT1 (28.95); IMPDH2 (5.26)	HPRT1 (40.62)
GO:0009156	ribonucleoside monophosphate biosynthetic process	-6.532	0.013	26.32	3.12	GART (21.05); PFAS (7.89); PRPS1 (10.53)	PRPS1 (3.12)
GO:0009167	purine ribonucleoside monophosphate metabolic process	-4.665	0.011	81.58	62.5	NDUFAB1 (5.26); NDUFB11 (7.89); SDHAF2 (7.89); COX7A2L (7.89); SDHD (10.53); GMPS (10.53); SLC25A23 (7.89); TPI1 (13.16); NUDT9 (13.16); ATP5G3 (10.53); PPIF (7.89); UQCC2 (15.79); CARD11 (2.63); COX15 (5.26); PFKFB1 (7.89); HKDC1 (7.89); COX8C (10.53); VCP (18.42); NMNAT1 (10.53); AMPD1 (5.26); ATP5B (2.63); CLPX (10.53); CCNB1 (15.79); HSPA8 (10.53); P2RX7 (2.63); MSH2 (7.89); NT5E (18.42); NDUF7 (5.26); CDK1 (7.89); HTR2A (18.42); BAD (7.89); MYH3 (7.89); SURF1 (10.53); ATP6V1B2 (5.26); NDUF8 (2.63); NDUF9	VCP (3.12); NMNAT1 (3.12); CCNB1 (3.12); HTR2A (6.25); DLG3 (31.25); SDHA (3.12); PGM1 (3.12); PARK7 (3.12); MECP2 (9.38); AK2 (3.12); COX7B (3.12); LEXM (3.12); ATP5EP2 (3.12); NDUF6 (3.12); NDUF5 (6.25); ADSL (3.12); AK4 (3.12); NDUF5 (3.12); NDUF3 (3.12); STOML2 (3.12); HPRT1 (40.62); ATP5H (3.12); ATP7A (12.5); ATP5L (3.12); ENPP1 (3.12); PRPS1 (3.12)

(50); UQCC3 (7.89); DLG3 (21.05); SDHA (10.53); UQCRB (47.37); PGAM1 (7.89); ATP5J (21.05); ALDOC (5.26); PGM1 (7.89); DNM1L (7.89); PGAM4 (7.89); SDHC (5.26); PARK7 (10.53); ATIC (5.26); ATP6V1A (5.26); GPI (5.26); GPD1 (7.89); COX6B1 (7.89); RHOA (5.26); GADD45GIP1 (5.26); NDUFA11 (7.89); MECP2 (2.63); ATP1A2 (5.26); NDUFA6 (13.16); EIF6 (10.53); MPP3 (5.26); FIGNL1 (2.63); COX6C (44.74); DLD (2.63); SLC25A25 (2.63); AMPD2 (5.26); NDUFV2 (5.26); OLA1 (10.53); AK2 (7.89); ALDOB (13.16); ENO2 (13.16); HK1 (7.89); ACTN3 (7.89); PRKAA1 (2.63); NUDT4 (7.89); COX7B (10.53); TEFM (5.26); NDUFV3 (2.63); PFAS (7.89); DLG4 (5.26); ATP5F1 (5.26); ATP5E (7.89); OGT (7.89); GMPS (5.26); NT5C2 (7.89); LEXM (7.89); ECD (5.26); NDUFB1 (10.53); ATP5EP2 (2.63); ARNT (5.26); NDUFS6 (13.16); NCOR1 (7.89); ADA (7.89); COQ9 (5.26); OGDHL (5.26); NDUFS5 (7.89); HIF1A (10.53); BPGM (2.63); ADSL (15.79); TIGAR (15.79); HSPA1B (15.79); UQCRHL (7.89); AK4 (7.89); NDUFAF1 (7.89); COX8A (7.89); PAICS (15.79); NDUFB7 (7.89); COA6 (5.26); AK1 (2.63); PGK1 (7.89); PGK2 (18.42); NDUFB5 (5.26); NDUFA2 (5.26); ATP5A1 (5.26); NDUFA7 (7.89); NDUFB4 (5.26); NDUFA3 (13.16); NUDT5 (7.89); COX6A1 (7.89); STOML2 (18.42); SLC25A13 (2.63); STAT3 (5.26); GART (21.05); NDUFC1 (13.16); NDUFB3 (7.89); HPRT1 (28.95); NDUFA12 (5.26); NUDT3 (15.79); COX4I2 (2.63); PFKL (2.63); ATP5H (10.53); IMPDH2 (5.26); MLXIPL (2.63); SIRT6 (7.89); CYC1 (7.89); NDUFA13 (7.89); COX6A2 (7.89); OGDH (2.63); ATP5G2 (2.63); NUDT10 (7.89); COX5A (7.89); DDIT4 (5.26); FLCN (7.89); ATP7A (15.79); ATP5L (13.16); TJP2 (2.63); ATP6V0A2 (7.89); CBFA2T3 (7.89); ENPP1 (18.42); ATP6V1B1 (7.89); IGF1 (2.63); ENO4 (7.89); PRPS1 (10.53); SCRIB (42.11); MYOG (5.26); ATP5J2 (2.63); UQCRQ (5.26)

GO:0009168	purine ribonucleoside monophosphate biosynthetic process	-6.476	0.013	31.58	3.12	ADA (7.89); ADSL (15.79); AMPD1 (5.26); AMPD2 (5.26); ATIC (5.26); GART (21.05);	ADSL (3.12)
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GO:0009185	ribonucleoside diphosphate metabolic process	-5.749	0.011	71.05	40.62	<p>GMPS (5.26); IMPDH2 (5.26); PAICS (15.79); PFAS (7.89)</p> <p>TPI1 (13.16); NUDT9 (13.16); CARD11 (2.63); PFKFB1 (7.89); HKDC1 (7.89); P2RX7 (2.63); HTR2A (18.42); BAD (7.89); DLG3 (21.05); PGAM1 (7.89); ALDOC (5.26); PGM1 (7.89); PGAM4 (7.89); GPI (5.26); GPD1 (7.89); EIF6 (10.53); MPP3 (5.26); AK2 (7.89); ALDOB (13.16); ENO2 (13.16); HK1 (7.89); ACTN3 (7.89); PRKAA1 (2.63); DLG4 (5.26); NUDT18 (5.26); OGT (7.89); ECD (5.26); ARNT (5.26); NCOR1 (7.89); OGDHL (5.26); HIF1A (10.53); BPGM (2.63); TIGAR (15.79); PGK1 (7.89); PGK2 (18.42); NUDT5 (7.89); ENTPD4 (5.26); STAT3 (5.26); PFKL (2.63); MLXIPL (2.63); SIRT6 (7.89); OGDH (2.63); ENTPD2 (2.63); DDIT4 (5.26); TJP2 (2.63); CBFA2T3 (7.89); IGF1 (2.63); ENO4 (7.89); SCRIB (42.11); MYOG (5.26)</p> <p>SLC25A23 (7.89); GNAI3 (5.26); GUCY1A3 (15.79); LPAR1 (2.63); CRH (47.37); DRD3 (5.26); PPIF (7.89); EDNRA (13.16); UQCC2 (15.79); CXCL9 (13.16); VCP (18.42); WFS1 (10.53); MC3R (7.89); CCNB1 (15.79); HRH3 (5.26); AKAP9 (2.63); GUCA1A (18.42); PTGIR (7.89); P2RX7 (2.63); NF1 (21.05); CDK1 (7.89); HTR2A (18.42); HTR1B (18.42); PDE5A (13.16); RXFP2 (31.58); GPR65 (15.79); GNAI2 (5.26); ACMSD (5.26); APLP1 (10.53); AVP (2.63); PGAM1 (7.89); TSHR (10.53); SSTR4 (13.16); ADCY7 (7.89); CCR2 (5.26); DNM1L (7.89); PGAM4 (7.89); GHRH (7.89); VIP (18.42); PTH (7.89); DRD1 (5.26); CALCA (7.89); PARK7 (10.53); GPD1 (7.89); OPR1 (2.63); PDZD3 (10.53); RHOA (5.26); GADD45GIP1 (5.26); TBL1XR1 (5.26); MRAP (2.63); RCVRN (2.63); EIF6 (10.53); RLN2 (18.42); ACTN3 (7.89); MAPK7 (5.26); PRKAA1 (2.63); CXCL10 (13.16); GUCA1B (18.42); GALR3 (15.79); APOE (7.89); ADCY1 (2.63); EDNRB (21.05); RAF1 (5.26); OGT (7.89); EGLN1 (7.89); GUCA2A (7.89); NOS1 (7.89); GIPR (5.26); LEXM (7.89); CHGA (7.89); NPR3 (15.79); ECD (5.26); MC4R (5.26); ARNT (5.26); AKAP5 (10.53); NPY2R (13.16); NCOR1 (7.89); ADRB2 (5.26); TMIGD3 (5.26);</p>	<p>HTR2A (6.25); DLG3 (31.25); PGM1 (3.12); AK2 (3.12)</p> <p>VCP (3.12); CCNB1 (3.12); AKAP9 (6.25); PTGIR (3.12); NF1 (34.38); HTR2A (6.25); RXFP2 (12.5); GPR65 (9.38); VIP (3.12); PARK7 (3.12); TBL1XR1 (3.12); RLN2 (3.12); APOE (3.12); EDNRB (3.12); GUCA2A (6.25); GIPR (3.12); LEXM (3.12); NPR3 (3.12); GUCA2B (6.25); HPCA (3.12); GALR2 (3.12); ATP7A (12.5); AKAP12 (3.12); ADGRG6 (3.12)</p>
GO:0006140	regulation of nucleotide metabolic process	-4.503	0.013	78.95	50		

GO:0006164	purine nucleotide biosynthetic process	-6.167	0.012	52.63	43,75	ADORA3 (5.26); ADNP (10.53); HIF1A (10.53); GUCA2B (7.89); BPGM (2.63); ADCY3 (7.89); TIGAR (15.79); RUNDC3A (5.26); GRM2 (5.26); NME2 (5.26); GABBR1 (2.63); HPCA (7.89); STAT3 (5.26); GALR2 (7.89); ADORA2B (7.89); LTB4R2 (10.53); MLXIPL (2.63); ADRB1 (7.89); SIRT6 (7.89); GPER1 (2.63); ADCY4 (10.53); DDIT4 (5.26); FLCN (7.89); ATP7A (15.79); ADGRD1 (7.89); P2RY11 (7.89); CBFA2T3 (7.89); GPR161 (5.26); AKAP12 (21.05); FZD2 (5.26); PTK2B (39.47); IGF1 (2.63); ADGRG6 (18.42); RAMP2 (5.26); MYOG (5.26); ADRB3 (5.26) ADSL (15.79); ATIC (5.26); GART (21.05); GMPT2 (10.53); GMPS (5.26); HPRT1 (28.95); IMPDH2 (5.26); MTHFD1 (10.53); OAS1 (2.63); PAICS (15.79); PFAS (7.89); PRPS1 (10.53) SLC25A23 (7.89); GNAI3 (5.26); GUCY1A3 (15.79); LPAR1 (2.63); CRH (47.37); DRD3 (5.26); PPIF (7.89); EDNRA (13.16); UQCC2 (15.79); CXCL9 (13.16); VCP (18.42); WFS1 (10.53); MC3R (7.89); CCNB1 (15.79); HRH3 (5.26); AKAP9 (2.63); GUCA1A (18.42); PTGIR (7.89); P2RX7 (2.63); NF1 (21.05); CDK1 (7.89); HTR2A (18.42); HTR1B (18.42); PDE5A (13.16); RXFP2 (31.58); GPR65 (15.79); GNAI2 (5.26); APLP1 (10.53); AVP (2.63); PGAM1 (7.89); TSHR (10.53); SSTR4 (13.16); ADCY7 (7.89); CCR2 (5.26); DNM1L (7.89); GHRH (7.89); VIP (18.42); PTH (7.89); DRD1 (5.26); CALCA (7.89); PARK7 (10.53); GPD1 (7.89); OPRL1 (2.63); PDZD3 (10.53); RHOA (5.26); GADD45GIP1 (5.26); TBL1XR1 (5.26); MRAP (2.63); RCVRN (2.63); EIF6 (10.53); RLN2 (18.42); ACTN3 (7.89); MAPK7 (5.26); PRKAA1 (2.63); CXCL10 (13.16); GUCA1B (18.42); GALR3 (15.79); APOE (7.89); ADCY1 (2.63); EDNRB (21.05); RAF1 (5.26); OGT (7.89); EGLN1 (7.89); GUCA2A (7.89); NOS1 (7.89); GIPR (5.26); LEXM (7.89); CHGA (7.89); NPR3 (15.79); ECD (5.26); MC4R (5.26); ARNT (5.26); AKAP5 (10.53); NPY2R (13.16); NCOR1 (7.89); ADRB2 (5.26); TMIGD3 (5.26); ADORA3 (5.26); ADNP (10.53); HIF1A (10.53); GUCA2B (7.89); ADCY3 (7.89); TIGAR (15.79); RUNDC3A (5.26); GRM2 (5.26); NME2 (5.26);	ADSL (3.12); HPRT1 (40.62); PRPS1 (3.12)
GO:1900542	regulation of purine nucleotide metabolic process	-4.326	0.013	78.95	50	VCP (3.12); CCNB1 (3.12); AKAP9 (6.25); PTGIR (3.12); NF1 (34.38); HTR2A (6.25); RXFP2 (12.5); GPR65 (9.38); VIP (3.12); PARK7 (3.12); TBL1XR1 (3.12); RLN2 (3.12); APOE (3.12); EDNRB (3.12); GUCA2A (6.25); GIPR (3.12); LEXM (3.12); NPR3 (3.12); GUCA2B (6.25); HPCA (3.12); GALR2 (3.12); ATP7A (12.5); AKAP12 (3.12); ADGRG6 (3.12)	

