**Gene Expression and Regulatory Webwork of POLR2K in Bladder Carcinogenesis by Integrated Bioinformatics Approaches**

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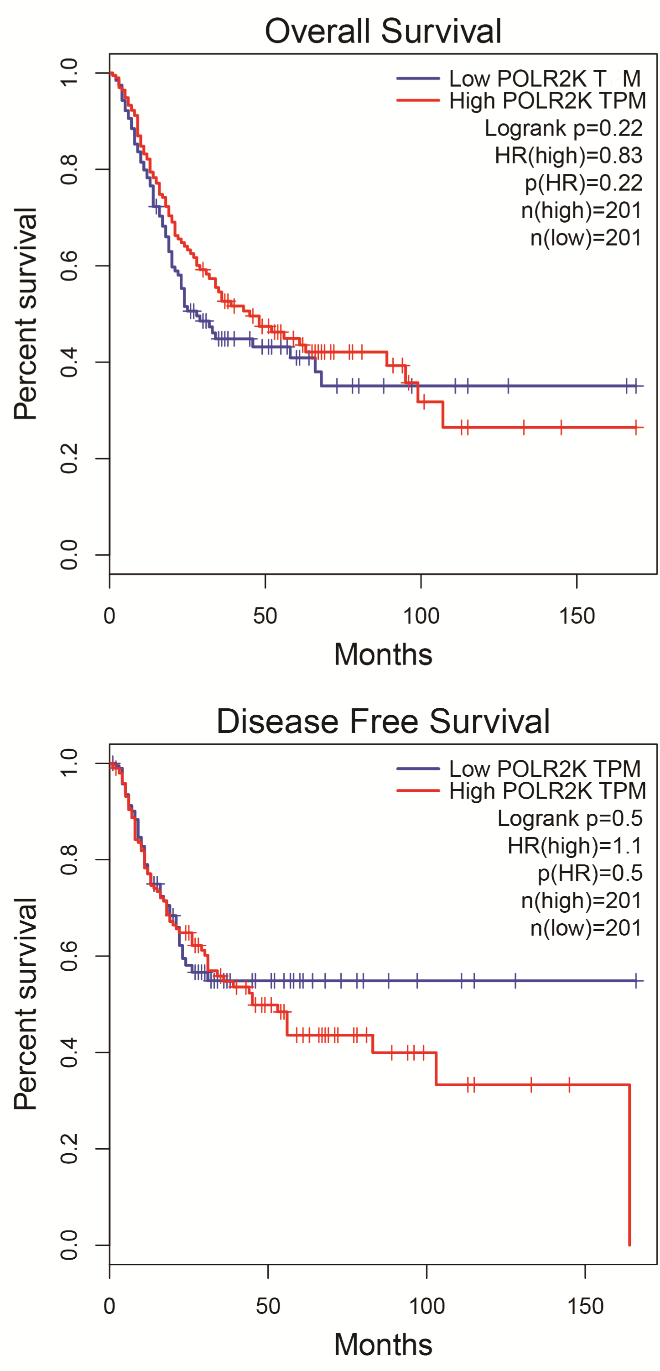
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**Supplementary Figure**

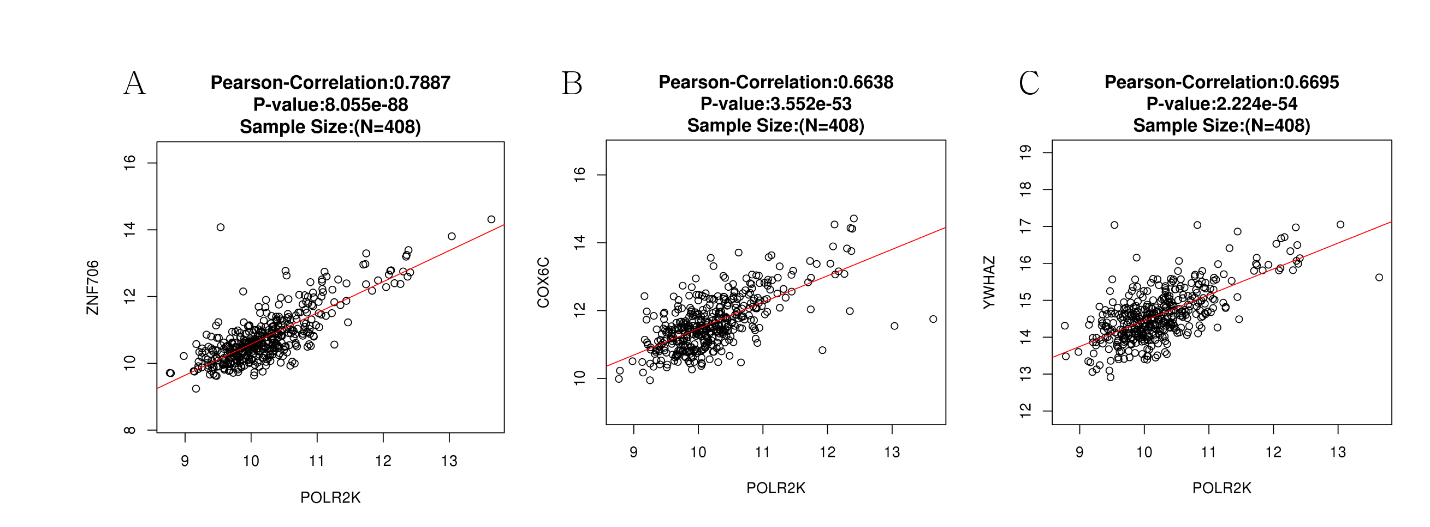
Supplementary Figure 1. Overall survival and Disease Free Survival (RFS) of POLR2K in the TCGA.



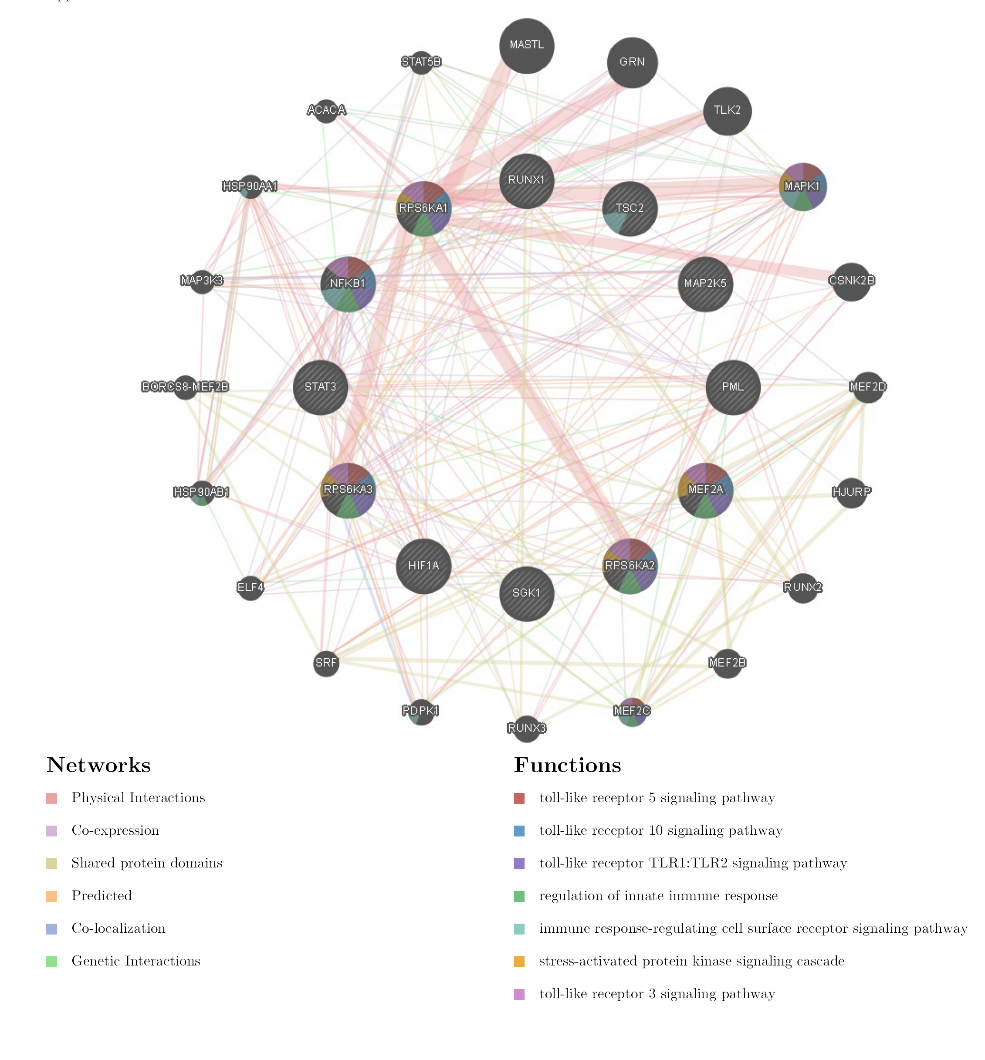
Supplementary Fig 2. The type and frequency of POLR2K neighbor gene alterations in bladder urothelial carcinoma (cBioportal). We used POLR2K as seed gene to get the neighboring genes and then applied to cBioportal to get the alteration frequencies of these neighborhood genes. Below shown is the top 15 of them.

