# Supplementary Material

# Identification of a histone family gene signature for predicting the prognosis of cervical cancer patients

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**Table S1 Information of the data resources**

| Groups | Cervix Uteri (number of samples) | Cervical Carcinoma (number of samples) | Experiment type |
|---|---|---|---|
| TCGA (TCGA-CESC) # | 3 | 252 | RNA-sequencing |
| Biewenga Cervix (GSE7410)[1]* | 5 | 40 | Micro array(mRNA) |
| Pyeon Multi-cancer (GSE6791)[2]* | 8 | 20 | Micro array(mRNA) |
| Scotto Cervix (GSE9750)[3]* | 3 | 32 | Micro array(mRNA) |

Abbreviations: TCGA: The Cancer Genome Atlas

#TCGA-CESC: project ID of the data we used from TCGA

*The three datasets we used for validation also can be searched in GEO(Gene Expression Omnibus microarray data repository), GEO accessions and references were shown.

**References:**

1 Biewenga, P. *et al.* Gene expression in early stage cervical cancer. *Gynecologic Oncology* **108**, 520-526, doi:10.1016/j.ygyno.2007.11.024.

2 Pyeon, D. *et al.* Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer research* **67**, 4605-4619, doi:10.1158/0008-5472.CAN-06-3619 (2007).

3 Scotto, L. *et al.* Identification of copy number gain and overexpressed genes on chromosome arm 20q by an integrative genomic approach in cervical cancer: Potential role in progression. *Genes, Chromosomes and Cancer* **47**, 755-765, doi:10.1002/gcc.20577 (2008).

## Table S2 Information of the DEGs corresponding to the heatmap (Figure 2)

| | logFC | logCPM | P-Value | FDR |
|---|---|---|---|---|
| **Up-DEGs** | | | | |
| **(cancer versus normal)** | | | | |
| FAM83C | 11.00726 | 4.921006 | 0.001449 | 0.012618 |
| UGT1A6 | 10.5887 | 1.75696 | 0.007979 | 0.048456 |
| EPGN | 10.43008 | 1.599564 | 0.008235 | 0.04946 |
| NANOGNBP3 | 10.208962 | 1.85087 | 0.000772 | 0.007596 |
| TERT | 10.04358 | 1.217666 | 3.68E-05 | 0.000559 |
| MAB21L3 | 9.786823 | 0.9653 | 0.000204 | 0.002506 |
| RP11-21B23.2 | 9.699783 | 0.87928 | 0.008012 | 0.048596 |
| KRT3 | 9.606661 | 0.788798 | 0.008165 | 0.049208 |
| KRT16P1 | 9.605554 | 0.786461 | 0.00532 | 0.035572 |
| CALML5 | 9.491751 | 7.428736 | 0.00544 | 0.036201 |
| PLA2G4E | 9.480202 | 4.407806 | 0.003248 | 0.024052 |
| HIST1H2BL | 9.372446 | 3.376436 | 0.006084 | 0.039312 |
| IGF2BP1 | 9.302071 | 3.031891 | 0.007071 | 0.044205 |
| PGLYRP3 | 9.283234 | 3.376436 | 0.006084 | 0.039312 |
| CH17-360D5.3 | 9.093475 | 2.292376 | 0.000504 | 0.005383 |
| HIST1H2BJ | 9.020184 | 3.250386 | 0.001613 | 0.013761 |
| OR2B6 | 9.008599 | 0.204147 | 3.27E-05 | 0.000503 |
| HIST1H2BM | 9.004763 | 2.004825 | 2.64E-05 | 0.000418 |
| CYP4F23P | 8.943169 | 0.140711 | 0.007992 | 0.048505 |
| RP11-161I6.2 | 8.844568 | 0.045341 | 0.001989 | 0.01626 |
| HIST1H2AI | 8.832465 | 0.033357 | 1.11E-06 | 2.34E-05 |
| ZIC2 | 8.736181 | 4.075299 | 3.05E-05 | 0.000474 |
| HIST1H2BD | 8.663077 | 4.532132 | 0.001339 | 0.011848 |
| TPSP2 | 8.661043 | -0.13167 | 0.005447 | 0.036211 |
| RP11-1038A11.3 | 8.606365 | -0.18447 | 0.00276 | 0.02112 |
| **Down-DEGs** | | | | |
| **(cancer versus normal)** | | | | |
| PGM5-AS1 | -9.16467 | -1.34416 | 1.62E-88 | 5.21E-84 |
| TCEAL6 | -8.61211 | -2.44778 | 7.55E-83 | 8.08E-79 |
| FRMD6-AS2 | -7.97443 | -2.01225 | 3.94E-49 | 3.42E-46 |
| TCF23 | -7.95359 | 0.658118 | 9.46E-41 | 4.22E-38 |
| RP11-475A13.1 | -7.91355 | -4.14075 | 3.47E-45 | 1.96E-42 |
| RP3-333A15.2 | -7.86555 | -3.21927 | 8.93E-63 | 1.91E-59 |
| AGTR2 | -7.7095 | -1.16863 | 5.24E-17 | 4.05E-15 |
| DES | -7.58321 | 6.095272 | 1.18E-56 | 1.57E-53 |
| CNN1 | -7.52521 | 5.393158 | 7.45E-77 | 5.98E-73 |
| ACTG2 | -7.35287 | 5.862155 | 2.33E-56 | 3.00E-53 |
| PTGER3 | -7.2886 | 1.997712 | 2.51E-74 | 1.61E-70 |
| DPP6 | -7.21308 | 1.150937 | 7.32E-42 | 3.46E-39 |
| RP11-887P2.5 | -7.17872 | -1.53145 | 1.71E-46 | 1.10E-43 |