GO:0006195	purine nucleotide catabolic process	-6.267	0.013	28,95	9,38	GABBR1 (2.63); HPCA (7.89); STAT3 (5.26); GALR2 (7.89); ADORA2B (7.89); LTB4R2 (10.53); MLXIPL (2.63); ADRB1 (7.89); SIRT6 (7.89); GPER1 (2.63); ADCY4 (10.53); DDIT4 (5.26); FLCN (7.89); ATP7A (15.79); ADGRD1 (7.89); P2RY11 (7.89); CBFA2T3 (7.89); GPR161 (5.26); AKAP12 (21.05); FZD2 (5.26); PTK2B (39.47); IGF1 (2.63); ADGRG6 (18.42); RAMP2 (5.26); MYOG (5.26); ADRB3 (5.26); DNPH1 (18.42); GDA (10.53); GPX1 (5.26); ITPA (2.63); NT5C (10.53); NT5C1A (7.89); NT5C2 (7.89); NT5E (18.42); NUDT15 (2.63)	NT5C (3.12); NT5C1A (6.25)
GO:0009259	ribonucleotide metabolic process	-5.708	0.011	18,42	3,12	ATIC (5.26); RNASEH2B (18.42)	RNASEH2B (3.12)
GO:0009260	ribonucleotide biosynthetic process	-6.587	0.012	84,21	59,38	GNAI3 (5.26); GUCY1A3 (15.79); ATP5G3 (10.53); LPAR1 (2.63); CRH (47.37); DRD3 (5.26); RFK (10.53); PANK3 (7.89); EDNRA (13.16); PANK2 (2.63); VCP (18.42); AMPD1 (5.26); ATP5B (2.63); WFS1 (10.53); MC3R (7.89); HRH3 (5.26); AKAP9 (2.63); GUCA1A (18.42); PTGIR (7.89); UMPS (5.26); NF1 (21.05); NPPB (10.53); HTR1B (18.42); SURF1 (10.53); DCAKD (5.26); RXFP2 (31.58); GPR65 (15.79); UQCC3 (7.89); GNAI2 (5.26); APLP1 (10.53); AVP (2.63); UCK1 (2.63); ATP5J (21.05); TSHR (10.53); GUCY2F (7.89); ADCY7 (7.89); CCR2 (5.26); GHRH (7.89); VIP (18.42); PTH (7.89); DRD1 (5.26); CALCA (7.89); ATIC (5.26); NPPA (10.53); OPRL1 (2.63); PDZD3 (10.53); PPCS (7.89); PANK1 (7.89); MRAP (2.63); GUCY2C (5.26); RCVRN (2.63); NME5 (5.26); RLN2 (18.42); AMPD2 (5.26); AK2 (7.89); COASY (5.26); GUCA1B (18.42); GALR3 (15.79); APOE (7.89); ADCY10 (5.26); PFAS (7.89); CMPK1 (7.89); ADCY1 (2.63); ACAT1 (7.89); ATP5F1 (5.26); EDNRB (21.05); RAF1 (5.26); ATP5E (7.89); TAAR1 (18.42); GUCA2A (7.89); NOS1 (7.89); GMPS (5.26); GIPR (5.26); NPR3 (15.79); ATP5EP2 (2.63); MC4R (5.26); AKAP5 (10.53); NPY2R (13.16); ADRB2 (5.26); TMIGD3 (5.26); ADORA3 (5.26); ADNP (10.53); GUCA2B (7.89); ADCY3 (7.89); ADSL (15.79); RUNDC3A (5.26); PAICS (15.79); CAD (7.89); NME1 (5.26); ATP5A1 (5.26); GRM2 (5.26); NME2 (5.26); STOML2 (18.42); SLC25A13	VCP (3.12); AKAP9 (6.25); PTGIR (3.12); NF1 (34.38); NPPB (3.12); RXFP2 (12.5); GPR65 (9.38); VIP (3.12); NPPA (3.12); PPCS (6.25); RLN2 (3.12); AK2 (3.12); APOE (3.12); CMPK1 (3.12); EDNRB (3.12); TAAR1 (3.12); GUCA2A (6.25); GIPR (3.12); NPR3 (3.12); ATP5EP2 (3.12); GUCA2B (6.25); ADSL (3.12); STOML2 (3.12); SLC26A1 (18.75); HPCA (3.12); GALR2 (3.12); HPRT1 (40.62); ATP5H (3.12); CTPS1 (6.25); ATP5L (3.12); AKAP12 (3.12); ADGRG6 (3.12); PRPS1 (3.12)



GO:0009261	ribonucleotide catabolic process	-6.581	0.013	65.79	40.62	<p>(2.63); GABBR1 (2.63); PAPSS2 (5.26); SLC26A1 (13.16); HPCA (7.89); STAT3 (5.26); GART (21.05); GALR2 (7.89); HPRT1 (28.95); ADORA2B (7.89); LTB4R2 (10.53); ATP5H (10.53); CTPS1 (7.89); IMPDH2 (5.26); ADRB1 (7.89); CYC1 (7.89); GPER1 (2.63); GUCY1B2 (2.63); ATP5G2 (2.63); ADCY4 (10.53); FLCN (7.89); ATP5L (13.16); PAPSS1 (13.16); NPR2 (15.79); ADGRD1 (7.89); ATP6V0A2 (7.89); P2RY11 (7.89); GPR161 (5.26); AKAP12 (21.05); PTK2B (39.47); GUCY2D (7.89); ADGRG6 (18.42); PRPS1 (10.53); RAMP2 (5.26); ATP5J2 (2.63); ADRB3 (5.26) NUDT9 (13.16); PDE7A (47.37); ITPA (2.63); NT5E (18.42); PDE5A (13.16); MAPK7 (5.26); PDE4C (7.89); NUDT4 (7.89); NUDT18 (5.26); EGLN1 (7.89); ENTPD4 (5.26); HPRT1 (28.95); NUDT3 (15.79); PDE1B (2.63); NUDT10 (7.89) NDUFAB1 (5.26); NDUFB11 (7.89); SDHAF2 (7.89); COX7A2L (7.89); SDHD (10.53); GMPR2 (10.53); SLC25A23 (7.89); GNAI3 (5.26); GUCY1A3 (15.79); TPI1 (13.16); NUDT9 (13.16); PDE7A (47.37); ATP5G3 (10.53); LPAR1 (2.63); CRH (47.37); DRD3 (5.26); PANK3 (7.89); PPIF (7.89); EDNRA (13.16); UQCC2 (15.79); CARD11 (2.63); ITPA (2.63); COX15 (5.26); CXCL9 (13.16); PANK2 (2.63); PFKFB1 (7.89); HKDC1 (7.89); COX8C (10.53); VCP (18.42); NMNAT1 (10.53); AMPD1 (5.26); ATP5B (2.63); CLPX (10.53); WFS1 (10.53); MC3R (7.89); CCNB1 (15.79); HRH3 (5.26); AKAP9 (2.63); GUCA1A (18.42); PTGIR (7.89); HSPA8 (10.53); P2RX7 (2.63); MSH2 (7.89); NF1 (21.05); NT5E (18.42); NDUFAF7 (5.26); CDK1 (7.89); NPPB (10.53); HTR2A (18.42); HTR1B (18.42); BAD (7.89); PDE5A (13.16); MYH3 (7.89); SURF1 (10.53); DCAKD (5.26); ATP6V1B2 (5.26); NDUFA8 (2.63); NDUFB9 (50); RXFP2 (31.58); GPR65 (15.79); UQCC3 (7.89); GNAI2 (5.26); DLG3 (21.05); APLP1 (10.53); AVP (2.63); SDHA (10.53); UQCRB (47.37); PGAM1 (7.89); ATP5J (21.05); ALDOC (5.26); TSHR (10.53); SSTR4 (13.16); GUCY2F (7.89); ADCY7 (7.89); CCR2 (5.26); PGM1 (7.89); DNM1L (7.89); PGAM4 (7.89); GHRH (7.89); VIP (18.42); PTH</p>	HPRT1 (40.62)
GO:0009150	purine ribonucleotide metabolic process	-5.418	0.011	84.21	62.5	<p>VCP (3.12); NMNAT1 (3.12); CCNB1 (3.12); AKAP9 (6.25); PTGIR (3.12); NF1 (34.38); NPPB (3.12); HTR2A (6.25); RXFP2 (12.5); GPR65 (9.38); DLG3 (31.25); SDHA (3.12); PGM1 (3.12); VIP (3.12); PARK7 (3.12); NPPA (3.12); PPCS (6.25); TBL1XR1 (3.12); MECP2 (9.38); RLN2 (3.12); AK2 (3.12); COX7B (3.12); APOE (3.12); EDNRB (3.12); TAAR1 (3.12); GUCA2A (6.25); GIPR (3.12); LEXM (3.12); NPR3 (3.12); ATP5EP2 (3.12); NDUFS6 (3.12); NDUFS5 (6.25); GUCA2B (6.25); ADSL (3.12); AK4 (3.12); NDUFB5 (3.12); NDUFA3 (3.12); STOML2 (3.12); SLC26A1 (18.75); HPCA (3.12); GALR2 (3.12); HPRT1 (40.62); ATP5H (3.12); MCCC2 (3.12); ATP7A (12.5); ATP5L (3.12); ENPP1 (3.12); AKAP12 (3.12); ADGRG6 (3.12); PRPS1 (3.12)</p>	

(7.89); DRD1 (5.26); CALCA (7.89); SDHC (5.26); PARK7 (10.53); ATIC (5.26); ATP6V1A (5.26); GPI (5.26); GPD1 (7.89); NPPA (10.53); COX6B1 (7.89); OPRL1 (2.63); PDZD3 (10.53); PPCS (7.89); RHOA (5.26); GADD45GIP1 (5.26); TBL1XR1 (5.26); NDUFA11 (7.89); PANK1 (7.89); MECP2 (2.63); MRAP (2.63); GUCY2C (5.26); ATP1A2 (5.26); RCVRN (2.63); NME5 (5.26); NDUFA6 (13.16); EIF6 (10.53); MPP3 (5.26); FIGNL1 (2.63); COX6C (44.74); DLD (2.63); SLC25A25 (2.63); RLN2 (18.42); AMPD2 (5.26); NDUFV2 (5.26); OLA1 (10.53); AK2 (7.89); ALDOB (13.16); ENO2 (13.16); HK1 (7.89); ACTN3 (7.89); MAPK7 (5.26); PDE4C (7.89); PRKAA1 (2.63); NUDT4 (7.89); CXCL10 (13.16); COX7B (10.53); COASY (5.26); TEFM (5.26); GUCA1B (18.42); GALR3 (15.79); APOE (7.89); NDUFV3 (2.63); ADCY10 (5.26); PFAS (7.89); DLG4 (5.26); ADCY1 (2.63); NUDT18 (5.26); ACAT1 (7.89); ATP5F1 (5.26); EDNRB (21.05); RAF1 (5.26); HMGCR (7.89); ATP5E (7.89); OGT (7.89); EGLN1 (7.89); TAAR1 (18.42); GUCA2A (7.89); NOS1 (7.89); GMPS (5.26); NT5C2 (7.89); GIPR (5.26); LEXM (7.89); NFS1 (2.63); CHGA (7.89); NPR3 (15.79); ECD (5.26); NDUFB1 (10.53); ATP5EP2 (2.63); MOCOS (5.26); MC4R (5.26); ARNT (5.26); AKAP5 (10.53); BPNT1 (7.89); NPY2R (13.16); NDUFS6 (13.16); NCOR1 (7.89); ADRB2 (5.26); TMIGD3 (5.26); ADORA3 (5.26); COQ9 (5.26); OGDHL (5.26); RAB23 (13.16); NDUFS5 (7.89); ADNP (10.53); HIF1A (10.53); GUCA2B (7.89); BPGM (2.63); SULT1E1 (13.16); ADCY3 (7.89); ADSL (15.79); TIGAR (15.79); HSPA1B (15.79); UQCRHL (7.89); AK4 (7.89); NDUFAF1 (7.89); RUNDC3A (5.26); COX8A (7.89); PAICS (15.79); NDUFB7 (7.89); COA6 (5.26); SULT1B1 (13.16); AK1 (2.63); PGK1 (7.89); PGK2 (18.42); NDUFB5 (5.26); NDUFA2 (5.26); NME1 (5.26); ATP5A1 (5.26); GRM2 (5.26); NDUFA7 (7.89); NDUFB4 (5.26); NDUFA3 (13.16); NME2 (5.26); NUDT5 (7.89); COX6A1 (7.89); STOML2 (18.42); SLC25A13 (2.63); GABBR1 (2.63); MOCS3 (10.53); PAPSS2 (5.26); SLC26A1 (13.16); HPCA