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Supplementary Figure 3. Gene expression correlation analysis for POLR2K, ZNF706, COX6C, and YWHAZ (LinkedOmics). The scatter plot shows Pearson correlation of POLR2Kexpression with expression of ZNF706 (A), COX6C (B), and YWHZA (C).



Supplementary Figure 4. Protein-protein interaction network of MAPK7-target networks (GeneMANIA).Protein-protein interaction (PPI) network and functional analysis indicating the gene set that was enriched in the target networks of kinase MAPK7. Different colors of the network edge indicate the bioinformatics methods applied: co-expression, physical interaction, co-localization, website prediction, pathway and shared protein domains. The different colors for the network nodes indicate the biological functions of the set of enrichment genes.

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Supplementary Figure 5. Protein-protein interaction network of miRNA 374-target networks (GeneMANIA). Protein-protein interaction (PPI) network and functional analysis indicating the gene set that was enriched in the target networks of miRNA 374. Different colors of the network edge indicate the bioinformatics methods applied: co-expression, website prediction, co-localization, shared protein domains, physical interaction, pathway and genetic interactions. The different colors for the network nodes indicate the biological functions of the set of enrichment genes.

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**Supplementary Table**

Supplementary Table 1. Significantly enriched GO annotations (cellular components) of POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |  |  |
| --- | --- | --- | --- |
| Description | LeadingEdgeNum | FDR | LeadingEdgeGene |
|  |  |  |  |
| mitochondrial protein complex | 140 | 0 | APOO,BAX,BCKDHA,BCKDHB,BCS1L,C12orf65,C15orf48,CHCHD1,CHCHD6,COX5A,COX5B,COX6A1,COX6A2,COX7A2,COX7A2L,COX7C,CYC1,DAP3,DNA2,DNAJC11,DNAJC19,FOXRED1,GRPEL1,HSD17B10,IMMP1L,IMMT,MCCC2,MPV17L2,MRPL10,MRPL11,MRPL12,MRPL13,MRPL14,MRPL15,MRPL16,MRPL18,MRPL19,MRPL2,MRPL20,MRPL21,MRPL22,MRPL27,MRPL3,MRPL30,MRPL32,MRPL33,MRPL34,MRPL35,MRPL36,MRPL37,MRPL38,MRPL39,MRPL4,MRPL40,MRPL41,MRPL42,MRPL47,MRPL48,MRPL49,MRPL50,MRPL51,MRPL52,MRPL53,MRPL55,MRPL9,MRPS11,MRPS12,MRPS14,MRPS15,MRPS16,MRPS17,MRPS18A,MRPS18B,MRPS2,MRPS21,MRPS22,MRPS24,MRPS26,MRPS28,MRPS30,MRPS33,MRPS34,MRPS35,MRPS36,MRPS5,MRPS6,MRPS7,MRPS9,MTG1,MTX1,NDUFA11,NDUFA2,NDUFA3,NDUFA4,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB2,NDUFB3,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB9,NDUFC2,NDUFS2,NDUFS5,NDUFS6,NDUFV2,NDUFV3,PARK7,PNPT1,POLRMT,PPIF,ROMO1,SDHB,SDHC,SUCLG1,SUPV3L1,TIMM10,TIMM13,TIMM17A,TIMM17B,TIMM50,TIMM8B,TOMM20L,TOMM22,TOMM40,TOMM5,TOMM6,UQCR10,UQCRB,UQCRFS1,UQCRH,UQCRHL,UQCRQ,VDAC1,WDR93 |
| condensed chromosome | 82 | 0 | AURKA,AURKB,BANF1,BIRC5,BLM,BOD1,BRCA1,BUB1,BUB1B,BUB3,CBX3,CCDC155,CCNB1,CCNB1IP1,CDCA5,CDK2,CDT1,CDX2,CENPA,CENPF,CENPH,CENPK,CENPM,CENPN,CENPO,CENPV,CENPW,CHEK1,DSN1,DYNC1I1,DYNC1LI1,DYNLT3,ERCC6L,FANCD2,H2AFX,H2AFY,HJURP,HMGB1,HMGB2,HSF1,ITGB3BP,KIF2C,LRPPRC,LRWD1,MAD2L1,MEAF6,NCAPG,NCAPH,NDC80,NEK2,NSMCE2,NUDCD2,NUF2,NUP107,NUP85,PES1,PLK1,RAD1,RAD21,RAD51,RCC1,RPA2,RRS1,SEH1L,SETMAR,SKA1,SKA3,SMC1B,SPAG5,SPC24,SPC25,SS18L1,STAG3,SYCE2,SYCP2,TEX12,TEX14,TOP2A,TOP3B,TUBG1,ZWILCH,ZWINT |
| replication fork | 26 | 0.0061 | BCAS2,BLM,CDC45,GINS2,GINS4,H2AFX,MCM10,MCM3,NBN,PCNA,PIF1,PRIM1,PRIM2,PRPF19,RAD18,RAD51C,RFC2,RFC3,RFC4,RFC5,RPA2,RPA3,TIMELESS,TIPIN,UHRF1,XRCC2 |
