Supplementary Information

Supplementary Figure 1. Screen shot of inquire about KRAS, TP53, CDKN2A and CDKN2B in TCGA pancreatic cancer samples on the website http://www.cbioportal.org/.

Supplementary Figure 2. Lentiviral vectors used in this study. **a,** Diagram of the lentiviral vectors. **b,** The knockdown efficiency of the shRNAs tested in MEFs by real-time PCR.

Supplementary Figure 3. Gross appearance of the mouse pancreatic cancers. **a,** All of the mouse pancreatic ductal adenocarcinomas were located in the head of the pancreas. **b,** The size of most tumors ranged from 0.5 to 1.5 cm. **c,** The cut surfaces were yellow to white and exhibited little hemorrhage and necrosis. **d,** Obstruction of the common bile duct and/or the main pancreatic duct cause by tumor mass. **e,** Additional abnormalities were observed in the digestive organs.

Supplementary Figure 4. The whole appearance of HE staining and CK-19 of pancreatic cancer. The frame region in “a” was shown as “b” and the frame region in “b” was shown as “c”. N: normal tissue; T: tumor.

Supplementary Figure 5. Cellular proliferation in pancreatic cancer. **a,** PCNA

expression. PCNA expression was not detected in normal pancreatic ducts and was significantly enhanced in pancreatic cancer. **b,** the quantification of ki67 positive cells in normal tissue, pancreatic cancer, adjacent tissues and distal tissues.

Supplementary Figure 6. Cell types infected by lentivirus. The lentivirus KRAS-shTp53-EGFP, KRAS-shTp53-EGFP-shCdkn2a, KRAS-shTp53-EGFP-shCdkn2b were injected and collect samples at day 7 for staining. The sections were staining with CK19 antibody and GFP antibody. Most EGFP positive cells are also CK-19 positive.

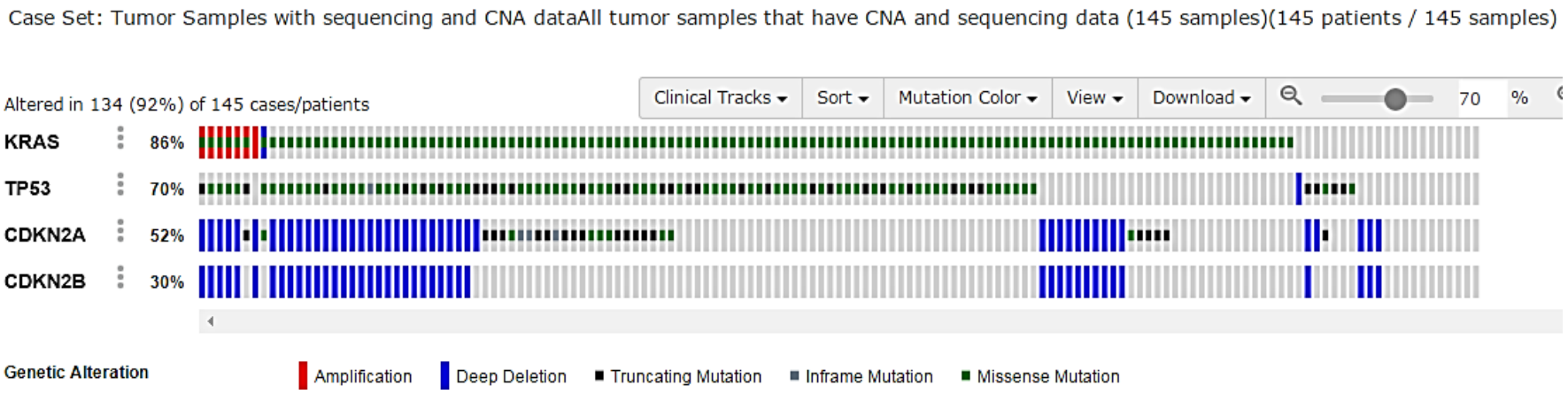
Supplementary Figure 7. Hematoxylin and eosin (H&E) staining of pancreatic cancer induced by cytokeratin-19 promoter-driven $KRAS^{G12D}$ expression. Duct-like structure was observed in tumor. Two fields (10x and 20x) were shown.

Supplementary Table 1. The quality of RNA-seq, reads mapping rate, and the correlation of 3 biological replicates.