						(7.89); STAT3 (5.26); GART (21.05); NDUFC1 (13.16); NDUFB3 (7.89); GALR2 (7.89); HPRT1 (28.95); NDUFA12 (5.26); NUDT3 (15.79); COX4I2 (2.63); PDE1B (2.63); ADORA2B (7.89); PFKL (2.63); LTB4R2 (10.53); ATP5H (10.53); IMPDH2 (5.26); MLXIPL (2.63); MCCC2 (13.16); MOCS1 (15.79); ADRB1 (7.89); SIRT6 (7.89); CYC1 (7.89); NDUFA13 (7.89); COX6A2 (7.89); OGDH (2.63); GPER1 (2.63); GUCY1B2 (2.63); ATP5G2 (2.63); NUDT10 (7.89); ADCY4 (10.53); COX5A (7.89); DDIT4 (5.26); FLCN (7.89); ATP7A (15.79); IMPAD1 (50); ATP5L (13.16); PAPSS1 (13.16); NPR2 (15.79); TJP2 (2.63); ADGRD1 (7.89); ATP6V0A2 (7.89); P2RY11 (7.89); CBFA2T3 (7.89); ENPP1 (18.42); GPR161 (5.26); SULT6B1 (5.26); AKAP12 (21.05); FZD2 (5.26); ATP6V1B1 (7.89); TPST2 (18.42); PTK2B (39.47); GUCY2D (7.89); IGF1 (2.63); GPHN (10.53); ENO4 (7.89); ADGRG6 (18.42); PRPS1 (10.53); SCRIB (42.11); RAMP2 (5.26); MYOG (5.26); ATP5J2 (2.63); ADRB3 (5.26); UQCQRQ (5.26)	
GO:0009152	purine ribonucleotide biosynthetic process	-6.177	0.012	15,79	3,12	ADSL (15.79)	ADSL (3.12)
GO:0009154	purine ribonucleotide catabolic process	-6.444	0.013	65,79	40,62	NUDT9 (13.16); PDE7A (47.37); ITPA (2.63); NT5E (18.42); PDE5A (13.16); MAPK7 (5.26); PDE4C (7.89); NUDT4 (7.89); NUDT18 (5.26); EGLN1 (7.89); HPRT1 (28.95); NUDT3 (15.79); PDE1B (2.63); NUDT10 (7.89); AKT1 (10.53); AKT2 (7.89); PEA15 (5.26); SLC2A1 (10.53); SLC2A10 (7.89); SLC2A11 (28.95); SLC2A12 (18.42); SLC2A2 (5.26); SLC2A4 (5.26); SLC2A5 (10.53); SLC2A6 (10.53); SLC2A8 (10.53); SLC35A4 (5.26); SLC35A5 (5.26); SLC35C1 (7.89); SLC35D1 (7.89); SLC35D2 (13.16); SLC35D3 (15.79); SLC37A1 (2.63); SLC37A2 (10.53); SLC37A4 (10.53); SLC45A1 (10.53); SLC5A11 (5.26); TMEM241 (5.26); NUDT9 (13.16); AHCY (13.16); GPD1L (5.26); PDE7A (47.37); NT5C (10.53); GBA2 (15.79); HYAL2 (5.26); OVGP1 (5.26); NEIL2 (44.74); CD44 (7.89); HYAL1 (5.26); SDC2 (7.89); ITPA (2.63); UNG (7.89); ACAN (7.89); SMUG1 (7.89); STAB2 (7.89); NT5E (18.42); CST3	HPRT1 (40.62)
GO:0008643	carbohydrate transport	-5.810	0.009	57,89	21,88	SLC2A1 (6.25); SLC2A11 (12.5); SLC2A12 (3.12); SLC2A2 (3.12); SLC2A5 (3.12); SLC35D3 (3.12); SLC45A1 (3.12)	
GO:1901136	carbohydrate derivative catabolic process	-4.572	0.011	84,21	78,12	NT5C (3.12); GLA (3.12); CEMIP (3.12); SGSH (3.12); GPC3 (65.62); FBXO6 (3.12); NT5C1A (6.25); FBXO2 (3.12); GBA3 (3.12); PGLYRP1 (3.12); HPRT1 (40.62); GPC4 (65.62)	

						(10.53); CHP1 (7.89); PDE5A (13.16); LYVE1 (7.89); OMD (13.16); SDC4 (7.89); GLA (10.53); CEMIP (10.53); NEU1 (15.79); TMEM2 (2.63); CSPG4 (10.53); SGSH (10.53); GPC3 (50); STT3B (5.26); DUT (7.89); LUM (7.89); GPD1 (7.89); NTHL1 (5.26); GNPDA1 (5.26); NUDT15 (2.63); CTBS (5.26); FBXO6 (10.53); MAPK7 (5.26); PDE4C (7.89); NUDT4 (7.89); ABHD10 (5.26); HYAL4 (2.63); ADAL (7.89); NUDT18 (5.26); NT5C1A (7.89); FUCA1 (10.53); CHIT1 (5.26); EDEM2 (10.53); KERA (7.89); EGLN1 (7.89); FMOD (5.26); FGF2 (13.16); DCTPP1 (7.89); APOBEC3C (13.16); DCN (2.63); ADA (7.89); PNLIPRP2 (7.89); GNS (2.63); PGLYRP3 (5.26); GALNS (7.89); GM2A (5.26); HGSNAT (5.26); ENPP4 (18.42); FBXO2 (10.53); BCAN (5.26); OGN (13.16); HYAL3 (5.26); GBA3 (15.79); HPSE (13.16); APOBEC2 (15.79); ENTPD4 (5.26); PGLYRP1 (7.89); HPRT1 (28.95); NEIL1 (10.53); NUDT3 (15.79); GPC4 (52.63); HEXB (10.53); PDE1B (2.63); NCAN (7.89); PRKCD (5.26); NUDT10 (7.89); NAGA (13.16); SAMHD1 (7.89); PGM2 (13.16); NEU2 (7.89); CSPG5 (5.26); NAGLU (5.26); DPYS (44.74)	
GO:0015758	glucose transport	-7.026	0.009	57,89	12,5	SLC2A1 (6.25); SLC2A12 (3.12); SLC2A2 (3.12); SLC2A5 (3.12)	
GO:0010827	regulation of glucose transport	-6.931	0.009	44,74	12,5	AAAS (7.89); FFAR4 (5.26); NDC1 (7.89); NUP133 (7.89); NUP155 (2.63); NUP188 (10.53); NUP210 (5.26); NUP214 (10.53); NUP37 (7.89); NUP43 (18.42); NUP58 (21.05); NUP85 (10.53); NUP98 (7.89); NUPL2 (5.26); RAE1 (5.26); RANBP2 (5.26); TPR (5.26); TRIB3 (10.53)	
GO:0010828	positive regulation of glucose transport	-6.953	0.009	13,16	0	CLIP3 (7.89); NR4A3 (13.16)	
GO:0046323	glucose import	-6.516	0.009	23,68	9,38	DRD1 (5.26); HNF1A (7.89); SLC2A10 (7.89); SLC2A12 (18.42); SLC2A4 (5.26); SLC2A6 (10.53); SLC2A8 (10.53); SORT1 (5.26); TSC1 (10.53)	

GO:0046324	regulation of glucose import	-6.451	0.009	18,42	6,25	APPL1 (5.26); ASPSCR1 (10.53); RTN2 (5.26); SLC25A27 (15.79)	ASPSCR1 (3.12); RTN2 (3.12)
GO:0046326	positive regulation of glucose import	-7.037	0.009	65,79	65,62	ADIPOQ (5.26); AKT1 (10.53); AKT2 (7.89); C1QTNF2 (5.26); CLTCL1 (18.42); GPC3 (50); IGF1 (2.63); ITLN1 (5.26); NFE2L2 (10.53); PIK3R1 (13.16); PTH (7.89); RAP1A (5.26); TERT (13.16)	ADIPOQ (3.12); GPC3 (65.62); TERT (3.12)
GO:0005977	glycogen metabolic process	-5.997	0.013	36,84	9,38	AKT1 (10.53); AKT2 (7.89); EPM2A (18.42); GNMT (15.79); IL6ST (7.89); PHKA1 (7.89); PPP1CA (7.89); PPP1CB (5.26); PPP1CC (7.89); PPP1R1A (2.63); PPP1R2P3 (5.26); PPP1R3B (5.26); PPP1R3C (7.89); PPP1R3D (7.89); PPP1R3E (10.53); PYGB (2.63); SLC37A4 (10.53); STBD1 (13.16); STK40 (7.89)	EPM2A (3.12); STK40 (6.25)
GO:1901607	alpha-amino acid biosynthetic process	-8.741	0.012	63.16	46.88	AHCY (13.16); MTHFD1 (10.53); CBS (2.63); SHMT2 (2.63); SLC1A3 (2.63); AGXT2 (2.63); SERINC3 (2.63); SEPHS2 (7.89); CPS1 (5.26); PLOD2 (5.26); GOT1L1 (44.74); NAGS (5.26); PARK7 (10.53); NOXRED1 (10.53); MRI1 (7.89); CTH (5.26); GLUD2 (10.53); CAD (7.89); GOT2 (5.26); OTC (34.21); ENOPH1 (13.16); GOT1 (7.89); ASNSD1 (10.53); GLS2 (2.63); AASS (2.63); AASDHPPT (10.53); ALDH4A1 (7.89)	PARK7 (3.12); OTC (46.88)
GO:0006525	arginine metabolic process	-9.549	0.013	18,42	3,12	ARG1 (18.42); ART4 (5.26); DDAH2 (15.79)	ARG1 (3.12)
GO:0009084	glutamine family amino acid biosynthetic process	-7.768	0.013	42.11	46.88	SLC1A3 (2.63); CPS1 (5.26); NAGS (5.26); NOXRED1 (10.53); GLUD2 (10.53); CAD (7.89); OTC (34.21); GLS2 (2.63); ALDH4A1 (7.89)	OTC (46.88)

**BIOENERGETICS**

GO:0030819	positive regulation of cAMP biosynthetic process	-6.418	0.013	73.68	21.88	ADCY7 (7.89); ADORA2B (7.89); ADRB1 (7.89); AKAP12 (21.05); AKAP5 (10.53); AVP (2.63); CALCA (7.89); CRH (47.37); DRD1 (5.26); GHRH (7.89); GIPR (5.26); GNAS (10.53); GPER1 (2.63); GPR161 (5.26); GPR65 (15.79); MC3R (7.89); MC4R (5.26); MRAP (2.63); NME2 (5.26); PTGIR (7.89); PTH (7.89); RAMP2 (5.26); RLN2 (18.42); RXFP2 (31.58); TSHR (10.53)	AKAP12 (3.12); GIPR (3.12); GPR65 (9.38); PTGIR (3.12); RLN2 (3.12); RXFP2 (12.5)
GO:0046395	carboxylic acid catabolic process	-9.206	0.015	2.63	0	PON1 (2.63); PON3 (2.63)	

**PROTEIN KINASE SIGNALING**

GO:0006469	negative regulation of protein kinase activity	-4.823	0.011	86.84	75	<p>AKT1 (10.53); ASPN (13.16); CAMK2N2 (5.26); CAV3 (5.26); CDKN2A (18.42); CEP85 (10.53); CHAD (5.26); CHP1 (7.89); DBNDD2 (7.89); DCN (2.63); DEPTOR (7.89); EPHA1 (2.63); FABP4 (7.89); FGFR1OP (15.79); FLRT1 (7.89); FLRT2 (10.53); FLRT3 (2.63); GADD45A (7.89); GADD45B (7.89); GMFB (10.53); GNAQ (13.16); IL6 (5.26); INPP5K (5.26); LRP6 (5.26); LRRC15 (5.26); LRRC3 (2.63); LRRC3C (5.26); LRRC4 (2.63); LRRC4B (10.53); LRRTM1 (7.89); MLLT1 (7.89); NCK1 (15.79); NF1 (21.05); NF2 (52.63); NYX (7.89); PARK7 (10.53); PKIA (47.37); PKIG (10.53); PODNL1 (7.89); PPM1E (10.53); PPP1R1A (2.63); PPP1R1B (5.26); PREX1 (2.63); PRKAR1A (10.53); PSEN1 (10.53); PTPRC (5.26); QARS (5.26); RB1 (57.89); RGN (7.89); RTN4RL2 (7.89); SOCS1 (5.26); SOCS2 (2.63); SOCS3 (10.53); TARBP2 (7.89); TESC (2.63); TRIB1 (55.26); TRIB2 (7.89); TRIB3 (10.53); TRIM27 (15.79); TSC2 (5.26); UBASH3B (10.53); WARS (10.53); WWTR1 (5.26)</p>	<p>CAMK2N2 (3.12); CDKN2A (3.12); CHAD (3.12); FGFR1OP (3.12); FLRT2 (3.12); LRRC15 (3.12); NCK1 (9.38); NF1 (34.38); NF2 (56.25); PARK7 (3.12); PPM1E (6.25); PRKAR1A (3.12); RB1 (59.38); SOCS3 (3.12)</p>
GO:0033673	negative regulation of kinase activity	-4.870	0.011	18.42	0	<p>AJUBA (10.53); CDKN1B (5.26); CSK (7.89); MSTN (10.53); MYCNOS (7.89); NPRL2 (5.26)</p>	
GO:0071901	negative regulation of protein serine/threonine kinase activity	-6.300	0.013	47.37	3.12	<p>ABL1 (10.53); CDK5RAP3 (5.26); CDKN1B (5.26); CDKN2D (7.89); DAB2IP (2.63); FAM212A (5.26); FAM212B (5.26); HEXIM2 (5.26); LRP6 (5.26); PKIA (47.37); PKIG (10.53); PPP1R1B (5.26); PYCARD (7.89)</p>	<p>CDK5RAP3 (3.12)</p>