| spliceosomal complex  MHC protein complex  extracellular matrix  cell leading edge  secretory granule membrane | 62  15  217    137  119 | 0  0.0035  0.0148  0.003  0.0031 | BCAS2,BUD13,BUD31,C9orf78,CRNKL1,CTNNBL1,GPATCH1,HNRNPA2B1,HNRNPC,HNRNPF,HNRNPK,HNRNPM,HNRNPR,HTATSF1,LSM2,LSM3,LSM4,LSM5,LSM6,LSM7,MAGOH,MAGOHB,PABPC1,PHF5A,PPIE,PPIH,PPIL1,PPP1R8,PRPF18,PRPF19,PRPF3,PRPF31,PRPF38A,PRPF4,RALY,RBM17,RBM28,RBM8A,RHEB,SF3B4,SF3B5,SNRNP25,SNRPA,SNRPA1,SNRPB,SNRPB2,SNRPC,SNRPD1,SNRPD2,SNRPD3,SNRPE,SNRPF,SNRPG,SYF2,TTF2,U2AF2,USP39,WAC,WDR83,YBX1,ZMAT5,ZNF830  B2M,CD74,HFE,HLA-DMB,HLA-DOA,HLA-DOB,HLA-DPA1,HLA-DQB2,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,HLA-F,HLA-G,MR1  A2M,ABI3BP,ADAMTS1,ADAMTS10,ADAMTS12,ADAMTS15,ADAMTS2,ADAMTS5,ADAMTS8,ADAMTS9,ADAMTSL4,ADAMTSL5,ADIPOQ,AGRN,AMTN,ANG,ANGPTL2,ANXA1,ANXA11,ANXA2,ANXA5,ANXA6,ANXA8,ASPN,BCAN,BGN,C1QA,C1QB,C1QC,CCDC80,CD151,CD180,CDH13,CDON,CILP,CLEC14A,CLU,CMA1,COL11A1,COL16A1,COL17A1,COL18A1,COL1A2,COL22A1,COL27A1,COL3A1,COL4A2,COL4A4,COL4A5,COL4A6,COL5A1,COL5A2,COL5A3,COL6A1,COL6A2,COL6A3,COL7A1,COL8A1,COL8A2,COLEC12,COMP,CPA3,CRISPLD2,CSPG4,CTSB,CTSC,CTSD,CTSG,CTSS,DCN,DMBT1,DPT,DST,ECM1,ECM2,EDIL3,EFEMP2,ELN,EMILIN1,F13A1,F3,FBLN5,FBN1,FCN1,FGF1,FGF10,FGF9,FGL2,FLG,FLRT2,FMOD,FN1,GDF10,GLG1,GPC1,GPC6,HAPLN3,HMCN1,HPSE,HPSE2,HRNR,HSD17B12,HSP90B1,HSPG2,HTRA1,ICAM1,IGFBP7,IL7,IMPG2,ITGA6,ITIH5,KERA,KRT1,L1CAM,LAD1,LAMA1,LAMA2,LAMA3,LAMA4,LAMA5,LAMB1,LAMB2,LAMB3,LAMC1,LAMC2,LEFTY2,LGALS3BP,LINGO4,LMAN1,LOX,LOXL1,LOXL2,LRIG1,LRIG2,LRIG3,LRRC17,LRRC32,LRRN2,LTBP2,LTBP3,LTBP4,MFAP1,MFAP5,MMP13,MMP14,MMP2,MMP21,MMP25,MMP28,MMP7,MMRN1,MUC4,MXRA5,MXRA7,NCAM1,NTN1,OGN,OMD,PF4,PHOSPHO1,PI3,PODNL1,PRELP,PRG4,PSAP,PTPRZ1,PXDN,RELN,S100A10,S100A8,S100A9,SCARA3,SDC3,SERPINA1,SERPINA3,SERPINA5,SERPINB1,SERPINB8,SERPINE1,SERPINE2,SERPINF1,SERPING1,SLPI,SMOC2,SOST,SPARC,SPARCL1,SPOCK2,SPON1,SSC5D,TECTA,TFPI2,TGFB1,TGFB1I1,TGFB2,TGFB3,TGFBI,TGM2,THBS1,THBS3,THBS4,THSD4,TIMP1,TIMP2,TIMP3,TLR3,TNC,TNR,TPSAB1,TPSB2,USH2A,VCAN,VIT,VWF,WNT5A,WNT5B,WNT7A  ABCA7,ABI2,ABI3,ABLIM1,ABLIM3,ACTN1,AMOTL1,ANXA2,APBB2,APP,ARAP3,ARHGAP31,ARHGEF2,ARHGEF4,ARPC2,ATP6V1B2,BAIAP2,BCAR1,BMX,CCDC88A,CD44,CDC42BPA,CDC42BPB,CDK6,CLIP1,CORO1A,CORO1C,CTNNA1,CTNND1,CTTN,CUBN,CXCR4,CYFIP1,DBNL,DDX58,DIAPH1,DPYSL3,DST,DUOX1,DUOX2,DUOXA2,DUSP22,DYSF,EEF1A1,EPHA2,EXOC8,EZR,FAT1,FER,FGD2,FGD5,FGD6,FGR,FRMD4B,FSCN1,GABRE,GBF1,IFIT5,ILK,IQGAP1,IQGAP2,ITGA5,ITGAV,ITGB3,ITGB4,KCNC4,KITLG,KLHL2,LAYN,LCP1,LDB1,LDB2,LIMA1,MACF1,MCC,MEFV,MKLN1,MTM1,MYO10,MYO1C,MYO1D,MYO1G,MYO5A,NCKAP1,NDEL1,PAFAH1B1,PAK1,PALLD,PDE4A,PDLIM7,PHLDB2,PIK3CA,PIP5K1C,PKD2,PLEK,PLEK2,PLEKHG5,PLEKHH2,PPP1R9B,PSD4,PSTPIP1,PTK2B,PTPRJ,PTPRK,PTPRO,PXN,RAB34,RAC1,RAC2,RAPGEF3,RAPH1,RHOA,ROCK1,S100B,SAMSN1,SHISA6,SLC1A2,SLC39A14,SLK,SNX1,SNX9,SORBS2,SPATA13,SPRY2,SPTBN1,SSH1,STX2,SWAP70,TIAM2,TIRAP,TLN1,TRPM7,USH2A,VIM,WASF2,WIPF1,WLS  ALDH3B1,AP1M1,AP2A2,ATP11A,ATP8A1,ATP8B3,ATP8B4,BST2,C3AR1,CAV1,CAV2,CD109,CD14,CD300A,CD33,CD36,CD38,CD44,CD46,CD47,CD53,CD58,CD59,CD68,CD93,CEACAM3,CHRNB4,CKAP4,CLEC4D,CLEC5A,COPB1,CXCR1,CXCR2,CYB5R1,CYBA,CYBB,DBH,DIAPH1,DNAJC13,EXOC3,FCAR,FCGR2A,FCGR3B,FPR1,FPR2,GAA,GLIPR1,GPR84,HVCN1,IGF2R,IQGAP1,IQGAP2,ITGAL,ITGAM,ITGAV,ITGB2,ITGB3,ITPR2,ITPR3,KCNAB2,LAIR1,LAMP1,LAMP2,LAMP3,LHFPL2,MGAM,MLEC,MMP25,MOSPD2,NCKAP1L,NFAM1,NFASC,P2RX1,PAM,PCDH7,PECAM1,PKP1,PLAU,PLAUR,PLD1,PRCP,PSAP,PSEN1,PTAFR,PTPRB,PTPRC,PTPRJ,PTPRN2,RAB27A,RAB31,RAB37,RAC1,RAP2B,RHOA,RHOF,RHOG,SERPINA5,SERPINB12,SIGLEC9,SIRPA,SIRPB1,SLC15A4,SLC2A3,SLC30A5,SNAP23,STK10,STOM,TBC1D10C,TCIRG1,TLR2,TMBIM1,TMED7-TICAM2,TMEM173,TMX3,TRIP11,TSPAN14,UBR4,VAMP2,VNN1 |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg fromgene set enrichment analysis (GSEA).