Supplementary Table 2. The enrichment of human pancreatic cancers core regulatory process or pathway of human pancreatic cancers.

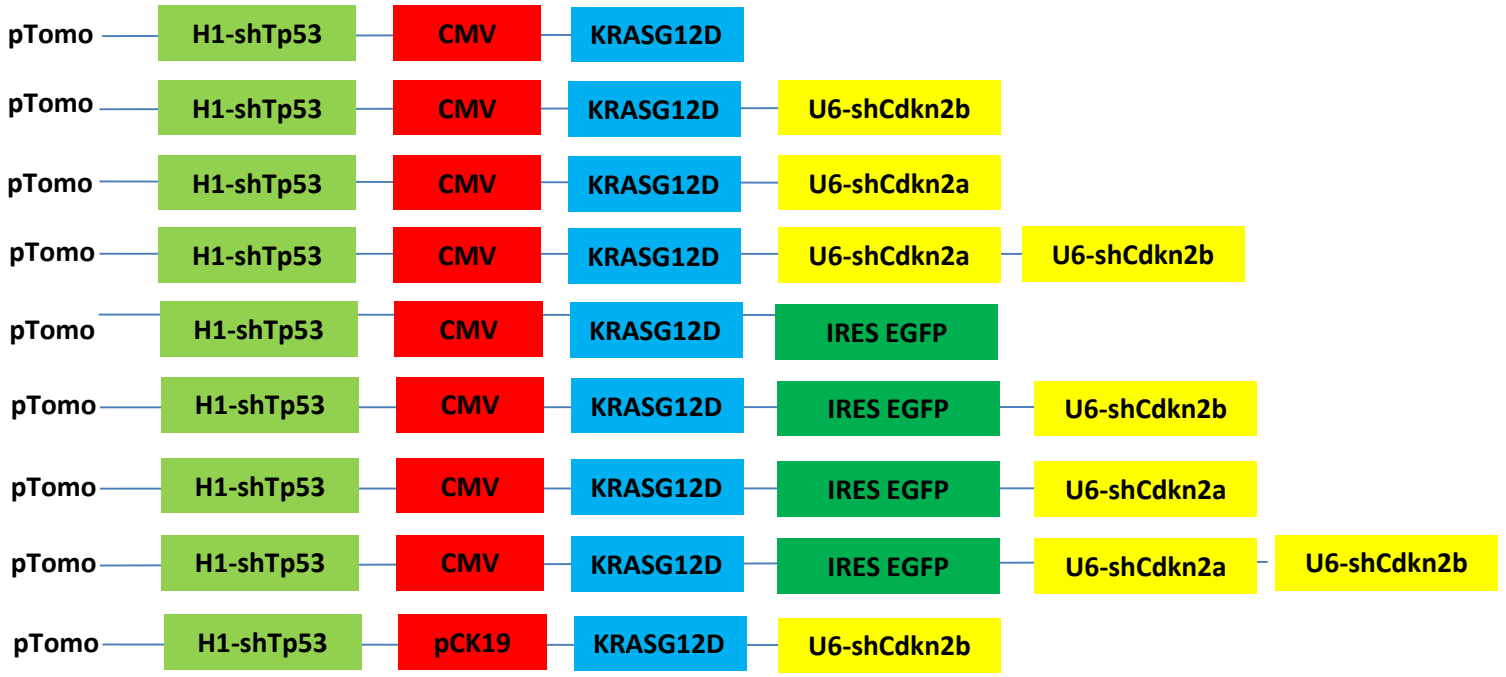
Supplementary Table 3. Sequence of all primers used in this study and target sequence of shRNA.