| | | | | |
|---|---|---|---|---|
| AC053503.12 | -7.12269 | -3.22431 | 3.51E-27 | 7.38E-25 |
| CHRDL1 | -7.09942 | 2.029395 | 9.46E-34 | 2.87E-31 |
| CLVS2 | -7.08581 | -2.73499 | 6.39E-28 | 1.40E-25 |
| PI16 | -7.07756 | 2.014868 | 4.14E-37 | 1.44E-34 |
| GPM6A | -6.9051 | -0.55645 | 4.90E-45 | 2.70E-42 |
| AC053503.6 | -6.90042 | -3.74084 | 1.05E-23 | 1.61E-21 |
| MYH11 | -6.89444 | 6.838917 | 1.02E-56 | 1.48E-53 |
| SERTM1 | -6.84045 | 0.87733 | 9.81E-16 | 6.44E-14 |
| ANGPTL1 | -6.80391 | 0.742043 | 5.09E-50 | 4.96E-47 |
| PLN | -6.71017 | 1.648954 | 8.63E-51 | 8.66E-48 |
| PRLHR | -6.69165 | -2.98097 | 3.67E-17 | 2.91E-15 |
| LCN6 | -6.67999 | -2.36527 | 1.63E-45 | 9.52E-43 |

## Table S3 Up-regulated KEGG pathways

| ID | Description | Gene Ratio | P-value | Q-value | Gene ID |
|---|---|---|---|---|---|
| hsa04110 | Cell cycle | 35/368 | 0.0000 | 0.0000 | BUB1/BUB1B/CCNA2/CCNB1/CCNB2/CCNE1/CCNE2/CDC20/CDC25A/CDC25C/CDC45/CDC6/CDC7/CDK1/CDKN2A/CDKN2B/CHEK1/E2F1/E2F2/ESPL1/MAD2L1/MCM2/MCM4/MCM5/ORC1/ORC6/PCNA/PKMYT1/PLK1/PTTG1/RBL1/SFN/SKP2/SMC1B/TTK |
| hsa05322 | Systemic lupus erythematosus | 28/368 | 0.0000 | 0.0000 | HIST1H2AD/HIST1H2AG/HIST1H2AI/HIST1H2AJ/HIST1H2AL/HIST1H2AM/HIST1H2BC/HIST1H2BD/HIST1H2BF/HIST1H2BG/HIST1H2BH/HIST1H2BI/HIST1H2BJ/HIST1H2BL/HIST1H2BO/HIST1H3B/HIST1H3C/HIST1H3D/HIST1H3F/HIST1H3G/HIST1H3H/HIST1H3J/HIST1H4D/HIST1H4E/HIST2H2AB/HIST2H2BF/HIST2H4A/HIST3H2BB |
| hsa05034 | Alcoholism | 33/368 | 0.0000 | 0.0000 | CALML3/CALML5/GNGT1/GRIN1/GRIN2D/HIST1H2AD/HIST1H2AG/HIST1H2AI/HIST1H2AJ/HIST1H2AL/HIST1H2AM/HIST1H2BC/HIST1H2BD/HIST1H2BF/HIST1H2BG/HIST1H2BH/HIST1H2BI/HIST1H2BJ/HIST1H2BL/HIST1H2BO/HIST1H3B/HIST1H3C/HIST1H3D/HIST1H3F/HIST1H3G/HIST1H3H/HIST1H3J/HIST1H4D/HIST1H4E/HIST2H2AB/HIST2H2BF/HIST2H4A/HIST3H2BB |
| hsa03030 | DNA replication | 12/368 | 0.0000 | 0.0000 | DNA2/FEN1/LIG1/MCM2/MCM4/MCM5/PCNA/POLD1/POLE/POLE2/RFC4/RNASEH2A |
| hsa05203 | Viral carcinogenesis | 30/368 | 0.0000 | 0.0000 | ATP6V0D2/BAK1/CCNA2/CCNE1/CCNE2/CCR8/CDC20/CDK1/CDKN2A/CDKN2B/CHEK1/HIST1H2BC/HIST1H2BD/HIST1H2BF/HIST1H2BG/HIST1H2BH/HIST1H2BI/HIST1H2BJ/HIST1H2BL/HIST1H2BO/HIST1H4D/HIST1H4E/HIST2H2BF/HIST2H4A/HIST3H2BB/IRF7/PMAIP1/RBL1/SKP2/SYK |
| hsa04115 | p53 signaling | 16/368 | 0.0000 | 0.0000 | CCNB1/CCNB2/CCNE1/CCNE2/CD8 |