Supplementary Table 2. Significantly enriched GO annotations (biological processes) of POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Description | LeadingEdgeNum | FDR | LeadingEdgeGene | |
|  |  |  | |  | |
| mitochondrial gene expression | 89 | 0 | | AURKAIP1,C1QBP,CDK5RAP1,CHCHD1,DAP3,ERAL1,FASTKD5,GADD45GIP1,GARS,HSD17B10,LRPPRC,MPV17L2,MRPL1,MRPL10,MRPL11,MRPL12,MRPL13,MRPL14,MRPL15,MRPL16,MRPL18,MRPL19,MRPL2,MRPL20,MRPL21,MRPL22,MRPL27,MRPL3,MRPL30,MRPL32,MRPL33,MRPL34,MRPL35,MRPL36,MRPL37,MRPL38,MRPL39,MRPL4,MRPL40,MRPL41,MRPL42,MRPL47,MRPL48,MRPL49,MRPL50,MRPL51,MRPL52,MRPL55,MRPL9,MRPS12,MRPS14,MRPS16,MRPS17,MRPS18A,MRPS18B,MRPS2,MRPS21,MRPS22,MRPS23,MRPS24,MRPS25,MRPS26,MRPS28,MRPS30,MRPS33,MRPS35,MRPS36,MRPS5,MRPS6,MRPS7,MRPS9,MTIF2,NDUFA7,PNPT1,POLRMT,PTCD3,PUS1,RPUSD3,SHMT2,SLC25A33,TARS2,TBRG4,TRIT1,TRMT61B,TRNT1,TRUB2,TSFM,TUFM,YARS2 | |
| ncRNA processing | 125 | 0 | | METTL6,MOCS3,MPHOSPH10,MRM1,MRPL1,MRPS9,MRTO4,NGDN,NHP2,NOL10,NOL11,NOP14,NOP2,NOP56,NOP58,NSUN6,OSGEPL1,PA2G4,PELP1,PES1,POLR3K,POP1,POP4,POP5,POP7,PUS1,PUS7,PUSL1,QTRT1,RCL1,REXO4,RPF1,RPL7,RPP21,RPP38,RPS16,RPS21,RPUSD2,RRP1,RRP1B,RRP7A,RRP9,RRS1,RSL1D1,SEPHS1,SEPHS2,SSB,TEX10,THUMPD3,TP53RK,TPRKB,TRIT1,TRMT112,TRMT12,TRMT6,TRMT61A,TRMT61B,TRMU,TRNT1,TSEN2,TSEN34,TSEN54,TSR2,URM1,UTP18,UTP23,UTP3,UTP6,WBP11,WDR12,WDR18,WDR43,WDR74,ZBTB8OS,ZNHIT3,ZNHIT6 | |
| mRNA processing | 142 | 0 | | AKAP8L,AURKAIP1,BCAS2,BRDT,BUD13,BUD31,C1QBP,C9orf78,CCNB1,CCNH,CELF5,CHERP,CPSF1,CPSF3,CPSF4,CPSF6,CRNKL1,CSTF1,CSTF2,CTNNBL1,DAZAP1,DBR1,DDX1,DDX47,DHX40,ELAVL1,ESRP1,FASTKD5,FIP1L1,GEMIN6,GEMIN7,GPATCH1,GRSF1,GTF2F2,GTF2H5,HMX2,HNRNPA2B1,HNRNPC,HNRNPF,HNRNPK,HNRNPL,HNRNPM,HNRNPR,HSF1,HTATSF1,KDM1A,KHDRBS1,KIN,LSM1,LSM10,LSM2,LSM3,LSM4,LSM5,LSM6,LSM7,MAGOH,MAGOHB,MTPAP,NCBP2,NONO,PABPC1,PABPC1L,PAF1,PAN2,PCBP1,PHF5A,PNPT1,POLR2C,POLR2D,POLR2F,POLR2G,POLR2H,POLR2I,POLR2J,POLR2K,PPIE,PPIH,PPIL1,PPP1R8,PRCC,PRPF18,PRPF19,PRPF3,PRPF31,PRPF38A,PRPF4,PTBP1,PUF60,RALY,RBM17,RBM28,RBM42,RBM8A,RNPS1,RPUSD3,RRP1B,RSRC1,SAFB,SAP18,SARNP,SF3B4,SF3B5,SFPQ,SLBP,SNRNP25,SNRNP27,SNRPA,SNRPA1,SNRPB,SNRPB2,SNRPC,SNRPD1,SNRPD2,SNRPD3,SNRPE,SNRPF,SNRPG,SSU72,STH,SYF2,TARDBP,TBRG4,TGS1,THOC1,THOC3,THOC5,TRUB2,TSEN2,TSEN34,TSEN54,TTF2,U2AF2,UBL5,USP39,WBP11,WDR83,YBX1,ZC3H3,ZMAT5,ZNF473,ZNF830 | |
| positive regulation of cell adhesion | 183 | 0.0004 | | ABI3BP,ADAM9,AIF1,AKT1,ANK3,AP3B1,AP3D1,ARPC2,ATM,BAG4,BCL10,BCL6,BTLA,CASS4,CAV1,CCDC80,CCDC88B,CCR2,CD1D,CD209,CD274,CD28,CD36,CD3E,CD4,CD40LG,CD44,CD46,CD47,CD5,CD6,CD74,CD86,CDK6,CEACAM6,CHRD,CIB1,CLECL1,COL16A1,COL8A1,CORO1A,CRK,CSF1,CX3CL1,CYLD,CYTH3,DOCK1,DOCK5,DUSP10,DYSF,EBI3,ECM2,EDIL3,EFNB1,ETS1,FLCN,FLNA,FMN1,FN1,FOXC2,FOXP3,FYN,GCNT2,GLI2,GLI3,GRAP2,HAS2,HLA-DMB,HLA-DPA1,HLA-DPB1,HLA-E,HLA-G,HLX,HSD17B12,HYAL1,ICAM1,IFNG,IGF1,IL12B,IL12RB1,IL15,IL18,IL1RL2,IL2,IL4R,IL6R,IL6ST,IL7,IL7R,ILK,IQGAP1,ITGA2,ITGA3,ITGA4,ITGA5,ITGA6,ITGAV,ITPKB,JAK2,JAK3,KIFAP3,LDB1,LGALS9,LILRB1,LIMS1,LYN,MALT1,MIP,MMRN1,MYO10,NCK1,NCKAP1L,NINJ1,NLRP3,NOD2,NODAL,NRP1,P2RY12,PAK1,PDCD1,PDCD1LG2,PDPK1,PIK3CA,PIK3R1,PIK3R6,PLEKHA2,PRKCA,PRKCQ,PRKD2,PTAFR,PTK2B,PTPN23,PTPRC,PTPRJ,PTPRU,PYCARD,RAC1,RARA,RASAL3,RASGRP1,RET,RHOA,RHOD,ROCK1,RREB1,RUNX1,RUNX3,S100A10,SAA1,SASH3,SIRPA,SIRPB1,SIRPG,SMAD3,SMAD7,SMOC2,SPOCK2,SPTA1,STAT5B,SYK,TEK,TFE3,TGFB1,TGFB2,TGFBR2,TGM2,TNFRSF14,TNFSF11,TNFSF13B,TNFSF14,TNFSF18,TNFSF4,TRAF6,TRIOBP,UTRN,VAV1,VNN1,WNT5A,ZAP70,ZBTB1,ZBTB16,ZBTB7B,ZMIZ1 | |
| NIK/NF-kappaB signaling | 51 | 0.0006 | | ADIPOR1,AKT1,APP,BIRC3,BTRC,CARD10,CD14,CYLD,EDA,EGFR,EZR,FBXW11,HDAC7,IKBKE,IL18,IL18R1,ILK,LGALS9,LIMS1,LITAF,MALT1,MAP3K7,NFKB2,NLRC3,NLRP12,NLRP3,NOD1,NOD2,NOL3,PPM1A,PTPN22,RC3H2,RHOA,RIPK3,SAMD5,TIRAP,TLR2,TLR3,TLR4,TLR6,TLR9,TNFRSF10A,TNFRSF10B,TNFSF14,TRADD,TRAF6,TRIM40,TRIM44,TRIP6,UACA,ZFP91 | |
|  |  |  | |  | |
| rRNA metabolic process | 85 | 0.0002 | | ABT1,BOP1,BYSL,C1D,CHD7,DCAF13,DDX27,DDX47,DDX49,DDX51,DDX52,DKC1,EBNA1BP2,EMG1,ERI3,ESF1,EXOSC2,EXOSC3,EXOSC4,EXOSC5,EXOSC7,EXOSC9,FBL,FTSJ3,GAR1,GTF2H5,GTF3A,GTF3C2,GTF3C5,GTPBP4,H2AFY,LAS1L,LSM6,LYAR,MAPT,MARS,MPHOSPH10,MRM1,MRPL1,MRPS9,MRTO4,NGDN,NHP2,NOL10,NOL11,NOL12,NOP14,NOP2,NOP56,NOP58,PA2G4,PELP1,PES1,POP4,POP5,RCL1,REXO4,RPF1,RPL7,RPS16,RPS21,RPUSD2,RRP1,RRP1B,RRP7A,RRP9,RRS1,RSL1D1,SMARCA4,SMARCB1,TEX10,TRMT112,TRMT61B,TSR2,UTP18,UTP23,UTP3,UTP6,WBP11,WDR12,WDR18,WDR43,WDR74,ZNHIT3,ZNHIT6 | |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochbergfrom gene set enrichment analysis (GSEA).