Supplementary Fig 1



Supplementary Fig 2

a



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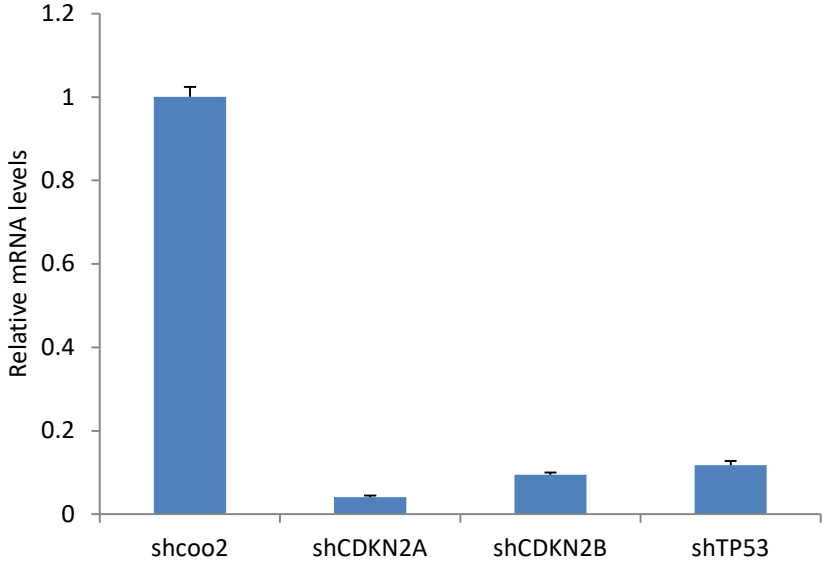
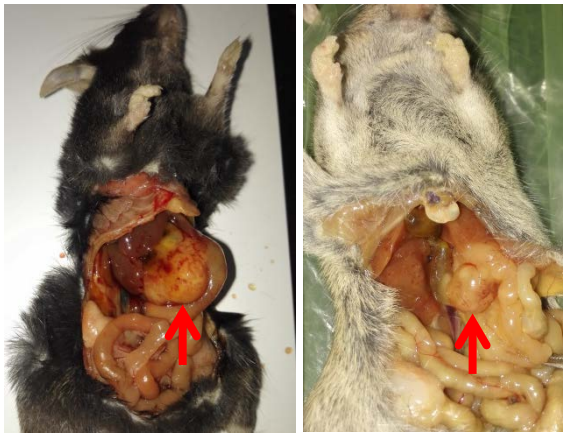


Supplementary Fig 3

a



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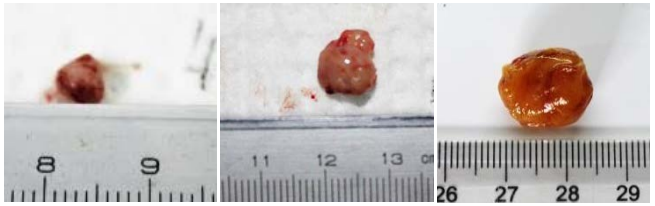

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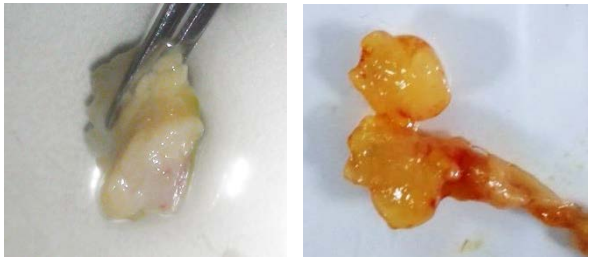

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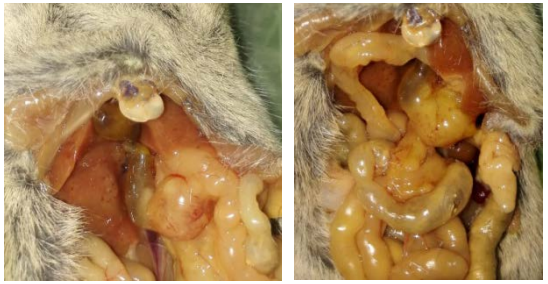