| | | | | | |
|---|---|---|---|---|---|
| | pathway | | | | 2/CDK1/CDKN2A/CHEK1/GTSE1/PERP/PMAIP1/RRM2/SERPINB5/SFN/TP53AIP1/TP73 |
| hsa03460 | Fanconi anemia pathway | 14/368 | 0.0000 | 0.0000 | BLM/BRCA1/BRCA2/BRIP1/EME1/FAAP24/FANCA/FANCB/FANCD2/FANCI/RAD51/RMI1/RMI2/UBE2T |
| hsa04114 | Oocyte meiosis | 21/368 | 0.0000 | 0.0000 | AURKA/BUB1/CALML3/CALML5/CCNB1/CCNB2/CCNE1/CCNE2/CDC20/CDC25C/CDK1/ESPL1/FBXO43/ITPR3/MAD2L1/PKMYT1/PLK1/PTTG1/RPS6KA1/SGOL1/SMC1B |
| hsa03440 | Homologous recombination | 11/368 | 0.0000 | 0.0001 | BLM/BRCA1/BRCA2/BRIP1/EME1/POLD1/RAD51/RAD54B/RAD54L/TOPBP1/XRCC2 |
| hsa04530 | Tight junction | 19/368 | 0.0010 | 0.0253 | CGN/CLDN14/CLDN4/CLDN7/CRB3/EPB41L4B/F11R/LLGL2/MARVELD2/MARVELD3/MICALL2/MYH14/OCLN/PCNA/PRKCZ/RUNX1/SLC9A3R1/TUBA1C/TUBA4A |
| hsa03410 | Base excision repair | 7/368 | 0.0012 | 0.0258 | FEN1/LIG1/NEIL3/PCNA/POLD1/POLE/POLE2 |