Supplementary Table 3. Significantly enriched GO annotations (molecular functions) of POLR2K in bladder urothelial carcinoma (LinkedOmics)

|  |  |  |  |
| --- | --- | --- | --- |
| Description | LeadingEdgeNum | FDR | LeadingEdgeGene |
|  |  |  |  |
| structural constituent of ribosome | 70 | 0 | DAP3,MRPL1,MRPL10,MRPL11,MRPL12,MRPL13,MRPL14,MRPL15,MRPL16,MRPL18,MRPL19,MRPL2,MRPL20,MRPL21,MRPL22,MRPL27,MRPL3,MRPL30,MRPL32,MRPL33,MRPL34,MRPL35,MRPL36,MRPL37,MRPL4,MRPL41,MRPL42,MRPL47,MRPL49,MRPL51,MRPL52,MRPL55,MRPL9,MRPS12,MRPS14,MRPS16,MRPS17,MRPS18A,MRPS18B,MRPS2,MRPS21,MRPS22,MRPS23,MRPS24,MRPS25,MRPS30,MRPS33,MRPS35,MRPS36,MRPS5,MRPS6,MRPS7,MRPS9,NDUFA7,RPL22,RPL23,RPL23A,RPL26L1,RPL27,RPL30,RPL32,RPL36A,RPL38,RPL7,RPL8,RPS16,RPS20,RPS21,RPS26,RSL24D1 |
| antigen binding | 32 | 0 | ABO,CD1A,CD1B,CD1C,CD1D,CD1E,CD209,CD40,CD48,EP400,HFE,HLA-DPA1,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-E,HLA-F,HLA-G,IL7R,ITGA4,KLRC1,KLRC2,KLRD1,LILRA1,LILRA2,SIRPA,SLAMF1,SLC7A8,TAP1,TAPBP,TGFB1 |
| cytokine binding | 68 | 0.0018 | A2M,ACVR1,ACVRL1,BMPR2,CCR1,CCR2,CCR4,CCR5,CCR6,CCRL2,CD109,CD36,CD4,CD74,CHRD,COMP,CRLF2,CSF1R,CSF2RA,CSF3R,CX3CR1,CXCR1,CXCR2,CXCR3,CXCR4,CXCR6,EBI3,ENG,GBP1,GHR,IFNAR1,IFNGR1,IL10RA,IL11RA,IL12RB1,IL13RA1,IL18BP,IL18R1,IL20RB,IL22RA2,IL2RB,IL2RG,IL31RA,IL3RA,IL6R,IL6ST,ITGA4,ITGAV,ITGB3,KIT,KLHL20,LEPR,LIFR,LRRC32,LTBP3,LTBP4,NRP1,NRP2,OSMR,PLP2,PXDN,TGFB3,TGFBR1,TGFBR2,THBS1,TNFRSF1A,TRIM16,ZFP36 |
| guanyl-nucleotide exchange factor activity | 107 | 0.0007 | ABR,AKAP13,ALS2CL,ARHGEF1,ARHGEF10,ARHGEF12,ARHGEF17,ARHGEF2,ARHGEF3,ARHGEF37,ARHGEF4,ARHGEF5,C9orf72,CAMK2A,CAMK2D,CSF2RA,CYTH1,CYTH4,DENND1B,DENND1C,DENND2C,DENND3,DENND4A,DENND5A,DIS3,DLG2,DOCK1,DOCK10,DOCK11,DOCK2,DOCK5,DOCK6,DOCK9,EGF,EGFR,FGD2,FGD5,FGF16,FLCN,FLT3,FLT3LG,FNIP1,GBF1,GFRA1,GFRA2,HBEGF,HERC1,HERC2,HPS1,IL2,IL2RB,IL2RG,IRS1,JAK1,JAK2,JAK3,KITLG,MET,MYCBP2,NCAM1,NEFL,NRG1,NRG2,NRG4,P2RY12,PDGFRA,PLEKHG3,PLEKHG5,PLEKHG7,PREX2,PSD4,RAB3GAP1,RAB3GAP2,RAPGEF2,RAPGEF3,RAPGEF5,RAPGEF6,RASGEF1B,RASGRF2,RASGRP3,RASGRP4,RCBTB2,RGL1,RGL4,RIC8A,RIC8B,RIN1,RIN2,RIN3,SBF1,SBF2,SERGEF,SHC1,SHC2,SMCR8,SOS2,SPATA13,SPTA1,SPTAN1,SPTB,ST5,TAGAP,TIAM2,TRAPPC6B,TRIO,VAV1,WDR41 |
|  |  |  |  |
| electron transfer activity | 35 | 0.0170 | AKR1A1,AOC2,CIAPIN1,COX11,COX5B,COX6A1,COX6A2,COX6B1,COX6C,COX7A2,COX7A2L,COX7B,COX7B2,CYB5A,CYC1,CYCS,CYP1A2,DHDH,FDX1,GLRX5,IDH3B,NDUFA4,NDUFS2,NDUFV2,PHGDH,PTGES2,SDHB,SDHC,SURF1,UQCR10,UQCRB,UQCRFS1,UQCRH,UQCRHL,UQCRQ |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