GO:0000187	activation of MAPK activity	-6.589	0.012	76.32	43.75	ADORA2B (7.89); ADRA2B (5.26); ALK (5.26); APP (26.32); ARRB1 (10.53); AVPI1 (7.89); BMP2 (2.63); C1QTNF2 (5.26); C5 (13.16); C5AR1 (10.53); CD74 (5.26); CDK1 (7.89); CHRNA7 (15.79); CSPG4 (10.53); CXCR4 (7.89); DUSP6 (7.89); EGF (13.16); ERP29 (7.89); FCER1A (5.26); FGF10 (2.63); FGF2 (13.16); GHR (2.63); GHRL (5.26); HGF (2.63); IGF1 (2.63); IL1B (5.26); IQGAP3 (5.26); KARS (7.89); KIT (18.42); LPAR1 (2.63); MAP2K1 (10.53); MAP2K2 (7.89); MAP2K6 (10.53); MAP3K2 (5.26); MAPK1 (21.05); MAPKAPK3 (5.26); MAPKAPK5 (2.63); MOS (7.89); NOD1 (5.26); NOD2 (7.89); NRG1 (50); NTRK3 (13.16); P2RX7 (2.63); PAK3 (18.42); PDE6H (5.26); PEA15 (5.26); PLA2G1B (7.89); PRKAA1 (2.63); PROK1 (5.26); PROK2 (7.89); PTPN11 (23.68); RIPK2 (42.11); S1PR2 (7.89); SAA1 (7.89); SHC1 (5.26); SOD1 (2.63); SYK (13.16); TAB1 (15.79); TAB2 (18.42); TAB3 (7.89); TDGF1 (5.26); TGFB3 (10.53); TLR4 (2.63); TNF (10.53); UBA52 (7.89); UBB (7.89); UBC (2.63); UBE2N (7.89); AJUBA (10.53); CD40 (2.63); CSK (7.89); DIRAS2 (13.16); EDN3 (7.89); EGF (13.16); EGFR (5.26); ELANE (5.26); ERBB2 (5.26); EZH2 (2.63); FGF2 (13.16); FGFR1 (44.74); FLT1 (23.68); FLT3 (31.58); HRAS (5.26); HTR2A (18.42); KIT (18.42); KITLG (2.63); KRAS (13.16); MST1R (5.26); NEK10 (5.26); PDCD10 (5.26); PDE5A (13.16); PDGFA (2.63); PDGFB (13.16); PDGFRB (5.26); PIK3CG (2.63); PIK3R5 (7.89); PSEN1 (10.53); S100A12 (5.26); SRC (2.63); TAB1 (15.79); TNF (10.53); TNFSF11 (2.63); C5AR1 (3.12); CHRNA7 (25); MAP2K6 (3.12); MAPK10 (6.25); PAK3 (21.88); PTPN11 (34.38); TAB2 (3.12)
GO:0043406	positive regulation of MAP kinase activity	-4.448	0.013	71.05	37.5	EGFR (15.62); FLT1 (3.12); FLT3 (25); HTR2A (6.25); TENM1 (12.5)

GO:0051056	regulation of small GTPase mediated signal transduction	-5.159	0.011	65.79	43.75	AMOT (7.89); ARAP1 (10.53); ARAP3 (5.26); ARHGAP1 (7.89); ARHGAP12 (7.89); ARHGAP19 (7.89); ARHGAP21 (7.89); ARHGAP22 (5.26); ARHGAP25 (7.89); ARHGAP26 (5.26); ARHGAP29 (5.26); ARHGAP30 (5.26); ARHGAP33 (7.89); ARHGAP40 (7.89); ARHGAP44 (7.89); ARHGAP6 (10.53); ARHGAP9 (2.63); ARHGEF12 (10.53); ARHGEF19 (7.89); ARHGEF2 (5.26); ARHGEF26 (5.26); ARHGEF3 (5.26); ARHGEF6 (18.42); ARHGEF7 (5.26); ARHGEF9 (10.53); BCR (28.95); CHN1 (10.53); DEPDC1B (7.89); ECT2 (5.26); FGD1 (7.89); GARNL3 (2.63); GMIP (7.89); GNA13 (13.16); INPP5B (7.89); PIK3R2 (7.89); PLEKHG2 (7.89); PREX1 (2.63); RAC1 (5.26); RALGAPA1 (10.53); RALGAPA2 (15.79); RALGAPB (2.63); RHOA (5.26); RHOBTB1 (7.89); RHOBTB2 (5.26); RHOF (7.89); RHOG (7.89); RHOH (13.16); RHOV (7.89); SIPA1 (7.89); SIPA1L3 (10.53); SRGAP3 (5.26); TAGAP (15.79); TIAM1 (2.63); TRIP10 (7.89); TSC2 (5.26); VAV2 (2.63); BRAP (7.89); CCNA2 (13.16); CDK2 (5.26); CDKN1A (13.16); CDKN2A (18.42); CNKSR1 (10.53); DNMT1 (7.89); DOK1 (7.89); DOK2 (39.47); DOK3 (5.26); FGF2 (13.16); G3BP1 (5.26); G3BP2 (13.16); HRAS (5.26); IGF1 (2.63); IQGAP3 (5.26); JUN (7.89); KRAS (13.16); MAPKAPK3 (5.26); MAPKAPK5 (2.63); NF1 (21.05); NRAS (5.26); PARK7 (10.53); PLD1 (5.26); PLK2 (7.89); RALA (5.26); RALGDS (10.53); RAPGEF6 (5.26); RASSF1 (5.26); RB1 (57.89); RFXANK (7.89); RGL2 (15.79); RIT1 (5.26); SHC1 (5.26); SHTN1 (7.89); SYNGAP1 (15.79); TP53 (7.89); ZNF304 (13.16)	ARHGAP26 (3.12); ARHGAP6 (6.25); ARHGEF6 (18.75); ARHGEF9 (18.75); BCR (3.12); DEPDC1B (3.12); ECT2 (3.12); GNA13 (3.12); INPP5B (6.25); MCF2 (6.25); OPHN1 (3.12); TAGAP (3.12)
GO:0007265	Ras protein signal transduction	-3.614	0.013	71.05	71.88	CDKN2A (3.12); JUN (3.12); NF1 (34.38); PARK7 (3.12); PLD1 (3.12); RB1 (59.38); ZNF304 (3.12)	
GO:0046578	regulation of Ras protein signal transduction	-4.619	0.013	13.16	0	FOXM1 (13.16); SQSTM1 (5.26)	
GO:0046580	negative regulation of Ras protein signal transduction	-8.542	0.015	55.26	37.5	DAB2IP (2.63); MFN2 (10.53); NF1 (21.05); PPP2CB (42.11); RABGEF1 (2.63); RASA2 (5.26); RASAL1 (2.63); RASAL3 (7.89); SPRY2 (5.26); SYNGAP1 (15.79); TNK1 (5.26); TRIM67 (7.89)	MFN2 (3.12); NF1 (34.38)



GO:1904893	negative regulation of STAT cascade	-5.210	0.013	65.79	62.5	SOCS3 (10.53); SOCS2 (2.63); LRRC4 (2.63); SOCS4 (10.53); LRRC15 (5.26); RTN4RL2 (7.89); LRRTM1 (7.89); LRRC3C (5.26); NF2 (52.63); LRRC4B (10.53); PIBF1 (21.05); PODNL1 (7.89); LRRC3 (2.63); FLRT1 (7.89); FLRT3 (2.63); SOCS1 (5.26); NYX (7.89); DCN (2.63); PTPN2 (5.26); FLRT2 (10.53); ADIPOR1 (5.26); BCL3 (7.89); SOCS5 (7.89); PPP2CA (5.26); ASPN (13.16); PPP2R1A (10.53); VHL (5.26); CHAD (5.26) ADIPOR1 (5.26); ASPN (13.16); BCL3 (7.89); CHAD (5.26); DCN (2.63); FLRT1 (7.89); FLRT2 (10.53); FLRT3 (2.63); HMGA2 (7.89); LRRC15 (5.26); LRRC3 (2.63); LRRC3C (5.26); LRRC4 (2.63); LRRC4B (10.53); LRRTM1 (7.89); NF2 (52.63); NYX (7.89); PODNL1 (7.89); RTN4RL2 (7.89); SOCS1 (5.26); SOCS2 (2.63); SOCS3 (10.53); SOCS4 (10.53); SOCS5 (7.89); VHL (5.26)	SOCS3 (3.12); LRRC15 (3.12); NF2 (56.25); PIBF1 (3.12); FLRT2 (3.12); BCL3 (3.12); PPP2R1A (3.12); CHAD (3.12)
GO:0046426	negative regulation of JAK-STAT cascade	-5.210	0.013	60.53	62.5	SOCS3 (10.53); SOCS2 (2.63); LRRC4 (2.63); SOCS4 (10.53); LRRC15 (5.26); RTN4RL2 (7.89); LRRTM1 (7.89); LRRC3C (5.26); NF2 (52.63); LRRC4B (10.53); PIBF1 (21.05); PODNL1 (7.89); LRRC3 (2.63); FLRT1 (7.89); FLRT3 (2.63); SOCS1 (5.26); NYX (7.89); DCN (2.63); PTPN2 (5.26); FLRT2 (10.53); ADIPOR1 (5.26); BCL3 (7.89); SOCS5 (7.89); PPP2CA (5.26); ASPN (13.16); PPP2R1A (10.53); VHL (5.26); CHAD (5.26) ADIPOR1 (5.26); ASPN (13.16); BCL3 (7.89); CHAD (5.26); DCN (2.63); FLRT1 (7.89); FLRT2 (10.53); FLRT3 (2.63); HMGA2 (7.89); LRRC15 (5.26); LRRC3 (2.63); LRRC3C (5.26); LRRC4 (2.63); LRRC4B (10.53); LRRTM1 (7.89); NF2 (52.63); NYX (7.89); PODNL1 (7.89); RTN4RL2 (7.89); SOCS1 (5.26); SOCS2 (2.63); SOCS3 (10.53); SOCS4 (10.53); SOCS5 (7.89); VHL (5.26)	BCL3 (3.12); CHAD (3.12); FLRT2 (3.12); LRRC15 (3.12); NF2 (56.25); SOCS3 (3.12)

#### RESPONSE TO REACTIVE OXYGEN SPECIES

GO:0072593	reactive oxygen species metabolic process	-5.626	0.013	60.53	18.75	ALOX12 (7.89); AOX1 (7.89); BCL2 (5.26); CTGF (18.42); CYBA (7.89); CYR61 (5.26); DDIT4 (5.26); EPHX2 (50); GLS2 (2.63); IL19 (5.26); NDUFA13 (7.89); P2RX7 (2.63); PDGFB (13.16); PDK4 (2.63); PLA2R1 (10.53); PMAIP1 (5.26); PREX1 (2.63); RFK (10.53); SOD1 (2.63) BMP7 (7.89); RGN (7.89); HSPH1 (2.63); TNF (10.53); PARK7 (10.53); MET (18.42); SESN3 (7.89); GPR37 (2.63); HGF (2.63); SZT2 (10.53); PAWR (7.89); ENDOG (10.53); PSAP (5.26); FOXO3 (31.58); FBLN5 (10.53); NFE2L2 (10.53); GCH1 (10.53); STK26 (7.89); GPR37L1 (5.26)	CTGF (3.12); EPHX2 (15.62)
GO:1901031	regulation of response to reactive oxygen species	-8.661	0.028	55.26	37.5	ALOX12 (7.89); AOX1 (7.89); BCL2 (5.26); CTGF (18.42); CYBA (7.89); CYR61 (5.26); DDIT4 (5.26); EPHX2 (50); GLS2 (2.63); IL19 (5.26); NDUFA13 (7.89); P2RX7 (2.63); PDGFB (13.16); PDK4 (2.63); PLA2R1 (10.53); PMAIP1 (5.26); PREX1 (2.63); RFK (10.53); SOD1 (2.63) BMP7 (7.89); RGN (7.89); HSPH1 (2.63); TNF (10.53); PARK7 (10.53); MET (18.42); SESN3 (7.89); GPR37 (2.63); HGF (2.63); SZT2 (10.53); PAWR (7.89); ENDOG (10.53); PSAP (5.26); FOXO3 (31.58); FBLN5 (10.53); NFE2L2 (10.53); GCH1 (10.53); STK26 (7.89); GPR37L1 (5.26)	PARK7 (3.12); MET (28.12); SZT2 (3.12); FOXO3 (15.62)

\* The coefficients reflect ORs<1; which indicates association of altered pathway state to A-AML, since the aneuploid state was set to 0 and euploid state was set to 1 in the model.

† Cut-off was set at 0.05.

‡ Percentages of patients who had at least one gene altered in a certain pathway.

§ Genes belonging to each pathway, with percentage of A-AML and E-AML patients having a CNV in that gene.