## Table S4 Down-regulated KEGG pathways

| ID | Description | Gene Ratio | P-value | Q-value | Gene ID |
|---|---|---|---|---|---|
| hsa04510 | Focal adhesion | 43/466 | 0.0000 | 0.0000 | AKT3/BCL2/CAV1/CHAD/COL1A2/COL4A6/COL6A1/COL6A2/COL6A3/COL6A6/FLNA/FLNC/FLT1/FLT4/FYN/HGF/ILK/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/KDR/LAMA2/LAMA4/LAMB2/MAPK10/MYL9/MYLK/PARVA/PDGFC/PDGFD/PDGFRA/PDGFRB/PPP1R12B/PRKCA/RELN/THBS1/THBS4/TNXB/FIGF/VWF/ZYX |
| hsa04270 | Vascular smooth muscle contraction | 31/466 | 0.0000 | 0.0000 | ACTA2/ACTG2/ADCY4/ADCY5/ADRA1A/ADRA1D/AGTR1/AVPR1A/CACNA1C/CALCRL/CALD1/EDNRA/GUCY1A2/ITPR1/KCNMA1/KCNMB1/KCNMB2/MRVI1/MYH11/MYL9/MYLK/NPR1/NPR2/PLA2G5/PPP1R12B/PPP1R14A/PRKCA/PRKG1/RAMP1/RAMP2/RAMP3 |
| hsa04080 | Neuroactive ligand-receptor interaction | 50/466 | 0.0000 | 0.0000 | ADCYAP1R1/ADRA1A/ADRA1D/ADRA2A/ADRA2C/ADRB3/AGTR1/AGTR2/AVPR1A/AVPR2/BRS3/CALCRL/CHRM2/CTSG/EDNRA/EDNRB/GH1/GLP2R/GRIA2/GRIA3/GRID1/GRIK5/GRM7/HTR1E/HTR2A/HTR2B/HTR4/LEPR/LPAR4/MAS1/MCHR1/NPY1R/NPY5R/P2RX1/PRL/PRLHR/PRLR/PTGER2/PTGER3/PTGFR/PTH1R/S1PR1/S1PR2/S1PR3/SSTR3/TACR1/TACR2/TBXA2R/THRA/VIPR2 |
| hsa04020 | Calcium signaling pathway | 37/466 | 0.0000 | 0.0000 | ADCY4/ADRA1A/ADRA1D/ADRB3/AGTR1/ATP2B4/AVPR1A/CACNA1C/CACNA1G/CACNA1H/CAMK2A/CHRM2/EDNRA/EDNRB/GNA14/HTR2A/HTR2B/HTR4/ITPKB/ITPR1/MYLK/NOS3/P2RX1/PDE1A/PDE1B/PDE1C/PDGFRA/PDGFRB/PLN/PRKCA/PTGER3/PTGFR/RYR3/SLC8A1/TACR1/TACR2/TBXA2R |
| hsa04022 | cGMP-PKG signaling pathway | 34/466 | 0.0000 | 0.0000 | ADCY4/ADCY5/ADRA1A/ADRA1D/ADRA2A/ADRA2C/ADRB3/AGTR1/AKT3/ATP1A2/ATP1B2/ATP2B4/CACNA1C/EDNRA/EDNRB/GUCY1A2/ITPR1/KCNJ8/KCNMA1/KCNMB1/KCNMB2/MEF2C/MRVI1/MYL9/MYLK/NFATC4/NOS3/NPR1/NPR2/PDE2A/PLN/PRKG1/RGS2 |

|  |  |  |  |  |  |
|---|---|---|---|---|---|
|  |  |  |  |  | /SLC8A1 |
| hsa04151 | PI3K-Akt signaling pathway | 51/466 | 0.0000 | 0.0000 | AKT3/ANGPT1/ANGPT4/BCL2/CHAD/CHRM2/COL1A2/COL4A6/COL6A1/COL6A2/COL6A3/COL6A6/EPO/FGF10/FGF13/FGF2/FGF7/FGFR1/FLT1/FLT4/GH1/GNG11/GNG7/HGF/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/KDR/LAMA2/LAMA4/LAMB2/LPAR4/NGF/NOS3/NR4A1/PDGFC/PDGFD/PDGFRA/PDGFRB/PRKCA/PRL/PRLR/RELN/TEK/THBS1/THBS4/TNXB/FIGF/VWF |
| hsa04512 | ECM-receptor interaction | 20/466 | 0.0000 | 0.0000 | CHAD/COL1A2/COL4A6/COL6A1/COL6A2/COL6A3/COL6A6/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/LAMA2/LAMA4/LAMB2/RELN/THBS1/THBS4/TNXB/VWF |
| hsa05414 | Dilated cardiomyopathy | 20/466 | 0.0000 | 0.0000 | ACTC1/ADCY4/ADCY5/CACNA1C/CACNB2/DES/DMD/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/LAMA2/MYL3/PLN/SGCA/SGCD/SLC8A1/TPM1/TPM2 |
| hsa04924 | Renin secretion | 16/466 | 0.0000 | 0.0001 | ADCY5/ADCYAP1/ADCYAP1R1/ADRB3/AGTR1/AQP1/CACNA1C/EDNRA/GUCY1A2/ITPR1/KCNMA1/NPR1/PDE1A/PDE1B/PDE1C/PTGER2 |
| hsa04261 | Adrenergic signaling in cardiomyocytes | 26/466 | 0.0000 | 0.0001 | ACTC1/ADCY4/ADCY5/ADRA1A/ADRA1D/AGTR1/AGTR2/AKT3/ATP1A2/ATP1B2/ATP2B4/BCL2/CACNA1C/CACNB2/CAMK2A/MYL3/PLN/PPP1R1A/PRKCA/RAPGEF4/SCN1B/SCN4B/SCN7A/SLC8A1/TPM1/TPM2 |
| hsa04911 | Insulin secretion | 18/466 | 0.0000 | 0.0001 | ABCC8/ADCY4/ADCY5/ADCYAP1/ADCYAP1R1/ATP1A2/ATP1B2/CACNA1C/CAMK2A/KCNMA1/KCNMB1/KCNMB2/KCNN2/KCNN3/PRKCA/RAPGEF4/SNAP25/VAMP2 |
| hsa05410 | Hypertrophic cardiomyopathy (HCM) | 17/466 | 0.0000 | 0.0003 | ACTC1/CACNA1C/CACNB2/DES/DMD/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/LAMA2/MYL3/SGCA/SGCD/SLC8A1/TPM1/TPM2 |
| hsa05412 | Arrhythmogenic right ventricular cardiomyopathy (ARVC) | 15/466 | 0.0000 | 0.0007 | ACTN2/CACNA1C/CACNB2/CTNNA3/DES/DMD/ITGA11/ITGA7/ITGA8/ITGA9/ITGB3/LAMA2/SGCA/SGCD/SLC8A1 |