Supplementary Table 4. Significantly enriched KEGG pathway annotations of POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Description | LeadingEdgeNum | FDR | LeadingEdgeGene | |
|  |  |  | |  |
| JAK-STAT signaling pathway | 53 | 0 | | AKT1,AOX1,BCL2,CCND2,CDKN1A,CREBBP,CRLF2,CSF2RA,CSF3R,EGF,EGFR,GHR,IFNA1,IFNA13,IFNAR1,IFNE,IFNGR1,IL10RA,IL10RB,IL11RA,IL12RB1,IL13RA1,IL15,IL15RA,IL2,IL2RB,IL2RG,IL4R,IL6R,IL6ST,IL7,IL7R,IRF9,JAK1,JAK2,JAK3,LEPR,MCL1,OSM,OSMR,PDGFRA,PIAS1,PIK3CA,PIK3CD,PIK3R1,PIK3R2,SOS2,STAM2,STAT1,STAT2,STAT3,STAT4,STAT6 |
| Toll-like receptor signaling pathway | 51 | 0 | | AKT1,AKT3,CASP8,CCL3L1,CCL4,CCL4L2,CD14,CD40,CD86,CHUK,CXCL9,IFNA1,IFNA13,IFNAR1,IFNAR2,IKBKB,IKBKE,IKBKG,IL12B,IRAK4,IRF7,JUN,LBP,MAP2K3,MAP3K7,MAPK1,MAPK11,MAPK14,NFKB1,PIK3CA,PIK3CD,PIK3R1,PIK3R2,RAC1,RIPK1,SPP1,STAT1,TAB2,TICAM2,TIRAP,TLR1,TLR2,TLR3,TLR4,TLR5,TLR6,TLR8,TLR9,TOLLIP,TRAF3,TRAF6 |
| NOD-like receptor signaling pathway | 70 | 0 | | AKT1,AKT3,CASP8,CCL3L1,CCL4,CCL4L2,CD14,CD40,CD86,CHUK,CXCL9,IFNA1,IFNA13,IFNAR1,IFNAR2,IKBKB,IKBKE,IKBKG,IL12B,IRAK4,IRF7,JUN,LBP,MAP2K3,MAP3K7,MAPK1,MAPK11,MAPK14,NFKB1,PIK3CA,PIK3CD,PIK3R1,PIK3R2,RAC1,RIPK1,SPP1,STAT1,TAB2,TICAM2,TIRAP,TLR1,TLR2,TLR3,TLR4,TLR5,TLR6,TLR8,TLR9,TOLLIP,TRAF3,TRAF6 |
| Spliceosome | 54 | 0 | | BCAS2,BUD31,CHERP,CRNKL1,CTNNBL1,HNRNPC,HNRNPK,HNRNPM,HSPA1B,LSM2,LSM3,LSM4,LSM5,LSM6,LSM7,MAGOH,MAGOHB,NCBP2,PCBP1,PHF5A,PPIE,PPIH,PPIL1,PRPF18,PRPF19,PRPF3,PRPF31,PRPF38A,PRPF4,PUF60,RBM17,RBM8A,RP9,SF3B4,SF3B5,SNRNP27,SNRPA,SNRPA1,SNRPB,SNRPB2,SNRPC,SNRPD1,SNRPD2,SNRPD3,SNRPE,SNRPF,SNRPG,SYF2,THOC1,THOC3,U2AF1,U2AF2,USP39,WBP11 |
| Ribosome | 49 | 0 | | MRPL1,MRPL10,MRPL11,MRPL12,MRPL13,MRPL14,MRPL15,MRPL16,MRPL18,MRPL19,MRPL2,MRPL20,MRPL21,MRPL27,MRPL3,MRPL30,MRPL32,MRPL33,MRPL34,MRPL35,MRPL36,MRPL4,MRPL9,MRPS12,MRPS14,MRPS16,MRPS17,MRPS18A,MRPS2,MRPS21,MRPS5,MRPS6,MRPS7,MRPS9,RPL22,RPL23,RPL23A,RPL26L1,RPL30,RPL32,RPL36A,RPL38,RPL7,RPL8,RPS16,RPS20,RPS21,RPS26,RSL24D1 |
| Cell cycle | 47 | 0.0002 | | ANAPC11,ANAPC7,BUB1,BUB1B,BUB3,CCNA2,CCNB1,CCNB2,CCNE1,CCNE2,CCNH,CDC20,CDC25A,CDC25C,CDC26,CDC45,CDC6,CDK1,CDK2,CDK4,CDKN2A,CDKN2D,CHEK1,CHEK2,DBF4,E2F1,E2F3,E2F5,ESPL1,HDAC2,MAD2L1,MAD2L2,MCM2,MCM3,MCM4,MCM7,PCNA,PKMYT1,PLK1,PTTG1,PTTG2,RAD21,SKP2,SMC1B,TFDP2,TTK,YWHAZ |
|  |  |  | |  |
| Cytokine-cytokine receptor interaction | 96 | 0.0002 | | ACVR1,ACVR1B,ACVRL1,BMPR2,CCL20,CCL4,CCR1,CCR2,CCR4,CCR5,CCR6,CD4,CD40,CD40LG,CLCF1,CRLF2,CSF1,CSF1R,CSF2RA,CSF3R,CX3CL1,CX3CR1,CXCL14,CXCL16,CXCR1,CXCR2,CXCR3,CXCR4,EDA,EDA2R,FAS,FASLG,GDF10,GDF6,GHR,IFNA1,IFNA13,IFNAR1,IFNE,IFNGR1,IL10RA,IL10RB,IL11RA,IL12RB1,IL13,IL13RA1,IL15,IL15RA,IL16,IL17RA,IL18,IL18R1,IL18RAP,IL1RAP,IL1RL2,IL2,IL20RB,IL2RB,IL2RG,IL31RA,IL32,IL33,IL3RA,IL4R,IL6R,IL6ST,IL7,IL7R,INHBB,LEPR,LTB,MSTN,NGFR,NODAL,OSM,OSMR,TGFB1,TGFB2,TGFB3,TGFBR2,TNFRSF10A,TNFRSF10B,TNFRSF10C,TNFRSF14,TNFRSF1A,TNFRSF6B,TNFRSF9,TNFSF10,TNFSF11,TNFSF12,TNFSF13,TNFSF13B,TNFSF14,TNFSF18,TNFSF4,TNFSF8 |
| DNA replication | 23 | 0.0157 | | DNA2,FEN1,LIG1,MCM2,MCM3,MCM4,MCM5,MCM7,PCNA,POLD1,POLE2,POLE3,POLE4,PRIM1,PRIM2,RFC2,RFC3,RFC4,RFC5,RNASEH1,RNASEH2A,RPA2,RPA3 |
| mRNA surveillance pathway | 31 | 0.0385 | | CPSF1,CPSF3,CPSF4,CPSF6,CSTF1,CSTF2,DAZAP1,FIP1L1,HBS1L,MAGOH,MAGOHB,MSI1,MSI2,NCBP1,NCBP2,NXT1,PABPC1,PABPC1L,PABPC3,PABPC4,PABPN1,PPP2R1A,PPP2R2D,PPP2R3B,RBM8A,RNPS1,SAP18,SMG5,SSU72,UPF2,UPF3B |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

Supplementary Table 5. Significantly enriched kinase-target networks of RBM8A in POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |
| --- | --- |
| Geneset | LeadingEdgeGene |
|  |  |
| Kinase\_HIPK2 | CTBP2,HIPK2,NOTCH1,PML,RUNX1,ZBTB4 |
| Kinase\_MAPK7 | HIF1A,MAP2K5,MEF2A,NFKB1,PML,RPS6KA1,RPS6KA2,RPS6KA3,RUNX1,SGK1,STAT3,TSC2 |
| Kinase\_MAPK6 | HIF1A,MAPK6,NFKB1,RPS6KA1,RPS6KA3,RUNX1,STAT3,TSC2 |
| Kinase\_ATR | BLM,BRCA1,CDKN2A,CHEK1,CHEK2,CHTF18,DBF4,DCK,E2F1,EWSR1,FANCD2,FANCI,FARSA,GINS2,GPS1,H2AFX,MARCKSL1,MCM2,MCM3,NBN,RAD1,RPA2,SIAH1,TDP1,ZSCAN5A |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