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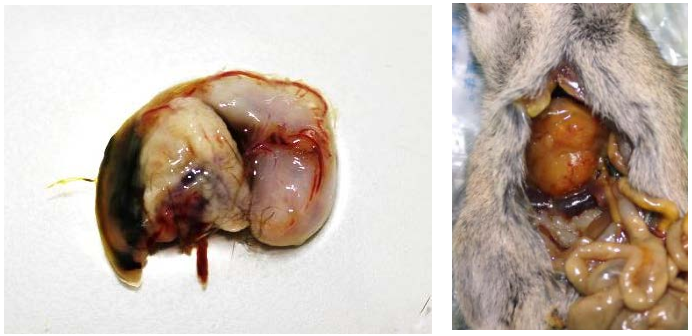
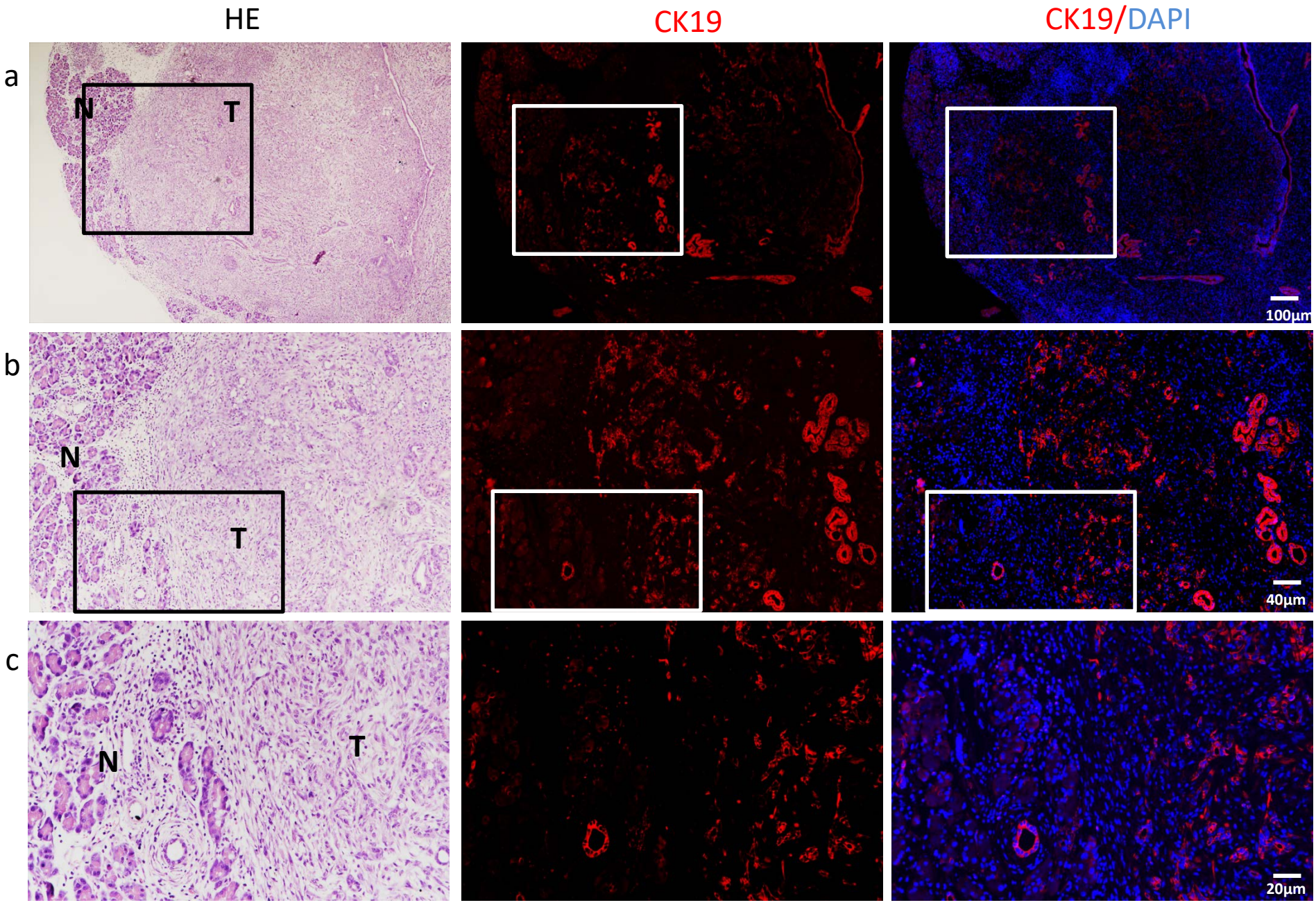
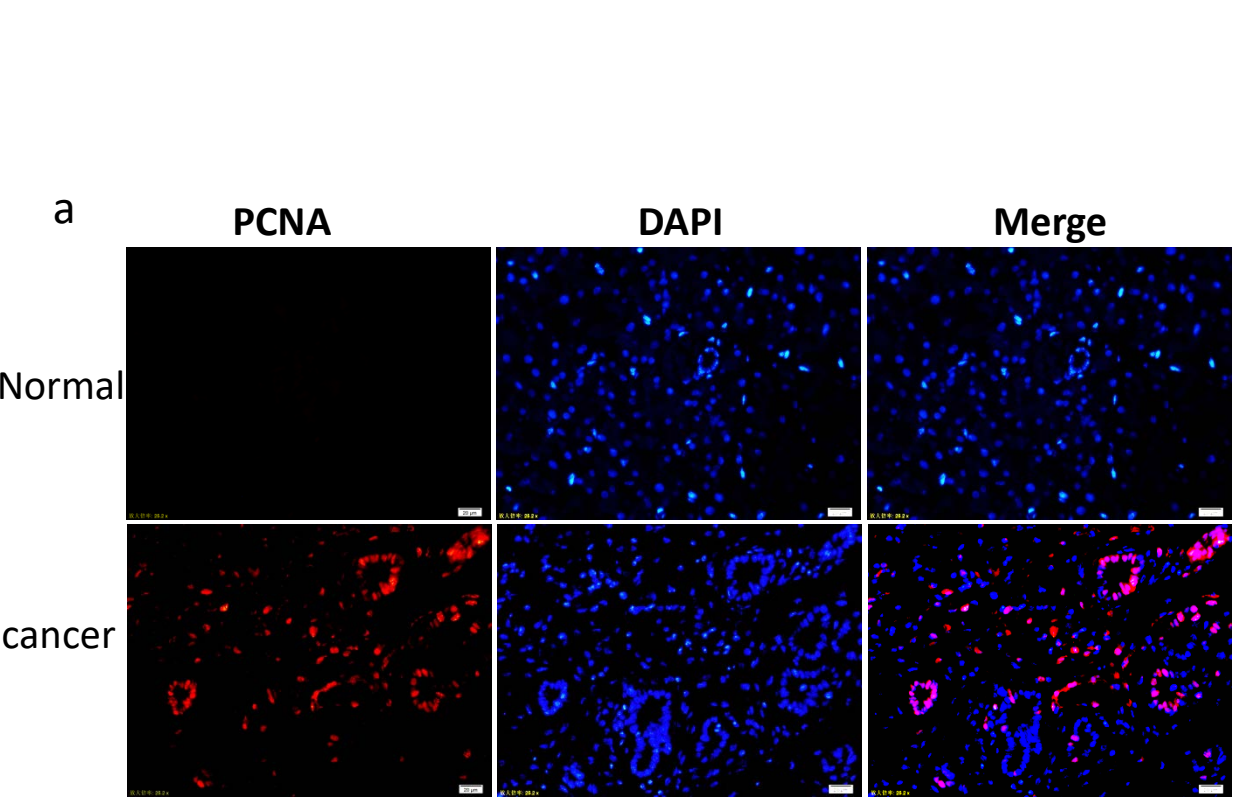
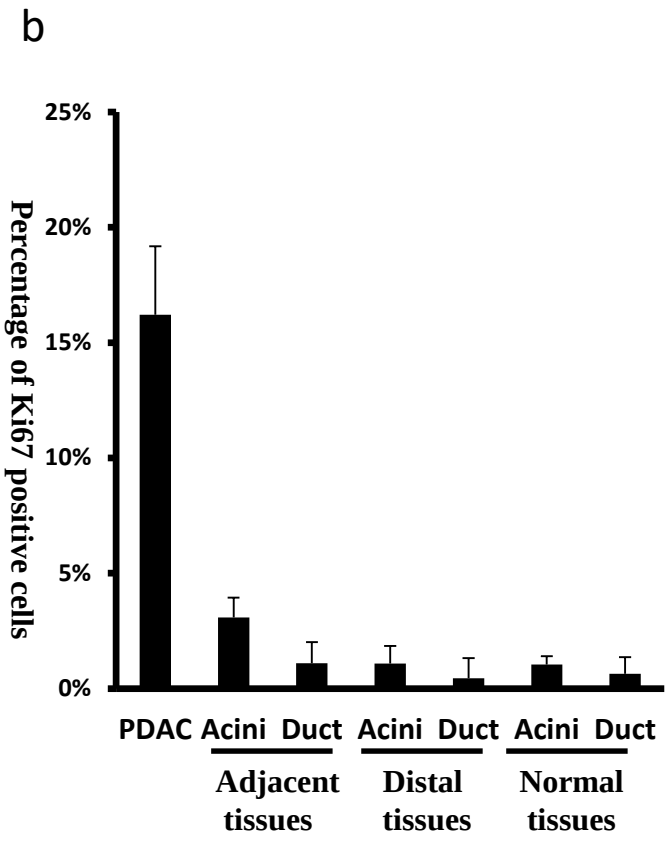