|  |  |  |  |  |  |
|---|---|---|---|---|---|
| hsa05205 | Proteoglycans in cancer | 29/466 | 0.0000 | 0.0007 | AKT3/ANK2/CAMK2A/CAV1/DCN/ESR1/FGF2/FGFR1/FLNA/FLNC/FZD4/HGF/HPSE2/HSPB2/IGF2/ITGB3/ITPR1/KDR/LUM/MMP2/PPP1R12B/PRKCA/SDC2/THBS1/TIMP3/TWIST1/TWIST2/WNT2/WNT9B |
| hsa04015 | Rap1 signaling pathway | 29/466 | 0.0001 | 0.0013 | ADCY4/ADCY5/AKT3/ANGPT1/ANGPT4/FGF10/FGF13/FGF2/FGF7/FGFR1/FLT1/FLT4/GNAO1/HGF/ITGB3/KDR/LPAR4/MAGI2/NGF/PDGFC/PDGFD/PDGFRA/PDGFRB/PRKCA/RAPGEF4/RASGRP2/TEK/THBS1/FIGF |
| hsa04713 | Circadian entrainment | 17/466 | 0.0001 | 0.0016 | ADCY4/ADCY5/ADCYAP1R1/CACNA1C/CACNA1G/CACNA1H/CAMK2A/GNAO1/GNG11/GNG7/GRIA2/GRIA3/GUCY1A2/ITPR1/PRKCA/PRKG1/RYR3 |
| hsa04514 | Cell adhesion molecules (CAMs) | 22/466 | 0.0001 | 0.0018 | CADM3/CD34/CDH5/CLDN5/CNTNAP1/ESAM/ICAM2/ITGA8/ITGA9/JAM2/JAM3/LRRC4B/MAG/NCAM1/NEGR1/NLGN3/NRXN2/NRXN3/PECAM1/PTPRM/SDC2/SELP |
| hsa04970 | Salivary secretion | 16/466 | 0.0002 | 0.0021 | ADCY4/ADCY5/ADRA1A/ADRA1D/ADRB3/ATP1A2/ATP1B2/ATP2B4/BST1/GUCY1A2/ITPR1/KCNMA1/PRKCA/PRKG1/RYR3/VAMP2 |
| hsa05200 | Pathways in cancer | 44/466 | 0.0003 | 0.0030 | ADCY4/ADCY5/AGTR1/AKT3/AR/AXIN2/BCL2/COL4A6/CTNNA3/CXCL12/EDNRA/EDNRB/FGF10/FGF13/FGF2/FGF7/FGFR1/FOXO1/FZD4/GLI1/GNG11/GNG7/HGF/LAMA2/LAMA4/LAMB2/LPAR4/MAPK10/MITF/MMP2/PDGFRA/PDGFRB/PRKCA/PTCH2/PTGER2/PTGER3/RASGRP2/RUNX1T1/STAT5B/TGFBR2/FIGF/WNT2/WNT9B/ZBTB16 |
| hsa04072 | Phospholipase D signaling pathway | 21/466 | 0.0004 | 0.0036 | ADCY4/ADCY5/AGTR1/AKT3/AVPR1A/AVPR2/DGKB/FYN/GAB2/GRM7/LPAR4/MS4A2/PDGFC/PDGFD/PDGFRA/PDGFRB/PPAP2A/PPAP2B/PRKCA/PTGFR/RAPGEF4 |
| hsa04014 | Ras signaling pathway | 29/466 | 0.0004 | 0.0036 | AKT3/ANGPT1/ANGPT4/FGF10/FGF13/FGF2/FGF7/FGFR1/FLT1/FLT4/GAB2/GNG11/GNG7/HGF/KDR/MAPK10/NGF/PDGFC/PDGFD/PDGFRA/PDGFRB/PLA2G5/PRKCA/RASA4/RASA4B/RASGRF2/ |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | RASGRP2/TEK/FIGF |
| hsa04614 | Renin-angiotensin system | 7/466 | 0.0004 | 0.0042 | AGTR1/AGTR2/CMA1/CPA3/CTSG/ENPEP/MAS1 |
| hsa04024 | cAMP signaling pathway | 26/466 | 0.0005 | 0.0042 | ADCY4/ADCY5/ADCYAP1R1/AKT3/ATP1A2/ATP1B2/ATP2B4/CACNA1C/CAMK2A/CHRM2/EDNRA/FXYD1/GLI1/GRIA2/GRIA3/HTR1E/HTR4/MAPK10/MYL9/NPR1/NPY1R/PLN/PTGER2/PTGER3/RAPGEF4/VIPR2 |
| hsa02010 | ABC transporters | 10/466 | 0.0005 | 0.0042 | ABCA10/ABCA6/ABCA8/ABCA9/ABCB1/ABCB5/ABCC8/ABCC9/ABCD2/ABCG2 |
| hsa05218 | Melanoma | 12/466 | 0.0018 | 0.0153 | AKT3/FGF10/FGF13/FGF2/FGF7/FGFR1/HGF/MITF/PDGFC/PDGFD/PDGFRA/PDGFRB |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications | 15/466 | 0.0020 | 0.0163 | AGTR1/AKT3/BCL2/COL1A2/COL3A1/COL4A6/EGR1/FOXO1/MAPK10/MMP2/NOS3/PRKCA/STAT5B/TGFBR2/FIGF |
| hsa04925 | Aldosterone synthesis and secretion | 13/466 | 0.0022 | 0.0169 | ADCY4/ADCY5/AGTR1/CACNA1C/CACNA1G/CACNA1H/CAMK1/CAMK2A/ITPR1/NPR1/NR4A1/PDE2A/PRKCA |
| hsa04724 | Glutamatergic synapse | 16/466 | 0.0026 | 0.0197 | ADCY4/ADCY5/CACNA1C/DLG4/GNAO1/GNG11/GNG7/GRIA2/GRIA3/GRIK5/GRM7/ITPR1/PRKCA/SHANK3/SLC1A7/TRPC1 |