Supplementary Table 6. Significantly enriched miRNA-target networks of POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |
| --- | --- |
| Geneset | LeadingEdgeGene |
|  |  |
| AACTGGA,MIR-145 | ABR,ACVR1B,AKAP9,AMOTL2,ANGPT2,AP1G1,ARHGAP24,BACH2,BAZ2A,CACHD1,CAMK1D,CCDC25,CD47,CDK6,CELF2,CFL2,CHKB,CLCA3P,CLINT1,CPEB4,CTNND1,DUSP6,EIF4A2,EIF4B,EIF4EBP2,ELMO1,ERG,ERLIN1,FLI1,FNDC3A,FNDC3B,FOXO1,GPHN,HERC4,HERC6,INHBB,INO80,IRS1,KIAA0355,LHFPL2,LMBRD2,MAF,MAP3K3,MYO5A,NBEAL1,NFE2L1,NUAK1,PHLDB2,PHRF1,PXN,RAPH1,RASA2,RASSF5,REV3L,RGS3,RIN2,RNF31,RREB1,SBF2,SCN3A,SEC31B,SLC1A2,SMAD3,SOX9,SRGAP3,TGFBR2,TIRAP,TRIM2,UBA6,UBE2Z,XRN1,ZC3H11A,ZFYVE26 |
| GTGCAAA,MIR-507 | AGFG1,ANO4,ATP1B1,BACH2,CCDC6,CHD9,CPEB4,DAB2IP,DGKH,DNAJC13,EIF4G2,EP300,ESRRG,FAM43A,GDF6,GRIK2,GTF2H1,IQSEC2,KCND2,LEF1,LPGAT1,MAF,MAP3K3,MBNL1,MED13L,MEIS1,MIP,NDFIP1,OSM,PCDH9,PJA2,PRDM1,RAPH1,RBMS3,REV3L,RGS17,RUNX1,SCN3A,SECISBP2L,SLC24A4,SORBS2,SP3,STAT5B,UNKL,USP47,WDR26,ZFX |
| ATAGGAA,MIR-202 | ACTN1,ACVR1,ARSB,ATP2B4,ATXN1,BAG4,BCL2,BTG1,CCDC88A,CD28,CPEB3,CREBBP,CTBP2,DDX3X,ELF1,ESR1,HLF,HOXB2,IQGAP1,KLF12,LUZP1,MAPK6,MED13L,NDRG1,PTEN,RPS6KA3,SCN2B,SPRED1,SSBP2,STAT3,TCF12,TGFBR2,USP15,USP8 |
| GTGCAAT,MIR-25,MIR-32,MIR-92,MIR-363,MIR-367 | ADAMTSL3,ADCY3,ADM,ARHGEF17,ARID1B,ARRDC3,ARRDC4,ATRX,BAZ2A,BAZ2B,BMPR2,BRMS1L,CBFA2T3,CD69,CDCA7L,CHMP7,CIC,CPEB2,CPEB3,CPEB4,DAB2IP,DDX3X,DLGAP2,DMXL1,DOCK9,DUSP10,FAM160B1,FASLG,FCHO2,FNDC3B,FNIP1,GLYR1,HERC2,HIVEP1,IBTK,ITGA5,ITGAV,LATS2,LHFPL2,LUZP1,LYST,MAN2A1,MEF2D,MYCBP2,MYO18A,NFIA,NOVA1,OTUD4,P2RY13,PAFAH1B1,PDS5B,PDZD2,PER2,PGAM1,PGAM4,PIKFYVE,PIP5K1C,POLK,PPP1R12A,PTPRO,REV3L,RFX1,RGS17,RGS3,RNF141,RPS6KA4,SESN3,SH3PXD2A,SLC24A3,SMAD7,TACC2,TEAD1,TECPR2,TEF,TOB2,TRAF3,TRAM2,TRIO,UBE2Z,UGP2,USP28,ZEB2 |
| TATTATA,MIR-374 | ABR,ACTN1,AFF4,ARHGAP5,ARHGAP6,ARL15,ATP1A1,ATP8B2,ATXN1,BACE1,BHLHE40,BMPER,CAPZA2,CD47,CEBPB,CHST2,CLIP4,CPEB4,CSMD2,DENND4A,DUSP6,DUSP8,EIF3A,EIF4G2,EN1,EP300,ESRRG,ETV5,FBXO42,FNDC3B,FNIP1,FOXO1,FOXP1,GOPC,GPM6A,HECTD1,HERC2,HIVEP2,HLF,HOXA1,HR,IL15RA,IQSEC2,KIAA2026,LARP1,LCA5,LRP1B,MAP2,MAPK6,MBNL2,MECP2,MEF2D,MEIS1,MMP14,MTMR12,NEO1,NFIX,NIPBL,NMT1,NOVA1,NR3C1,NUAK1,NUMB,OCRL,PAPPA,PARP8,PDE4B,PDE4D,PDPK1,PHF21A,PHRF1,PIKFYVE,PLAG1,PMEPA1,PNRC1,PPARGC1A,PPP2R2C,PRDM1,PURA,QKI,RAB38,RAI1,RSF1,RUNX2,SCN2B,SF1,SP1,SP3,SPRY2,SRPK2,ST8SIA4,STARD13,STYX,SYNE1,TCF12,TLE4,TMEM47,UBE2H,VAMP2,WDR11,WNT5A,ZC3H7B,ZCCHC14,ZDHHC5,ZEB2,ZNF236 |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

Supplementary Table 7. Significantly enriched transcription factor-target networks of POLR2K in bladder urothelial carcinoma (LinkedOmics).