**Table S5. Chromosome regions enriched for CNAs in the aneuploid cohort.**

<b>Cytoband</b>	<b>p value (adj)</b>	<b>Genes</b>
gain(6p12.1)	0.003	ICK;FBXO9;HCRTR2;KLHL31;BMP5;GCM1
gain(6p12.2)	0.003	EFHC1;TMEM14A;GSTA3;GSTA4;TRAM2
gain(6p12.3)	<0.001	CRISP3;C6orf141;CRISP1;OPN5;ADGRF4;ADGRF5;TDRD6;ADGRF2;DEFB110;DEFB112;DEFB113;DEFB114;ADGRF1;TNFRSF21;GLYATL3;DEFB133;CYP39A1;PGK2;RHAG;CRISP2;TFAP2D;SLC25A27
gain(6p21.1)	<0.001	TOMM6;DNPH1;CNPY3;FRS3;SLC22A7;APOBEC2;CAPN11;TAF8;PTCRA;SPATS1;C6orf223;RSPH9;TSPO2;UNC5CL;ENPP4;CUL9;GLTSCR1L;ZNF318;USP49;GNMT;RPL7L1;GUCA1A;GUCA1B;PRICKLE4;HSP90AB1;CRIP3;MDFI;C6orf226;NFKBIE;PEX6;TREM1;POLH;GTPBP2;MRPS18A;MRPS10;PPP2R5D;TMEM63B;TRERF1;AARS2;PTK7;ENPP5;PRPH2;C6orf132;MRPL14;DLK2;TBCC;BYSL;TFEB;TTBK1;CCND3;ABCC10;TJAP1;NCR2;MED20;MAD2L1BP
gain(6p21.2)	<0.001	DAAM2;MOCS1;SAYSD1;CPNE5;TDRG1;KCNK16;KCNK5;KCNK17
gain(6p21.31)	<0.001	RPS10-NUDT3;NUDT3;IP6K3;C6orf1;LEMD2;SCUBE3;HMGA1;MLN;GGNBP1;DEF6;MAPK13;BAK1;TCP11;UQCC2
gain(6p21.32)	<0.001	PFDN6;C6orf10;COL11A2;DAXX;ZBTB9;HLA-DMA;HLA-DMB;HLA-DOA;HLA-DOB;HLA-DPA1;HLA-DPB1;HLA-DPB2;HLA-DQA1;HLA-DQA2;HLA-DQB1;HLA-DQB2;HLA-DRA;HLA-DRB1;HLA-DRB5;HLA-DRB6;KIFC1;HCG23;HCG25;CUTA;PHF1;PSMB8;PSMB9;RGL2;RING1;RPS18;RXRB;VPS52;TAP1;TAP2;SLC39A7;HSD17B8;B3GALT4;SYNGAP1;WDR46;ZBTB22
gain(6p21.33)	<0.001	EHMT2;CLIC1;CSNK2B;DDAH2;LY6G6F;HLA-B;HLA-C;HSPA1B;HSPA1L;SAPCD1;MSH5;NEU1;C6orf48;POU5F1;APOM;LSM2;C6orf47;LY6G5B;LY6G6D;VAR5;PRRC2A;BAG6;GPANK1;ABHD16A;SLC44A4;VWA7;C6orf25;LY6G6C;LY6G5C
gain(6p22.1)	<0.001	TRIM10;ZBED9;MAS1L;TRIM40;TRIM39-RPP21;ZSCAN23;HLA-E;HLA-F;HLA-L;ZKSCAN4;HCG17;TRIM27;ZSCAN31;ZNF192P1;TRIM26;ZKSCAN8;ZSCAN9;ZKSCAN3;PGBD1;TRIM15;ZSCAN12
gain(6p22.2)	<0.001	SLC17A4;SLC17A2;TRIM38;SCGN;SLC17A3;HIST1H2AA;HIST1H2BA;HIST1H2C;HIST1H2D;HIST1H2AE;HIST1H2BB;HIST1H1A;SLC17A1;HIST1H2AB;HIST1H2BG;HIST1H2BH;HIST1H2BI;HIST1H3A;HIST1H3C;HIST1H3E;HIST1H3G;HIST1H3B;HIST1H4A;HIST1H4F;HIST1H4H;HIST1H4B;HIST1H4G;HIST1H3F
gain(6p22.3)	<0.001	C6orf229;NRSN1;MBOAT1;E2F3;RBM24;GMPT;MYLIP;KAAG1;JARID2;STMND1;ACOT13;PRL;MRS2;SOX4;DEK;KIAA0319
gain(6p23)	<0.001	RANBP9;RNF182;SIRT5;NOL7;MUR1;CD83
gain(6p24.2)	<0.001	TMEM170B;SMIM13;SYCP2L;ERVFRD-1;ELOVL2;GCM2
gain(6p25.2)	<0.001	ECI2;FAM217A;FAM50B;TUBB2B;C6orf201;SERPINB6;SERPINB9;WRNIP1;SLC22A23;PRPF4B
gain(6q13)	<0.001	KHDC1L;MB21D1;SDHAF4;KHDC3L;DPPA5;OOEP;DDX43;LMBRD1;OGFRL1;KHDC1
gain(6q14.1)	<0.001	RWDD2A;COX7A2;IRAK1BP1;DOPEY1;SEN6;HTR1B;IMPG1;PGM3;FAM46A;ELOVL4;TPBG;TTK;SH3BGRL2;UBE3D
gain(6q14.3)	0.004	SYNCRIP;CEP162;NT5E;TBX18
gain(6q15)	<0.001	PNRC1;PM20D2;SRSF12;CFAP206;ORC3;GABRR2;GJB7;UBE2J1;RARS2;SMIM8;LYRM2;RRAGD;SPACA1;RNGTT

gain(6q16.1)	<0.001	KLHL32;UFL1;MMS22L;NDUFAF4;GPR63;FHL5
gain(8p11.21)	<0.001	AP3M2;CHRNA3;SMIM19;GPAT4;NKX6-3;IDO2;DKK4;ANK1;IKBKB;IDO1;GOLGA7;PLAT;POLB;THAP1;C8orf4;SLC20A2;VDAC3;KAT6A;RNF170;GINS4;HOOK3;CHRNA6
gain(8p11.22)	0.004	HTRA4;ADAM2;PLEKHA2;TM2D2
gain(8p11.23)	<0.001	ERLIN2;PROSC;GOT1L1;LETM2;FGFR1;DDHD2;ADGRA2;LSM1;WHSC1L1;BRF2;STAR;RAB11FIP1;PLPP5;ASH2L;BAG4
gain(8p12)	<0.001	DUSP4;PURG;NRG1;SARAF;PPP2CB;WRN;DUSP26;RNF122;UBXN8;TTI2;MAK16;FUT10
gain(8p21.1)	0.009	EXTL3;NUGGC;ELP3;INTS9;FZD3
gain(8p21.2)	<0.001	PNMA2;CHRNA2;NKX2-6;EPHX2;PTK2B;TRIM35;GNRH1;NEFM;NKX3-1;ADAM7
gain(8p21.3)	<0.001	SORBS3;NPM2;R3HCC1;DMTN;C8orf58;CSGALNACT1;CCAR2;PDLIM2;TNFRSF10B;FGF17;DOK2;CHMP7
gain(8q11.21)	<0.001	CEBPD;MCM4;C8orf22;SNAI2;EFCAB1
gain(8q11.23)	0.002	OPRK1;ATP6V1H;RP1;SOX17;TCEA1
gain(8q12.1)	<0.001	SBF1P1;CYP7A1;SDR16C5;SDR16C6P;PENK;PLAG1;IMPAD1;RAB2A;CHCHD7;FAM110B;TOX
gain(8q12.3)	0.015	BHLHE22;UG0898H09;TTPA;GGH
gain(8q13.1)	<0.001	TCF24;C8orf44-SGK3;COPS5;ADHFE1;CRH;MCMDC2;RRS1;C8orf46;PPP1R42;MYBL1;PDE7A;C8orf44;CSPP1;VCPIP1;TRIM55;DNAJC5B
gain(8q13.3)	<0.001	NCOA2;TRAM1;XKR9;LACTB2;MSC
gain(8q21.11)	<0.001	C8orf89;RDH10;LY96;GDAP1;UBE2W;RPL7;ELOC
gain(8q21.13)	<0.001	STMN2;FABP5;HEY1;ZC2HC1A;PKIA;PEX2;ZBTB10;ZFHX4
gain(8q21.3)	<0.001	C8orf88;WWP1;TMEM64;NBN;RMDN1;NECAB1;OSGIN2;RUNX1T1;RIPK2;CPNE3
gain(8q22.1)	<0.001	FSBP;FAM92A;NDUFAF6;C8orf37;RAD54B;KIAA1429;GEM;DPY19L4;RBM12B;GDF6;MTERF3;PDP1;ESRP1;INTS8;UQCRB;PLEKHF2;TSPYL5;TMEM67;CCNE2;TP53INP1;PTDSS1
gain(8q22.2)	<0.001	OSR2;COX6C;ERICH5;RNF19A;FBXO43;KCNS2;POLR2K;RPL30;SPAG1
gain(8q22.3)	<0.001	CTHRC1;DPYS;DCAF13;RRM2B;UBR5;AZIN1;KLF10;SLC25A32;DCSTAMP;FZD6
gain(8q23.1)	<0.001	ABRA;RSPO2;EIF3E;ENY2;TRHR;NUDCD1;PKHD1L1;EMC2
gain(8q24.11)	0.002	EXT1;RAD21;EIF3H;MED30
gain(8q24.13)	<0.001	ZHX1-C8orf76;TRIB1;RNF139;ZHX1;ZNF572;ZHX2;NSMCE2;ATAD2;HAS2;NDUFB9;WDYHV1;SQLE;DERL1;TATDN1;C8orf76;FAM83A;TBC1D31;WASHC5
gain(8q24.21)	<0.001	CASC11;CCAT2;PRNCR1;PCAT2;CCDC26;FAM84B;MYC;POU5F1B;GSDMC;TMEM75;CASC8
gain(8q24.3)	<0.001	CCDC166;MINCR;TOP1MT;CYP11B2;PUF60;ARC;SCRIB;GLI4;ZNF707;ZFP41;COMMD5;ZNF517;WDR97;LY6E;HGH1;ADGRB1;ZNF250;RPL8;SCX;ZNF7;ZNF34;NAPRT;RECQL4;ZNF623
gain(9p13.3)	<0.001	GNE;CREB3;CLTA;ATP8B5P;SPAG8;FAM221B;NPR2;TMEM8B;GBA2;HRCT1;MSMP;TLN1;TPM2;FAM166B;CA9;RECK;HINT2;ARHGEF39;CCIN;CD72;RGP1;RUSC2
gain(12p13.32)	0.005	GALNT8;KCNA5;KCNA6;TIGAR;CCND2

gain(13q33.1)	0.032	ERCC5;CCDC168;KDELC1;TEX30
gain(20q11.21)	0.022	ABALON;TPX2;FOX51;POFUT1;PLAGL2;MYLK2;TM9SF4
gain(21q21.3)	<0.001	RWDD2B;USP16;CCT8;ADAMTS5;GABPA;LTN1;APP;ATP5J;MRPL39;BACH1;JAM2
gain(21q22.11)	<0.001	OLIG2;OLIG1;TCP10L;GART;DONSON;IFNAR2;SMIM11A;DNAJC28;C21orf62;C21orf59;SON;SYNJ1;PAXBP1;CRYZL1
gain(21q22.12)	0.007	MORC3;SETD4;CLIC6;CHAF1B;RUNX1
gain(21q22.13)	<0.001	DYRK1A;DSCR10;KCNJ6;KCNJ15;PIGP;SIM2
gain(21q22.2)	<0.001	LCA5L;ERG;ETS2;HMG1;PCP4;BRWD1;WRB;PSMG1
gain(21q22.3)	<0.001	TCONS_00029157;FRGCA;CRYAA;CSTB;RRP1B;AATBC;MX1;FAM3B;RIPK4;AGPAT3;PWP2;TMPRSS3;SUMO3;TFF1;TFF2;TFF3;TMPRSS2;SSR4P1;U2AF1;UBE2G2;C21orf33;FAM207A;RRP1
gain(22q12.1)	<0.001	CHEK2;CRYBB1;PITPNB;TFIP11;C22orf31;SRRD;MIAT;ASPHD2;XBP1;KREMEN1;ZNF3;TPST2;HPS4
gain(22q12.2)	<0.001	PIK3IP1;RNF215;EWSR1;MORC2;SEC14L2;PATZ1;PISD;PRR14L;SEC14L3;INPP5J;SEC14L4;LIMK2;DRG1;PLA2G3;MTFP1;CDC157;SEC14L6;RNF185;GAL3ST1;DEPDC5;SFI1
gain(22q12.3)	<0.001	HMGXB4;TOM1;IFT27;C1QTNF6;FBXO7;HMOX1;MCM5;MYH9;TIMP3;YWHAH
loss(5q14.3)	<0.001	LUCAT1;CETN3;LYSMD3;TMEM161B;ARRDC3;RASA1;ADGRV1;CCNH
loss(5q15)	<0.001	POU5F2;RHOBTB3;ELL2;KIAA0825;RGMB;LNPEP;PCSK1;SPATA9;SLF1
loss(5q21.1)	<0.001	CHD1;PPIP5K2;GIN1;ST8SIA4;C5orf30
loss(5q22.3)	<0.001	TMED7-TICAM2;CDO1;TICAM2;TMED7;FEM1C;ATG12
loss(5q23.1)	<0.001	HNCAT21;LVRN;HSD17B4;FAM170A;LOX;FTMT
loss(5q23.2)	<0.001	MARCH3;ZNF474;MGC32805;CEP120;TEX43;C5orf63;ALDH7A1;PHAX;ZNF608;GRAMD3;SNX2;SNCAIP
loss(5q23.3)	<0.001	KIAA1024L;HINT1;ISOC1;SLC12A2;LYRM7
loss(5q31.1)	<0.001	RAD50;TH2LCRR;WSPAR;DCANP1;CSF2;SEPT8;ACSL6;AFF4;HSPA4;IL3;IL5;IL13;IRF1;NEUROG1;TIFAB;CDKL3;C5orf15;TRPC7;SLC22A4;SLC22A5;MEIKIN;UBE2B;VDAC1;PDLIM4;P4HA2;CDKN2AIPNL;CXCL14;FNIP1
loss(5q31.2)	<0.001	KIF20A;BRD8;CTNNA1;ETF1;LRRTM2;GFRA3;PKD2L2;PROB1;MZB1;PAIP2;FAM13B;FAM53C;KDM3B;SIL1;WNT8A;NME5;CDC23;MYOT;MATR3;CDC25C;SLC23A1
loss(5q31.3)	<0.001	GNPDA1;ARHGAP26;RELL2;IK;DND1;ANKHD1-EIF4EBP3;NDUFA2;PCDH1;PCDH18P;WDR55;ANKHD1;TMCO6;PCDHAC2;VTRNA1-3;VTRNA1-2;VTRNA1-1;KCTD16;HMHB1;PURA;ARAP3;NDFIP1;YIPF5;SPRY4;SLC4A9;EIF4EBP3;FCHSD1;CD14;RNF14;KIAA0141
loss(5q32)	<0.001	TCERG1;SCGB3A2;GPR151;CSNK1A1;SH3RF2;PLAC8L1;ABLIM3;ARSI;C5orf46;PDGFRB;POU4F3;GRXCR2;SPINK1;JAKMIP2
loss(5q33.1)	<0.001	G3BP1;CTB-113P19.1;CTB-12O2.1;SLC36A2;SLC36A1;CCDC69;GPX3;ANXA6;ATOX1;SPARC;CD74
loss(5q33.2)	<0.001	FAXDC2;FAM114A2;LARP1;GEMIN5;KIF4B;MRPL22;MFAP3;GALNT10;CNOT8
loss(5q33.3)	<0.001	FAM71B;EBF1;HAVCR1;ITK;HAVCR2;TIMD4;MED7
loss(7q21.12)	<0.001	DBF4;KIAA1324L;SLC25A40;SRI;STEAP4;DMTF1
loss(7q21.2)	<0.001	AKAP9;CDK6;CYP51A1;SAM9L;FAM133B;LRRD1;SAM9;VPS50;GATAD1;MTERF1;RBM48;KRIT1
loss(7q21.3)	<0.001	SLC25A13;BET1;DLX5;DLX6;PEG10;GNG11;PDK4;ASB4;SDHAF3;CASD1;SHFM1;TFPI2;SGCE