## Table S5 Up-regulated GSEA pathways

| NAME | Size | ES | NES | NOM p-value | FDR q-value |
|---|---|---|---|---|---|
| KEGG_ DNA replication | 36 | 0.8605 | 3.1050 | 0.0000 | 0.0000 |
| KEGG_ Cell cycle | 124 | 0.6606 | 3.0257 | 0.0000 | 0.0000 |
| KEGG_ Base excision repair | 35 | 0.7141 | 2.5420 | 0.0000 | 0.0000 |
| KEGG_ Mismatch repair | 23 | 0.7528 | 2.3964 | 0.0000 | 0.0000 |
| KEGG_ Systemic lupus erythematosus | 109 | 0.5416 | 2.3960 | 0.0000 | 0.0000 |
| KEGG_ Homologous recombination | 27 | 0.7291 | 2.3908 | 0.0000 | 0.0000 |
| KEGG_ Nucleotide excision repair | 44 | 0.6368 | 2.3785 | 0.0000 | 0.0000 |
| KEGG_ P53 signalling pathway | 66 | 0.5705 | 2.2898 | 0.0000 | 0.0000 |
| KEGG_ Proteasome | 43 | 0.6214 | 2.2817 | 0.0000 | 0.0000 |
| KEGG_ Spliceosome | 123 | 0.4627 | 2.0906 | 0.0000 | 0.0004 |
| KEGG_ Pyrimidine metabolism | 93 | 0.4729 | 2.0471 | 0.0000 | 0.0006 |
| KEGG_ Aminoacyl TRNA biosynthesis | 41 | 0.5508 | 2.0251 | 0.0000 | 0.0006 |
| KEGG_ Steroid biosynthesis | 16 | 0.6876 | 1.9574 | 0.0000 | 0.0017 |
| KEGG_ One carbon pool by folate | 17 | 0.6671 | 1.9326 | 0.0000 | 0.0025 |
| KEGG_ Oocyte meiosis | 107 | 0.4266 | 1.8932 | 0.0000 | 0.0041 |
| KEGG_ Progesterone mediated oocyte maturation | 83 | 0.4359 | 1.8765 | 0.0000 | 0.0045 |
| KEGG_ Antigen processing and presentation | 50 | 0.4820 | 1.8220 | 0.0024 | 0.0073 |
| KEGG_ Glycolysis gluconeogenesis | 57 | 0.4505 | 1.7825 | 0.0000 | 0.0112 |
| KEGG_ Primary immunodeficiency | 35 | 0.5102 | 1.7760 | 0.0044 | 0.0115 |
| KEGG_ Non-homologous end joining | 12 | 0.6760 | 1.7697 | 0.0084 | 0.0118 |
| KEGG_ RNA degradation | 55 | 0.4491 | 1.7403 | 0.0000 | 0.0154 |
| KEGG_ Cytosolic DNA sensing pathway | 42 | 0.4678 | 1.7170 | 0.0047 | 0.0185 |
| KEGG_ Bladder cancer | 40 | 0.4490 | 1.6409 | 0.0046 | 0.0357 |
| KEGG_ Folate biosythesis | 11 | 0.6127 | 1.5703 | 0.0314 | 0.0631 |