|  |  |  |
| --- | --- | --- |
| Geneset | LeadingEdgeGene | |
|  |  | |
| V$CDC5\_01 | | APH1A,ATAD2,ATAD5,C19orf57,CBX3,CD3EAP,CDC25A,CDC6,CDK1,CDT1,CORT,DCK,DCTPP1,DNAJC9,E2F1,E2F3,EZH2,FANCD2,FANCG,GEN1,GINS3,GMNN,GPN3,H2AFV,H2AFZ,HIST1H2AH,HIST1H2BK,HIST1H3A,HNRNPA2B1,HNRNPR,ILF3,MAZ,MCM2,MCM3,MCM4,MCM7,MCM8,MRPL40,MSH2,MSH5,MTF2,MXD3,NASP,NUP62,PAN2,PCNA,PHC1,PHF13,PHF5A,PIM1,PKMYT1,POLD1,POLE2,POLE4,PPM1D,PRPF38A,RANBP1,RBBP4,RPS20,SASS6,SEMA6A,SNRPD1,SSBP3,STK35,STMN1,SUMO1,SUV39H1,TFAP4,TMPO,TRMT6,UNG,WDR62,YBX2,ZBTB8OS |
| V$CDC5\_01 | | ABLIM1,ADAMTS9,AP1S2,ARNTL,ARRDC3,ATRX,B3GNT6,BACH2,BCL6,BMPR2,C15orf41,C1orf21,CACNA1C,CALD1,CCL20,CDH6,CDKN2C,CHD2,CLASP1,CLDN1,COL16A1,CPEB4,CREB5,CTNND1,CUX1,DGKB,DLG2,DLL4,EDA,EGR2,ELP3,ENPP2,ESRRG,FGF10,FNBP1,FOXP1,FOXP2,FUT11,FYN,GFRA1,GLI3,GPR87,HIPK1,HIVEP3,HOXD10,HOXD9,ING3,INPP4B,ITPKB,KCTD15,KLF12,KLF4,KLHL4,LMNA,LYN,MAML1,MBNL1,MGLL,MINK1,MN1,MXI1,NOVA1,NRP1,NRXN3,PBX1,PBX2,PCDHGC3,PHF21A,PIK3R1,PLAG1,PLEKHH3,POT1,PPARGC1A,PRKACB,PURA,RARA,RASAL2,RBM26,RCOR1,RGS1,RORA,RREB1,SAMSN1,SAT1,SCN7A,SESN3,SLCO2A1,STAT3,TCF21,TGFB3,TMPRSS3,TNFSF10,TNNI3K,TRPS1,UNC13D,VANGL1,VDR,XIAP,ZBTB20,ZFPM2,ZNF827 |
| V$FOXO1\_02 | | ARID4A,CACNA2D1,CD109,CDKN1A,CELF6,CFL2,CHD2,CLEC4D,CLSTN1,CSRNP3,DDIT4,DHRS3,DIXDC1,DNAJB12,DTNA,EIF4EBP2,ERG,ETV1,ETV5,EZH1,FGF10,FGF9,FOXN3,FOXO1,FOXP2,FSTL1,GCNT2,GFI1B,GNAO1,GRAP2,HBP1,HLX,HOXA1,HR,ID2,IL6ST,ITGB8,JAG1,KLF12,KLF9,LAMC2,LEMD1,LIFR,LIMK2,LIX1L,MDGA1,MEIS2,MITF,MMP13,NDRG1,NFIX,NR2F1,NRG1,NTN1,NUB1,OSBPL5,PAK1,PELI2,PHF21A,PI4K2A,PIK3C2A,PIK3IP1,PLAG1,PRDM1,PSEN1,PTCH1,PURA,RASD1,RFX1,ROGDI,ROR1,RORA,RSF1,SATB2,SERINC3,SH3RF1,SIN3A,SQSTM1,ST5,TBX4,TEK,TET2,TGFB3,THBS3,THRA,TMEM71,TRERF1,TRIM8,TSC22D3,TSHZ3,UTY,XPO7,ZADH2 |
| V$IRF\_Q6 | | ADAR,ADORA3,ARHGAP5,ATXN7L1,B2M,BATF2,BBX,BST2,BTAF1,C15orf41,CASP7,CCDC6,CDK6,CIITA,CPEB4,CXCR4,CYBB,DAPP1,DDX60,DGKA,DHX58,DNASE1L3,DTX3L,DUSP10,ECM2,EIF4A2,ESR1,ETV5,EXT1,F3,FCGR2B,FCGR2C,FLI1,HIPK1,HLA-F,HMCN1,IFI35,IFI44,IFIT2,IL18BP,IRF2,IRF9,ITGB7,KCNIP3,KLHL13,KYNU,LGALS8,LGALS9,LSP1,LY86,MEIS2,MLLT3,MOV10,NFATC1,NOD2,NPR3,NRP1,NUB1,OSM,PARP12,PCDH7,PCDHGC3,PCGF5,PLEKHH2,PLXNC1,PRKD2,PSMB10,PSMB8,PTPRO,PURA,RAPGEF6,RARG,RBMS2,RTP4,RUNX1T1,SAT1,SH2B3,SIK3,SIX1,SLC15A3,SLC40A1,STAT6,TAPBP,TAPBPL,TCIRG1,THBS1,TMEM229B,TNFSF13B,TOR1AIP1,TRIM21,UBE2L6,WDR82,ZADH2,ZBP1,ZEB2,ZNF366 |
| V$ISRE\_01 | | AKAP6,APOOL,ASPA,ATXN7L1,B2M,BATF2,BBX,BST2,BTAF1,CCDC6,CD151,CDK6,CRK,CXCR4,CXorf21,DAPP1,DDX58,DDX60,DGKA,DHX58,DTX3L,DUSP10,EPSTI1,ERC1,ERG,ESR1,FYCO1,GPR55,GPR65,HDAC4,HEPACAM,HLA-F,HMCN1,IFI44,IFIH1,IFIT2,IFIT3,IRF2,IRF9,KCNIP3,KY,KYNU,LCOR,LMO1,LSP1,MACC1,MAP2,MEF2C,MEIS1,MET,MMP25,MOV10,NPR3,NUB1,OPTN,OSM,PARP8,PCDH7,PCDHGC3,PCGF5,PLAG1,PLXNC1,PML,PPARGC1A,PPP2R5C,PRKD2,PTCH1,PURA,RTP4,SCN2A,SH2B3,SH3BGRL,SIK3,SIX1,SLC24A1,SLC25A28,SORBS1,SSBP2,STAT6,TAPBP,TBX21,TCIRG1,THBS1,TNFSF13B,TRIM21,TSKU,UBA7,UNC5C,XAF1,ZBP1,ZBTB7A,ZEB2 |
|  | |  |
| V$IRF7\_01  V$IRF1\_01 | | ABI3,ADAR,AGPAT4,AMY2A,ARRDC3,BATF2,BNC2,BST2,C19orf66,CALD1,CASP7,CCDC6,CD40LG,CXCL16,CXCR4,CXorf21,DAPP1,DDX58,DDX60,DTX3L,EPSTI1,ERG,ESR1,FLI1,FLRT2,GNGT2,HIVEP1,HMBOX1,IFIT2,IRF2,ITGB7,KDM3A,KIF13A,LDB2,LGALS3BP,MAP2K5,MOV10,NFIX,NPR3,NRP1,OPTN,OSM,PARP12,PARP8,PCGF5,PDE1B,PDE4D,PDGFC,PIK3CD,PLEK2,PLXNC1,PPP2R2A,PSMB9,PSME1,RAPGEF6,RUNX1T1,SAT1,SECISBP2L,SIPA1L1,SLC25A28,SOX5,SP110,SRPX2,STX11,TAP1,TAPBP,TCF12,TMEM229B,TRIM21,UBA7,UBR4,XAF1,ZFP36L1,ZMYND15  ARHGAP5,ASPA,B2M,BBX,BNC2,BST2,CD200R1,CD40LG,CDK6,CLCA3P,CREB1,CXorf21,DDX58,DNASE1L3,DOCK9,DTX3L,DUSP10,EDA,EIF4A2,EN1,ESR1,F3,FLT3LG,GNAO1,HDAC4,HLX,HOXA6,HOXB6,HOXD9,IL15RA,IRF9,ITPKB,JKAMP,KDM3A,KYNU,LCOR,LDB1,LDB2,LEMD1,LTBP2,43525,MBD6,MGAT2,MITF,NFIX,NPR3,NR3C2,PCGF5,PDGFC,PHF21A,PITX1,PLXNC1,PPARGC1A,PRDM10,PRKCB,PSMB10,PSMB8,PSMB9,RAPGEF6,RIMS2,RIT1,ROCK1,RUNX1T1,SAT1,SH3BGRL,SLAMF8,SLC22A25,SORBS1,STX11,TAP1,TAPBP,TGFB3,TMEM229B,TNFSF13B,TRIM21,UBD,VAMP3,XAF1,ZADH2,ZBED5,ZNF366 |

Abbreviations: LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA). V$, the annotation found in Molecular Signatures Database (MSigDB) for transcription factors (TF).

Supplementary Table 8. Significantly enriched neighborhood networks of *POLR2K* in Human Gene Atlas (Enrichr)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Term | Overlap | Adjusted P-value | Genes |  |  |
| CD34+ | 7/645 | 0.088287884 | RBM17,TAF15,COPS5,CPSF1,CSTF1,INTS8,CTNNBL1 | | |
| CD71+\_EarlyErythroid | 6/553 | 0.103385775 | CUL4A,USP7,BRF2,POLR3C,EP300,ASH2L | | |
| 721\_B\_lymphoblasts | 9/1543 | 0.37177576 | SF3B4,GTF3C2,RFC4,NCBP2,NCOA3,CSTF1,XRCC1,INTS9,POLR2K | | |
| CD56+\_NKCells | 5/752 | 0.820187761 | BRF2,RBM8A,NCOA6,DHX38,TAF4 | | |