loss(7q22.1)	<0.001	ATP5J2-PTCD1;CYP3A7-CYP3A51P;STAG3L5P-PVRIG2P-PILRB;CYP3A4;CYP3A5;ZSCAN25;FAM200A;TMEM130;GATS;NPTX2;SMURF1;ZNF655;PVRIG;TRRAP;TRIM4
loss(7q22.3)	0.008	HBP1;GPR22;PIK3CG;CBLL1
loss(7q31.1)	<0.001	HRAT17;THAP5;LSMEM1;IFRD1;DNAJB9;PNPLA8;GPR85;TMEM168
loss(7q31.2)	<0.001	ASZ1;TES;ST7-OT4;MET;WNT2;CAPZA2;CAV1;CAV2;ST7-OT3
loss(7q31.31)	0.014	LVCAT5;TSPAN12;LSM8
loss(7q32.1)	<0.001	SMKR1;FLNC;SND1;TPI1P2;FSCN3;TSPAN33;FAM71F2;ARF5;LEP;PAX4;STRIP2;LRRC4;SMO;GCC1;FAM71F1
loss(7q32.2)	<0.001	CPA2;KLF14;SSMEM1;KLHDC10;CPA4;TMEM209
loss(7q33)	<0.001	SLC13A4;WDR91;FAM180A;C7orf73;CREB3L2;C7orf49;SLC35B4;TRIM24
loss(7q34)	<0.001	C7orf55-LUC7L2;PRSS37;CLEC2L;FMC1;TRY2P;UBN2;ATP6V0A4;LUC7L2;KIAA1147;KIAA1549;MGAM2;FAM131B
loss(11p13)	0.023	FJX1;PAMR1;TRIM44;SLC1A2;WT1
loss(12p12.3)	<0.001	STRAP;HIST4H4;ERP27;C12orf60;ARHGDIB;ART4;MGP;MGST1;SMCO3;PDE6H;WBP11;H2AFJ;LMO3;RERG
loss(12p13.1)	<0.001	CDKN1B;CREBL2;EMP1;GPR19;RPL13AP20;DDX47;FAM234B;PLBD1;GSG1;GPRC5A
loss(12p13.2)	<0.001	SMIM10L1;KLRC4-KLRK1;BORCS5;TMEM52B;ETV6;GABARAPL1;CLEC9A;KLRD1;CLEC12B;OLR1;LOH12CR2;TAS2R9;TAS2R8;TAS2R7;CLEC7A;YBX3
loss(17p13.1)	<0.001	RPL29P2;FBXO39;EFNB3;SLC13A5;GUCY2D;C17orf100;TNFSF12-TNFSF13;RNASEK;MED31;XAF1;TP53;TEKT1;NAA38;TXNDC17;KIAA0753
loss(17p13.2)	<0.001	ZFP3;NLRP1;AIPL1;ALOX15;SMTNL2;SCIMP;FAM64A;NCBP3;DHX33;C1QBP;ZNF232;RPAIN;ZNF594;USP6;RABEP1

**Table S6. Chromosome regions enriched for CNAs in AML-related genes in the aneuploid cohort.**

<b>Cytoband</b>	<b>A-AML (% of cases)</b>	<b>E-AML (% of cases)</b>	<b>Candidate genes</b>	<b><i>p</i> value</b>
gain(6p22.3)	15.8	0	<i>E2F3, SOX4, DEK</i>	<0.05
loss(5q31.1)	36.8	6.3	<i>RAD50, TIFAB, PDLIM4</i>	<0.05
loss(5q31.2)	36.8	6.3	<i>KIF20A, CTNNA1, KDM3B</i>	<0.01
loss(5q31.3)	36.8	6.3	<i>DND1, PURA, SPRY4</i>	<0.05
loss(12p13.1)	18.4	0	<i>CDKN1B, EMP1</i>	<0.05

**Table S7. Top 5 disease-related pathways ranked according to their degree and betweenness centrality in the A-AML and E-AML networks.**

Pathway ID	Pathway name	Degree	Betweenness centrality
<b>Aneuploid AML</b>			
GO:0034723	DNA replication-dependent nucleosome organization	124	0.136
GO:0006335	DNA replication-dependent nucleosome assembly	123	0.136
GO:1903706	regulation of hemopoiesis	113	0.050
GO:0030099	myeloid cell differentiation	107	0.027
GO:0002521	leucocyte differentiation	107	0.027
<b>Euploid AML</b>			
GO:1903706	regulation of hemopoiesis	34	0.029
GO:0045879	negative regulation of smoothed signaling pathway	26	0.141
GO:0008589	regulation of smoothed signaling pathway	23	0.031
GO:0001953	negative regulation of cell-matrix adhesion	18	0.077
GO:0030099	myeloid cell differentiation	17	0.036

**Table S8. Pathway enrichment analysis for genes upregulated in A-AML.**

Source	Term	Fold Enrichment	p value	Genes
GO-BP	GO:0006334~nucleosome assembly	24.5	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0031497~chromatin assembly	23.7	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0065004~protein-DNA complex assembly	22.6	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0034728~nucleosome organization	22.1	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0006323~DNA packaging	17.6	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0006333~chromatin assembly or disassembly	16.2	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0016043~cellular component organization	2.5	<0.001	HIST1H2AB, LDLR, HIST1H2AE, ITSN1, APP, HIST1H2BM, HIST1H2BI, TGFBI, RUNX3, EHD4, PRKCA, H1F0, HIST1H3J, HIST1H2BB, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, CCNF, NID1, CDC20, MCM2, UBE2C, PLK1, HIST1H3A, HIST1H3B, TUBA4A, SETD7, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0034622~cellular macromolecular complex assembly	7.4	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, TUBA4A, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I



GO-BP	GO:0006325~chromatin organization	6.2	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, SETD7, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0051276~chromosome organization	4.9	0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, SETD7, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
REACTOME	REACT_7970:Telomere Maintenance	17.8	<0.001	HIST1H2AB, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0034621~cellular macromolecular complex subunit organization	6.6	<0.001	HIST1H2AB, H1F0, HIST1H2BB, HIST1H3J, HIST1H2BC, HIST1H2BE, HIST1H2BF, HIST1H2BG, HIST1H2AE, MCM2, HIST1H2BM, HIST1H2BI, HIST1H3A, HIST1H3B, TUBA4A, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I
GO-BP	GO:0032268~regulation of cellular protein metabolic process	4.3	0.005	PRKCA, APP, PLK1, MKNK2, PAX5, CDC20, UBE2C
GO-BP	GO:0031400~negative regulation of protein modification process	9.9	0.007	PRKCA, PAX5, CDC20, UBE2C
GO-BP	GO:0051246~regulation of protein metabolic process	3.8	0.009	PRKCA, APP, PLK1, MKNK2, PAX5, CDC20, UBE2C
GO-BP	GO:0031399~regulation of protein modification process	5.0	0.016	PRKCA, PLK1, PAX5, CDC20, UBE2C
GO-BP	GO:0051437~positive regulation of ubiquitin-protein ligase activity during mitotic cell cycle	13.0	0.022	PLK1, CDC20, UBE2C
GO-BP	GO:0032269~negative regulation of cellular protein metabolic process	6.5	0.022	PRKCA, PAX5, CDC20, UBE2C
GO-BP	GO:0051443~positive regulation of ubiquitin-protein ligase activity	12.6	0.023	PLK1, CDC20, UBE2C
GO-BP	GO:0051439~regulation of ubiquitin-protein ligase activity during mitotic cell cycle	12.4	0.023	PLK1, CDC20, UBE2C
GO-BP	GO:0051248~negative regulation of protein metabolic process	6.3	0.024	PRKCA, PAX5, CDC20, UBE2C
GO-BP	GO:0031401~positive regulation of protein modification process	6.3	0.024	PRKCA, PLK1, CDC20, UBE2C
GO-BP	GO:0051351~positive regulation of ligase activity	12.1	0.025	PLK1, CDC20, UBE2C

GO-BP	GO:0051438~regulation of ubiquitin-protein ligase activity	11.3	0.028	PLK1, CDC20, UBE2C
GO-BP	GO:0051340~regulation of ligase activity	10.9	0.030	PLK1, CDC20, UBE2C
GO-BP	GO:0031398~positive regulation of protein ubiquitination	10.5	0.032	PLK1, CDC20, UBE2C
GO-BP	GO:0031396~regulation of protein ubiquitination	8.8	0.044	PLK1, CDC20, UBE2C
GO-BP	GO:0051247~positive regulation of protein metabolic process	4.8	0.047	PRKCA, PLK1, CDC20, UBE2C
GO-BP	GO:0032270~positive regulation of cellular protein metabolic process	5.0	0.042	PRKCA, PLK1, CDC20, UBE2C
GO-BP	GO:0031399~regulation of protein modification process	5.0	0.016	PRKCA, PLK1, PAX5, CDC20, UBE2C
GO-BP	GO:0000278~mitotic cell cycle	4.8	0.007	APP, CDKN2C, PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0022403~cell cycle phase	4.3	0.012	APP, CDKN2C, PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0007049~cell cycle	3.0	0.014	APP, UHRF1, CDKN2C, PLK1, CCNF, CDC20, MCM2, UBE2C
KEGG	hsa04110:Cell cycle	6.3	0.022	CDKN2C, PLK1, CDC20, MCM2
GO-BP	GO:0000280~nuclear division	5.3	0.037	PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0007067~mitosis	5.3	0.037	PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0000087~M phase of mitotic cell cycle	5.3	0.038	PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0022402~cell cycle process	3.1	0.039	APP, CDKN2C, PLK1, CCNF, CDC20, UBE2C
GO-BP	GO:0048285~organelle fission	5.1	0.041	PLK1, CCNF, CDC20, UBE2C
REACTOME	REACT_152:Cell Cycle, Mitotic	3.3	0.048	PLK1, TUBA4A, CDC20, MCM2, UBE2C
GO-BP	GO:0030198~extracellular matrix organization	8.5	0.047	APP, TGFBI, NID1
GO-BP	GO:0010324~membrane invagination	5.3	0.037	APP, LDLR, ITSN1, EHD4
GO-BP	GO:0006897~endocytosis	5.3	0.037	APP, LDLR, ITSN1, EHD4
GO-BP	GO:0006917~induction of apoptosis	4.6	0.022	PRKCA, APP, CDKN2C, ITSN1, RUNX3
GO-BP	GO:0012502~induction of programmed cell death	4.6	0.022	PRKCA, APP, CDKN2C, ITSN1, RUNX3

**Table S9. Pathway enrichment analysis for genes downregulated in A-AML.**

Category	Term	Fold Enrichment	p value	Genes
GO-BP	GO:0048562~embryonic organ morphogenesis	8.7	<0.001	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, HOXA6, HOXB5, HOXA7, ZEB1
GO-BP	GO:0048568~embryonic organ development	6.7	<0.001	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, HOXA6, HOXB5, HOXA7, ZEB1
GO-BP	GO:0003002~regionalization	5.9	<0.001	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, HOXA6, HOXB5, HOXA7, HOXA10
GO-BP	GO:0007389~pattern specification process	4.8	<0.001	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, HOXA6, HOXB5, HOXA7, HOXA10, ZEB1
GO-BP	GO:0048598~embryonic morphogenesis	4.2	0.001	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, HOXA6, HOXB5, HOXA7, HOXA10, ZEB1
GO-BP	GO:0009887~organ morphogenesis	2.7	0.004	HOXB3, HOXB4, HOXB2, HOXA3, BRAF, HOXA5, HOXA6, HOXB5, HOXA7, ANGPT1, ZEB1, NKX2-3
GO-BP	GO:0009790~embryonic development	2.5	0.012	HOXB3, HOXB4, HOXB2, HOXA3, HOXA5, PIK3CB, HOXA6, HOXB5, HOXA7, HOXA10, ZEB1
GO-BP	GO:0006139~nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.6	0.001	SUPT3H, OCLN, ZKSCAN1, NFIX, ZEB1, MEIS1, NAA38, WT1, POT1, ZFC3H1, WDR36, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, TWISTNB, LUC7L3, HIP1, ATP8B4, NKX2-3, ESCO1, ZNF33A, GMDS, MAT2A, ZNF25, ATR, RAD50, NME7, HOXB3, ZNF138, MED31, HOXB4, HOXB2, RPAIN, DMTF1, ATP2C1, HOXB5, NFE2L3, ZNF33B
GO-BP	GO:0019219~regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.5	0.021	SUPT3H, NFIX, ZKSCAN1, ZEB1, MEIS1, WT1, POT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, RFX7, ZNF25, ATR, RAD50, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0009119~ribonucleoside metabolic process	8.4	0.049	OCLN, MAT2A, NME7
GO-BP	GO:0044249~cellular biosynthetic process	1.6	0.001	SUPT3H, ZKSCAN1, NFIX, ZEB1, ALG8, MEIS1, WT1, POT1, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, OGT, TWISTNB, HIP1, ATP8B4, NKX2-3, ZNF33A, TBXAS1, GMDS, MAT2A, ZNF25, ATR, RAD50, NME7, HOXB3, ZNF138, MED31, HOXB4, HOXB2, RPAIN, ST8SIA6, DMTF1, ATP2C1, HOXB5, NFE2L3, ZNF33B, MRPL45
GO-BP	GO:0034645~cellular macromolecule biosynthetic process	1.6	0.002	SUPT3H, ZKSCAN1, NFIX, ZEB1, ALG8, MEIS1, WT1, POT1, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, OGT, TWISTNB, HIP1, NKX2-3, ZNF33A, ZNF25, ATR, RAD50, MED31,