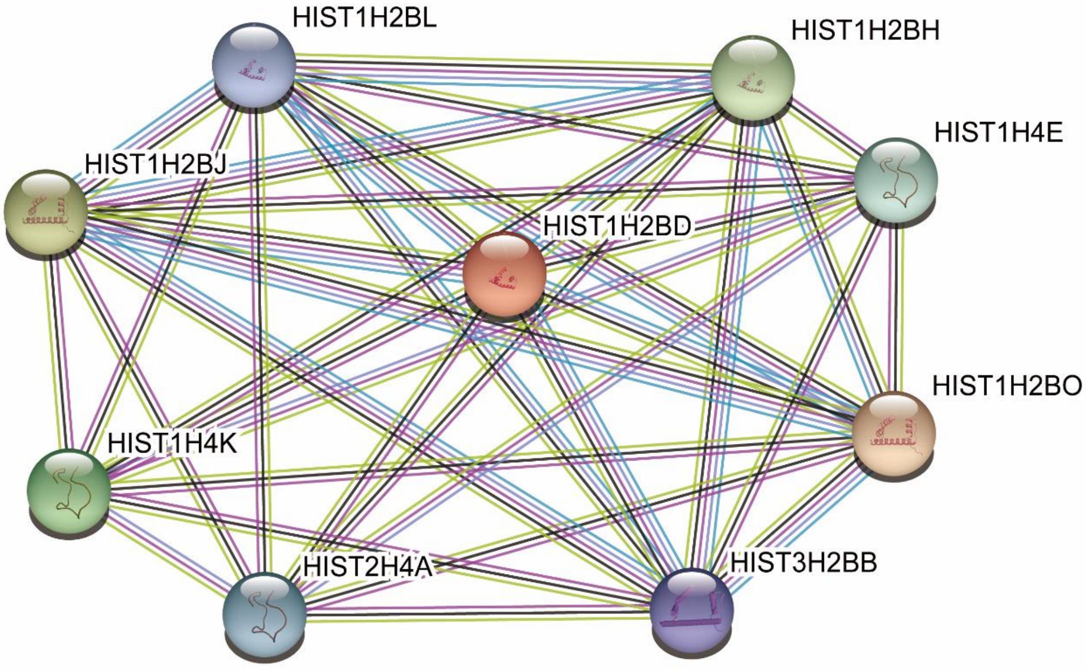
## Table S6 Down-regulated GSEA pathways

| NAME | Size | ES | NES | NOM p-value | FDR q-value |
|---|---|---|---|---|---|
| KEGG_ Ribosome | 87 | -0.6146 | -2.4324 | 0.0000 | 0.0000 |
| KEGG_ Vascular smooth muscle contraction | 112 | -0.5767 | -2.4139 | 0.0000 | 0.0000 |
| KEGG_ Focal adhesion | 196 | -0.4470 | -2.0197 | 0.0000 | 0.0038 |
| KEGG_ Neuroactive ligand-receptor interaction | 240 | -0.4275 | -1.9753 | 0.0000 | 0.0054 |
| KEGG_ Calcium signalling pathway | 169 | -0.4386 | -1.9248 | 0.0000 | 0.0070 |
| KEGG_ Cell adhesion molecules (CAMs) | 109 | -0.4646 | -1.9331 | 0.0000 | 0.0074 |
| KEGG_TGF-β signalling pathway | 85 | -0.4575 | -1.8121 | 0.0000 | 0.0193 |
| KEGG_ Dilated cardiomyopathy | 87 | -0.4580 | -1.8185 | 0.0000 | 0.0203 |
| KEGG_ Hypertrophic cardiomyopathy (HCM) | 81 | -0.4433 | -1.7179 | 0.0017 | 0.0451 |
| KEGG_ MAPK signalling pathway | 256 | -0.3608 | -1.6794 | 0.0000 | 0.0581 |
| KEGG_ ECM-receptor interaction | 83 | -0.4174 | -1.6421 | 0.0000 | 0.0726 |
| KEGG_ Gap junction | 89 | -0.4106 | -1.6290 | 0.0032 | 0.0764 |
| KEGG_ Complement and coagulation cascades | 67 | -0.4223 | -1.5935 | 0.0085 | 0.0874 |
| KEGG_ Glycophingolipid biosynthesis ganglio series | 15 | -0.5868 | -1.6005 | 0.0251 | 0.0887 |
| KEGG_ ABC transporters | 43 | -0.4525 | -1.5815 | 0.0139 | 0.0899 |
| KEGG_ Arrhythmogenic right ventricular cardiomyopathy (ARVC) | 72 | -0.4034 | -1.5508 | 0.0081 | 0.1067 |