				HOXB3, ZNF138, HOXB4, HOXB2, RPAIN, ST8SIA6, DMTF1, HOXB5, MRPL45, ZNF33B, NFE2L3
GO-BP	GO:0009059~macromolecule biosynthetic process	1.6	0.002	SUPT3H, ZKSCAN1, NFIX, ZEB1, ALG8, MEIS1, WT1, POT1, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, OGT, TWISTNB, HIP1, NKX2-3, ZNF33A, ZNF25, ATR, RAD50, MED31, HOXB3, ZNF138, HOXB4, HOXB2, RPAIN, ST8SIA6, DMTF1, HOXB5, MRPL45, ZNF33B, NFE2L3
GO-BP	GO:0009058~biosynthetic process	1.5	0.002	SUPT3H, ZKSCAN1, NFIX, ZEB1, ALG8, MEIS1, WT1, POT1, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, OGT, TWISTNB, HIP1, ATP8B4, NKX2-3, ZNF33A, TBXAS1, GMDS, MAT2A, ZNF25, ATR, RAD50, NME7, HOXB3, ZNF138, MED31, HOXB4, HOXB2, RPAIN, ST8SIA6, DMTF1, ATP2C1, HOXB5, NFE2L3, ZNF33B, MRPL45
GO-BP	GO:0043170~macromolecule metabolic process	1.3	0.005	DNAJC10, ZKSCAN1, ZEB1, ALG8, WDR36, RRN3, P4HA1, PIK3C3, CAT, OGT, TWISTNB, LUC7L3, ESCO1, ZNF33A, BRAF, TRPM7, PIK3CB, RPS6KC1, RAD50, TBCK, ZNF138, PROK2, RPAIN, MAPK6, NFE2L3, ZNF33B, MRPL45, PMPCB, SUPT3H, ERMP1, CLU, NFIX, MEIS1, NAA38, WT1, POT1, ZFC3H1, ZNF600, HOXA3, HOXA5, UFM1, HOXA6, HOXA7, LARS, HOXA10, LMLN, HIP1, NKX2-3, ZNF25, ATR, MSRB3, HOXB3, MED31, HOXB4, HOXB2, ST8SIA6, DMTF1, HOXB5, UBA3
GO-BP	GO:0044260~cellular macromolecule metabolic process	1.4	0.005	DNAJC10, ZKSCAN1, ZEB1, ALG8, WDR36, RRN3, P4HA1, PIK3C3, OGT, CAT, TWISTNB, LUC7L3, ESCO1, ZNF33A, BRAF, TRPM7, PIK3CB, RPS6KC1, RAD50, TBCK, ZNF138, PROK2, RPAIN, MAPK6, NFE2L3, ZNF33B, MRPL45, SUPT3H, NFIX, MEIS1, NAA38, WT1, POT1, ZFC3H1, HOXA3, ZNF600, HOXA5, UFM1, HOXA6, HOXA7, HOXA10, LARS, HIP1, NKX2-3, ZNF25, ATR, MSRB3, HOXB3, MED31, HOXB4, HOXB2, ST8SIA6, DMTF1, HOXB5, UBA3
GO-BP	GO:0044238~primary metabolic process	1.3	0.006	OCLN, DNAJC10, ZKSCAN1, ZEB1, ALG8, WDR36, RRN3, P4HA1, PIK3C3, CAT, OGT, TWISTNB, LUC7L3, ATP8B4, ESCO1, ZNF33A, BRAF, TRPM7, PIK3CB, RPS6KC1, RAD50, NME7, TBCK, ZNF138, PROK2, RPAIN, MAPK6, ATP2C1, NFE2L3, ZNF33B, MRPL45, PMPCB, SUPT3H, ERMP1, CLU, NFIX, MEIS1, NAA38, POT1, WT1, ZFC3H1, ZNF600, HOXA3, HOXA5, UFM1, HOXA6, HOXA7, LARS, HOXA10, HSD17B4, LMLN, NKX2-3, HIP1, TBXAS1, GMDS, PLEK, MAT2A, ZNF25, ATR, MSRB3, HOXB3, MED31, HOXB4, HOXB2, ST8SIA6, DMTF1, HOXB5, UBA3
GO-BP	GO:0044237~cellular metabolic process	1.2	0.015	OCLN, DNAJC10, ZKSCAN1, ZEB1, ALG8, WDR36, RRN3, P4HA1, PIK3C3, CAT, OGT, TWISTNB, LUC7L3, ATP8B4, ESCO1, ZNF33A, BRAF, TRPM7, PIK3CB, RPS6KC1, RAD50, NME7, TBCK, ZNF138, PROK2, RPAIN, MAPK6, ATP2C1, NFE2L3, ZNF33B, MRPL45, SUPT3H,

				NFIX, MEIS1, NAA38, POT1, WT1, ZFC3H1, ZNF600, HOXA3, HOXA5, UFM1, HOXA6, HOXA7, LARS, HOXA10, HSD17B4, NKX2-3, HIP1, TBXAS1, GMDS, PLEK, MAT2A, ZNF25, ATR, MSRB3, HOXB3, MED31, HOXB4, HOXB2, ST8SIA6, DMTF1, HOXB5, UBA3
GO-BP	GO:0010556~regulation of macromolecule biosynthetic process	1.4	0.037	SUPT3H, NFIX, ZKSCAN1, ZEB1, MEIS1, WT1, POT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, RFX7, ZNF25, ATR, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0031326~regulation of cellular biosynthetic process	1.4	0.037	SUPT3H, ZKSCAN1, NFIX, ZEB1, MEIS1, WT1, POT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, PLEK, RFX7, ZNF25, ATR, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0009889~regulation of biosynthetic process	1.4	0.040	SUPT3H, ZKSCAN1, NFIX, ZEB1, MEIS1, WT1, POT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, PLEK, RFX7, ZNF25, ATR, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0031323~regulation of cellular metabolic process	1.3	0.045	SUPT3H, ZKSCAN1, NFIX, ZEB1, MEIS1, WT1, POT1, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, PDGFD, HIP1, NKX2-3, ZNF33A, PLEK, PIK3CB, RFX7, ZNF25, ATR, RAD50, MED31, HOXB3, ZNF138, PROK2, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0050789~regulation of biological process	1.2	0.048	HINT1, DNAJC10, ZKSCAN1, ZEB1, CD47, AGAP6, RRN3, PIK3CB, ANGPT1, CAT, PDGFD, OGT, RAB27B, AGAP4, ZNF33A, BRAF, PIK3CB, G3BP1, RINT1, RPS6KC1, IPO8, RAD50, TBCK, ZNF138, PROK2, MAPK6, ATP2C1, KRIT1, NFE2L3, ZNF33B, SUPT3H, RALGPS2, CLU, NFIX, ABHD2, MEIS1, FAM13B, POT1, WT1, ZNF600, HOXA3, RASGRP3, HOXA5, HOXA6, SOS1, HOXA7, HOXA10, EXOC4, RHOBTB1, SUCNR1, NKX2-3, HIP1, PLEK, RFX7, ZNF25, ATR, TAX1BP1, ITPR2, HOXB3, MED31, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, RAP1B
GO-BP	GO:0006807~nitrogen compound metabolic process	1.5	0.003	SUPT3H, OCLN, ZKSCAN1, NFIX, ZEB1, MEIS1, NAA38, WT1, POT1, ZFC3H1, WDR36, ZNF600, HOXA3, RRN3, HOXA5, P4HA1, HOXA6, HOXA7, LARS, HOXA10, TWISTNB, LUC7L3, HIP1, ATP8B4, NKX2-3, ESCO1, ZNF33A, GMDS, MAT2A, ZNF25, ATR, RAD50, NME7, HOXB3, ZNF138, MED31, HOXB4, HOXB2, RPAIN, DMTF1, ATP2C1, HOXB5, NFE2L3, ZNF33B
GO-BP	GO:0034641~cellular nitrogen compound metabolic process	1.5	0.003	SUPT3H, OCLN, ZKSCAN1, NFIX, ZEB1, MEIS1, NAA38, WT1, POT1, ZFC3H1, WDR36, ZNF600, HOXA3, RRN3, HOXA5, HOXA6, HOXA7, LARS, HOXA10, TWISTNB, LUC7L3, HIP1, ATP8B4, NKX2-3, ESCO1, ZNF33A, GMDS, MAT2A, ZNF25, ATR, RAD50, NME7, HOXB3, ZNF138,

				MED31, HOXB4, HOXB2, RPAIN, DMTF1, ATP2C1, HOXB5, NFE2L3, ZNF33B
GO-BP	GO:0051171~regulation of nitrogen compound metabolic process	1.4	0.023	SUPT3H, NFIX, ZKSCAN1, ZEB1, MEIS1, WT1, POT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, RFX7, ZNF25, ATR, RAD50, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0046486~glycerolipid metabolic process	4.0	0.037	PLEK, PIK3CB, PIK3C3, CAT, NKX2-3
GO-BP	GO:0006355~regulation of transcription, DNA-dependent	1.7	0.016	SUPT3H, ZNF33A, RFX7, ZNF25, ZKSCAN1, NFIX, ZEB1, MEIS1, WT1, HOXB3, ZNF138, HOXB4, HOXB2, HOXA3, HOXA5, DMTF1, HOXA6, HOXB5, HOXA7, HOXA10, ZNF33B, NFE2L3, NKX2-3
GO-BP	GO:0006350~transcription	1.6	0.009	SUPT3H, NFIX, ZKSCAN1, ZEB1, MEIS1, WT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, TWISTNB, NKX2-3, HIP1, ZNF33A, ZNF25, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, ZNF33B, NFE2L3
GO-BP	GO:0045449~regulation of transcription	1.4	0.037	SUPT3H, NFIX, ZKSCAN1, ZEB1, MEIS1, WT1, HOXA3, ZNF600, RRN3, HOXA5, HOXA6, HOXA7, HOXA10, CAT, NKX2-3, HIP1, ZNF33A, RFX7, ZNF25, MED31, HOXB3, ZNF138, HOXB4, HOXB2, DMTF1, HOXB5, UBA3, ZNF33B, NFE2L3
GO-BP	GO:0051252~regulation of RNA metabolic process	1.6	0.020	SUPT3H, ZNF33A, RFX7, ZNF25, ZKSCAN1, NFIX, ZEB1, MEIS1, WT1, HOXB3, ZNF138, HOXB4, HOXB2, HOXA3, HOXA5, DMTF1, HOXA6, HOXB5, HOXA7, HOXA10, ZNF33B, NFE2L3, NKX2-3
GO-BP	GO:0007264~small GTPase mediated signal transduction	3.8	0.002	RALGPS2, RASGRP3, BRAF, SOS1, KRIT1, G3BP1, RHOBTB1, RAP1B, RAB27B
PANTHER	P00047:PDGF signaling pathway	4.4	0.003	MAPK6, BRAF, PIK3CB, SOS1, PIK3C3, RPS6KC1, ITPR2
KEGG	hsa04722:Neurotrophin signaling pathway	5.7	0.030	BRAF, PIK3CB, SOS1, RAP1B
PANTHER	P00034:Integrin signalling pathway	3.1	0.032	MAPK6, BRAF, PIK3CB, SOS1, PIK3C3, RAP1B
PANTHER	P04393:Ras Pathway	5.1	0.038	BRAF, PIK3CB, SOS1, PIK3C3
PANTHER	P00056:VEGF signaling pathway	5.9	0.026	MAPK6, BRAF, PIK3CB, PIK3C3
GO-BP	GO:0015031~protein transport	2.5	0.002	RPGR, PLEK, SNX14, RINT1, IPO8, WDR19, COG5, RPAIN, COG6, PEX1, NUP205, EXOC4, EXOC6, RAB27B, MRPL45
GO-BP	GO:0045184~establishment of protein localization	2.5	0.002	RPGR, PLEK, SNX14, RINT1, IPO8, WDR19, COG5, RPAIN, COG6, PEX1, NUP205, EXOC4, EXOC6, RAB27B, MRPL45
GO-BP	GO:0008104~protein localization	2.2	0.008	RPGR, PLEK, SNX14, RINT1, IPO8, WDR19, COG5, RPAIN, COG6, PEX1, NUP205, EXOC4, EXOC6, RAB27B, MRPL45
GO-BP	GO:0006886~intracellular protein transport	2.7	0.026	WDR19, RPGR, RPAIN, PEX1, NUP205, EXOC4, IPO8, MRPL45

GO-BP	GO:0034613~cellular protein localization	2.5	0.040	WDR19, RPGR, RPAIN, PEX1, NUP205, EXOC4, IPO8, MRPL45
GO-BP	GO:0006904~vesicle docking during exocytosis	16.0	0.015	PLEK, EXOC4, EXOC6
GO-BP	GO:0048278~vesicle docking	14.8	0.017	PLEK, EXOC4, EXOC6
GO-BP	GO:0022406~membrane docking	12.4	0.024	PLEK, EXOC4, EXOC6
KEGG	hsa05221:Acute myeloid leukemia	12.1	0.004	BRAF, PIK3CB, SOS1, CCNA1
KEGG	hsa04510:Focal adhesion	4.4	0.023	BRAF, PIK3CB, SOS1, RAP1B, PDGFD

**Table S10. *TP53* mutational status in the aneuploid and euploid GEP cohorts.**

<b>Patient ID</b>	<b>Aneuploid/Euploid</b>	<b><i>TP53</i></b>
1	Aneuploid	wt
5	Aneuploid	wt
12	Aneuploid	wt
13	Aneuploid	c.742C>T, p.R248W
21	Aneuploid	wt
23	Aneuploid	wt
24	Aneuploid	-17
25	Aneuploid	-17
37	Aneuploid	wt
54	Aneuploid	wt
55	Aneuploid	wt
56	Aneuploid	wt
58	Aneuploid	wt
68	Aneuploid	wt
69	Aneuploid	wt
70	Aneuploid	wt
71	Aneuploid	c. C577>T, p.H193Y
1006	Aneuploid	wt
2002	Aneuploid	wt
2030	Aneuploid	wt
2036	Aneuploid	wt
2040	Aneuploid	wt
6	Euploid	wt
14	Euploid	wt
15	Euploid	wt
16	Euploid	wt
18	Euploid	wt
20	Euploid	wt
0022	Euploid	wt
26	Euploid	wt
0037	Euploid	wt
39	Euploid	wt
40	Euploid	wt
41	Euploid	wt
44	Euploid	wt
45	Euploid	wt
46	Euploid	wt
47	Euploid	wt
48	Euploid	wt
49	Euploid	wt
50	Euploid	wt
51	Euploid	wt
59	Euploid	wt