## Table S7 KEGG pathway analysis of PPI modules

| Term | Count | P-value | Genes |
|---|---|---|---|
| hsa04080: Neuroactive ligand-receptor interaction | 17 | 0.0000 | MCHR1, PTGER3, NPBWR1, LPAR3, NPY1R, NPY5R, S1PR2, S1PR3, S1PR1, SSTR3, CHRM2, SSTR1, CNR1, GRM7, GALR2, S1PR5, ADRA2C |
| hsa05322: Systemic lupus erythematosus | 11 | 0.0000 | HIST1H3J, HIST1H4L, HIST1H2BD, HIST1H2AG, HIST1H2AD, HIST1H2BH, HIST2H4A, HIST1H2BO, HIST1H2BM, HIST1H4B, HIST1H2BL, HIST1H2BJ, HIST1H2AI, HIST1H3C, HIST1H2AJ, HIST3H2BB, HIST1H3F, HIST1H2AL |
| hsa04512: ECM-receptor interaction | 10 | 0.0000 | LAMA2, LAMB3, LAMB2, LAMC3, COL6A3, ITGB6, COL6A2, COL6A1, LAMC2, CHAD |
| hsa04510: Focal adhesion | 10 | 0.0000 | LAMA2, LAMB3, LAMB2, LAMC3, COL6A3, ITGB6, COL6A2, COL6A1, LAMC2, CHAD |
| hsa04110: Cell cycle | 9 | 0.0000 | CCNE2, CDC6, CDC45, MCM7, TP53, PKMYT1, TTK, CDK6, MCM5 |
| hsa04062: Chemokine signaling pathway | 8 | 0.0000 | ADCY4, ADCY7, CXCL5, CCR1, ADCY5, CXCR3, CCL16, CXCL10 |
| hsa04114: Oocyte meiosis | 6 | 0.0002 | ADCY4, ADCY7, ADCY5, SGOL1, CDC20, ESPL1 |
| hsa05200: Pathways in cancer | 6 | 0.0139 | LAMA2, E2F2, LAMB3, LAMB2, LAMC3, LAMC2 |
| hsa04060: Cytokine-cytokine receptor interaction | 5 | 0.0475 | CXCL5, CCR1, CXCR3, CCL16, CXCL10 |
| hsa04020: Calcium signaling pathway | 4 | 0.0349 | ADCY4, PTGER3, ADCY7, CHRM2 |
| hsa04270: Vascular smooth muscle contraction | 4 | 0.0056 | EDNRA, AVPR1A, ADRA1B, ADRA1D |
| hsa04115: p53 signaling pathway | 4 | 0.0079 | CCNE2, RRM2, TP53, CDK6 |
| hsa00230: Purine metabolism | 4 | 0.0350 | PDE7B, PDE2A, RRM2, PDE11A |
| hsa04914: Progesterone-mediated oocyte maturation | 3 | 0.0356 | ADCY4, ADCY7, ADCY5 |
| hsa04540: Gap junction | 3 | 0.0402 | ADCY4, ADCY7, ADCY5 |
| hsa05414: Dilated cardiomyopathy | 3 | 0.0449 | ADCY4, ADCY7, ADCY5 |

## Supplementry Figure S1：



Supplementary Figure 1

Protein-PPI network analysis of histone genes enriched in the SLE pathway. Each circle represents a node and each line represents an edge. The different color of the lines represents different types of interactions: light blue: curated databases; pink: experimentally determined; green: gene neighborhood; red: gene fusions; blue: gene co-occurrence; yellow: textmining; dark: co-expression; grey: protein homology.