64	Euploid	wt
65	Euploid	wt
66	Euploid	wt
83	Euploid	wt
85	Euploid	wt
2195	Euploid	wt

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**Table S11. List of WES mutations analyzed by Sanger Sequencing or Next Generation Sequencing.**

Start	End	Reference base(s)	Altered base(s)	Gene	Detection Method	Validation Method	Tumour status	Germline status	Sanger Sequencing Forward Primer (5'-3')	Sanger Sequencing Reverse Primer (5'-3')
35033566	35033566	G	T	AGXT2	MuTect	SS	mut	na	TGCGTTCTTAGAAATCAGAGGTG	CAGAGCCTTGCAGTTTACTTGAT
105407657	105407657	A	G	AHNAK2	VarScan	SS	mut	wt	TGTCTTCTCTGAAATCGAAGGA	GATTCAAAGTGAGGACCAGTGAG
46246569	46246569	G	T	ARID2	MuTect	SS	wt	na	TCCCCGACTCAGGATCAAAAGTAT	ATGAGACATGGAAAACAGTGCAT
31023076	31023079	TGAT	-	ASXL1	VarScan	SS	mut	wt	AGAGGACCTGCCTTCTCTGAGAAA	TTCGATGGGATGGGTATCCAATGC
17314703	17314703	G	A	ATP13A2	MuTect	SS	mut	wt	GAGCATGGCCAGTATTGAGTG	ACGTCATCTATTCTGGGACCTG
25022705	25022705	C	T	CENPO	MuTect	SS	mut	na	AATTGTTAGCTCCCCTGGTTTTA	CCCAAATCACGTTTGTTCATTAT
57743938	57743938	T	G	CLTC	Both	SS	mut	na	ATGCGCCTCAAGTATGTGTTTTA	GGTTAAGAAGATGGGTGTGAACC
165542528	165542528	G	-	COBLL1	VarScan	SS	mut	na	TGCTCTTGTCTTTGTGTTGATT	GGCATTAAAAGCCACAACACAAA
135487552	135487552	G	A	DDX31	Both	SS	mut	na	TAATTGTCCTGCTCATGTTTCGT	AGTGCTTGTATTGGGAGAAGG
6350850	6350850	G	A	FAM64A	MuTect	SS	mut	na	TGGTTTTGTCTGTGCTAACCTTT	GGATTGTGCCCAGGTTAAAAGG
15937239	15937239	G	T	FBXL7	MuTect	SS	mut	wt	AGAAGTGCACCAAACCTCAAATCC	TTTGCTTTGTTCAGGTTTGTGTG
28592642	28592642	C	A	FLT3	VarScan	SS	mut	na	CCGCCAGGAACGTGCTTG	GCAGACGGGCATTGCCCC
75874786	75874786	C	G	GLIPR1	MuTect	SS	mut	wt	CTCCAATTATTCACACACAGCAA	CAGAAAACAGGAAGTGTCCAAAG
51749144	51749144	G	A	GRM2	MuTect	SS	mut	wt	GGTTCATGTTAGGGTGAATGTT	GAATTCGTCCAATCGGTACTCAT
1960012	1960012	-	ACT	HIC1	VarScan	SS	mut	na	CTCCTGCTCCTTCTCCTGGTC	CATGTCATGGTCCAGGTTGAG
176316714	176316714	T	C	HK3	Both	SS	mut	na	ATGTATCTCCTTCAAAGCCAGGG	GGTATGGTCGAAGGTGGTCAG
37524829	37524829	C	A	IL2RB	MuTect	SS	wt	na	GGGAGTGCGGGGCTATAATC	TTCCTCTGAGTAGGGGTCGT
98662167	98662167	G	A	IPO5	MuTect	SS	mut	na	TTCTGGTCTTTGTGTTTTGCCTC	ACCGATAGCTCCTTCTAAAGACA
41620056	41620056	G	T	L3MBTL2	MuTect	SS	mut	wt	AACACCACACCTTCCCTGTC	ACTCTTCAGCCCTCGAAACC
29820029	29820029	G	A	MAZ	MuTect	SS	mut	na	TGTCACTCCCATTTCTACAGAT	GAAGTGGCTTTCTTGACTACTCC
99966347	99966347	C	T	METAP1	MuTect	SS	mut	na	GAGCTTCTGTTGGGCAATAACTA	CCAAGAGATTCCCAGATCATCCT
82335748	82335748	G	T	MEX3B	MuTect	SS	mut	wt	CGGTATCTTCTTCTGCTCTTCT	CCGCTGCCTTTAAGAAAAGAT
158819011	158819011	C	T	MNDA	VarScan	SS	mut	na	ACTAACGAGCTTTCATAGGGGAT	GCCTCGTGAATGTCATAAAAGCA
18258091	18258091	C	T	NAT2	VarScan	SS	mut	wt	ATTGACGGCAGGAATTACATTGT	ACTTCTTCAACCTCTTCTCAGT
29562747	29562747	G	A	NF1	Both	SS	mut	na	AATGGGATTGTTTGCCTAACCT	CTAACATGTTGCCAATCAGAGGA
25457049	25457054	CTCCCA	-	NINL	VarScan	SS	mut	na	CTGTGGAGTGGATGGGGATATT	CATGTCATCCTTCTCTCTCCA
57080473	57080473	G	A	NLRC5	MuTect	SS	mut	wt	TCCAAGTCTGGGAGTCCAAT	ACCCACGCCTCTTCTTTTC

120474836	120474836	A	G	PDE5A	Both	SS	mut	wt	AACTGCACAGAGGGA	ACTCA	TGCAAATAAGGCAAAACTCTAGC A
81242148	81242149	TT	-	PKD1L2	VarScan	SS	mut	na	GTGGGGTCTGGAATATGGTATCT		CATGCCATAAAATCAGAGGGACA
42281236	42281236	A	C	PKDCC	VarScan	SS	mut	na	ATAGAAAATCACTGGCCTCCTCT		TAGGCATTATAGAGGTTCCGCTT
42284989	42284989	C	A	PLA2G4E	Both	SS	mut	na	GTTAGGGTTCTCAATGGCCTG		TCTAACCTAATCCCCTGTGTGC
79785404	79785404	G	C	POLR3A	MuTect	SS	mut	na	GCTTCCTTCCATCTCCTCAATTC		CACCACTCACAGTTCCTAAGTTC
106857363	106857363	T	C	POLR3B	Both	SS	mut	na	ACTCTATGGTAGGCATGAAATGA		GACAGCATAGAGGAGCAAGTCTA
58740498	58740498	C	G	PPM1D	MuTect	SS	mut	wt	TGAATGCATACCCCGTTTTT		TCTTTTCGCTGTGAGGTTGTG
54153157	54153157	C	T	PSME4	VarScan	SS	mut	wt	CTTGACTTCTGTATTTGGCCCTT		TCCTTTTATAACTTCAGGAGCACC
43111336	43111336	G	T	PTK7	MuTect	SS	wt	na	CCTCATGTTCTACTGCAAGAAGC		CCAGGTTGCTCAGAAGACGAG
37628876	37628876	A	G	RAC2	Both	SS	mut	na	ACGGGTAGGAAAAGGATTAAGAG A		CCTAAGGGGAGAGGTAGGGTTTC
37640155	37640155	C	G	RAC2	MuTect	SS	mut	wt	AGCTTGAGTAAGTTCCCCTTCC		TGCATCCACAGAGTAAAGACTGA
38967300	38967300	A	C	RICTOR	MuTect	SS	mut	wt	AATTAATAGGAATGGGCCAAAA		CCTGGCATGAAAGAATCTGTTAG
1551180	1551193	GCTGCTT CCGGAC A	-	RILP	VarScan	SS	mut	na	GAGAGGGACAGTACAAAGGGTT		GTCATCAGGCTCAGCAGAATG
122265671	122265671	A	T	SETD1B	Both	SS	mut	na	CAGTGACCTGCTCAAGTTCAAC		CACTTGGTGGCGTCGATGATG
134491555	134491555	G	A	SGK1	Both	SS	mut	na	GCTTGAAGTGGGTGATTATGGAA		GCTCCACCAAAGGCTAACTAAA
124517319	124517319	G	A	SIAE	Both	SS	mut	na	GGAGGAGAGTAATGTGTGGTCAT		GACCAGCACATTATGAGGACAAA
96964395	96964395	G	A	SNRNP200	Both	SS	mut	na	TGCCTGGTACTTTTATAGCTCG		AAGACCCACCATATACTCACTC
101245695	101245695	G	-	SPAG1	VarScan	SS	mut	wt	GGTCTGTCTCTTCCACTTGATTG		TAACCTCAATCCCATCCCAAGAT
40474366	40474366	G	-	STAT3	VarScan	SS	mut	na	CATGATCTTTCCTTCCCATGTCC		GCTGTATCCCCTCTTTAGACTCA
7578190	7578190	T	C	TP53	Both	SS	mut	na	CACTTGTGCCCTGACTTTCA		TTGCACATCTCATGGGGTTA
7578535	7578535	T	C	TP53	MuTect	SS	mut	na	CACTTGTGCCCTGACTTTCA		TTGCACATCTCATGGGGTTA
7577574	7577574	T	C	TP53	VarScan	SS	mut	na	CACTTGTGCCCTGACTTTCA		TTGCACATCTCATGGGGTTA
68834972	68834972	A	C	TPCN2	MuTect	SS	mut	wt	GAGATCCTGAGTTTGGTCCTGTC		TGTCACCTTTCTTCTCCACTTA
98524941	98524941	G	A	TRRAP	MuTect	SS	mut	wt	GAAAAGACCATCCCCAATGTTAT		GAAAATCAATCAGCCAACTCAG
42288436	42288436	A	T	UBTF	MuTect	SS	mut	wt	GAGATAGGGCACCATGCAGT		CTCAGACAGGTCGTTCCACA
6303900	6303900	G	A	WFS1	MuTect	SS	mut	na	ATCAACATGCTCCCGTTCTTCAT		AGGATGGTGTGAACTCGATG
32417913	32417913	-	TT	WT1	VarScan	SS	mut	wt	AGGGAGTAGTTAGACTTTGGGAC		TATCTCTTATTGCAGCCTGGGTA
75245170	75245170	T	A	YLPM1	MuTect	SS	mut	mut	ATTTGGGGGAGGAACTGAAA		TTACCGGCTCTGGTGTATCC
37618563	37618563	A	G	ZNF420	Both	SS	mut	na	TCAGACGAGCCTCACACCTA		ACTTTTTGATGTCGGGTAAGTTGT

39923059	39923059	G	A	BCOR	MuTect	NGS	mut	na
39911649	39911649	G	A	BCOR	MuTect	NGS	mut	na
39911499	39911499	T	C	BCOR	MuTect	NGS	mut	na
119148966	119148966	T	C	CBL	MuTect	NGS	mut	na
33792321	33792321	C	T	CEBPA	MuTect	NGS	mut	na
25462068	25462068	A	G	DNMT3A	VarScan	NGS	mut	na
25470551	25470551	C	A	DNMT3A	Both	NGS	mut	na
25467482	25467482	C	T	DNMT3A	Both	NGS	mut	na
25457242	25457242	C	T	DNMT3A	VarScan	NGS	mut	na
25457242	25457242	C	T	DNMT3A	VarScan	NGS	mut	na
25463271	25463271	G	C	DNMT3A	MuTect	NGS	mut	na
25467198	25467198	G	T	DNMT3A	MuTect	NGS	mut	na
28608327	28608327	G	C	FLT3	MuTect	NGS	mut	na
90631934	90631934	C	T	IDH2	MuTect	NGS	mut	na
44945176	44945176	T	G	KDM6A	MuTect	NGS	mut	na
25398284	25398284	C	T	KRAS	MuTect	NGS	mut	na
25398284	25398284	C	T	KRAS	MuTect	NGS	wt	na
25398281	25398281	C	T	KRAS	MuTect	NGS	wt	na
25398281	25398281	C	T	KRAS	MuTect	NGS	mut	na
25398284	25398284	C	T	KRAS	MuTect	NGS	mut	na
25380285	25380285	G	A	KRAS	MuTect	NGS	mut	na
170837543	170837543	-	TCTG	NPM1	VarScan	NGS	mut	na
170837543	170837543	-	TCTG	NPM1	VarScan	NGS	mut	na
115256529	115256529	T	C	NRAS	Both	NGS	mut	na
115258748	115258748	C	T	NRAS	MuTect	NGS	mut	na
198273279	198273279	C	A	SF3B1	MuTect	NGS	wt	na
198266834	198266834	T	C	SF3B1	MuTect	NGS	mut	na
198267371	198267371	G	C	SF3B1	MuTect	NGS	wt	na
106196267	106196267	C	T	TET2	VarScan	NGS	mut	na
7577120	7577120	C	T	TP53	Both	NGS	mut	na
7577538	7577538	C	T	TP53	Both	NGS	mut	na

7577505	7577505	T	A	TP53	VarScan	NGS	mut	na
7577082	7577082	C	T	TP53	Both	NGS	mut	na
7578388	7578388	C	T	TP53	VarScan	NGS	mut	na
7577557	7577557	G	-	TP53	VarScan	NGS	mut	na
7577136	7577136	C	-	TP53	VarScan	NGS	mut	na
7577570	7577570	C	T	TP53	MuTect	NGS	mut	na
7578265	7578265	A	G	TP53	MuTect	NGS	mut	na

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