Supplementary Fig 4

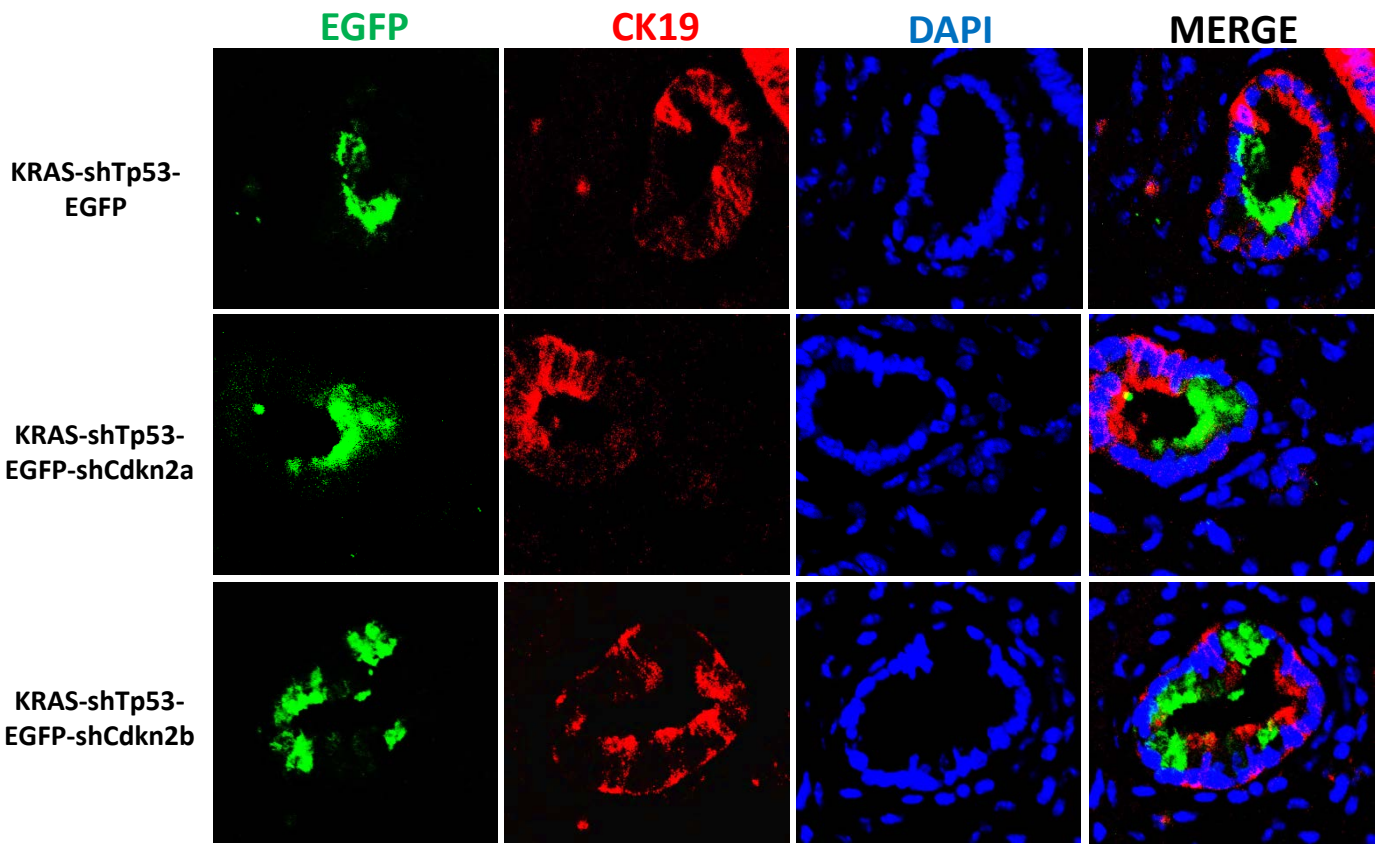


Supplementary Fig 5

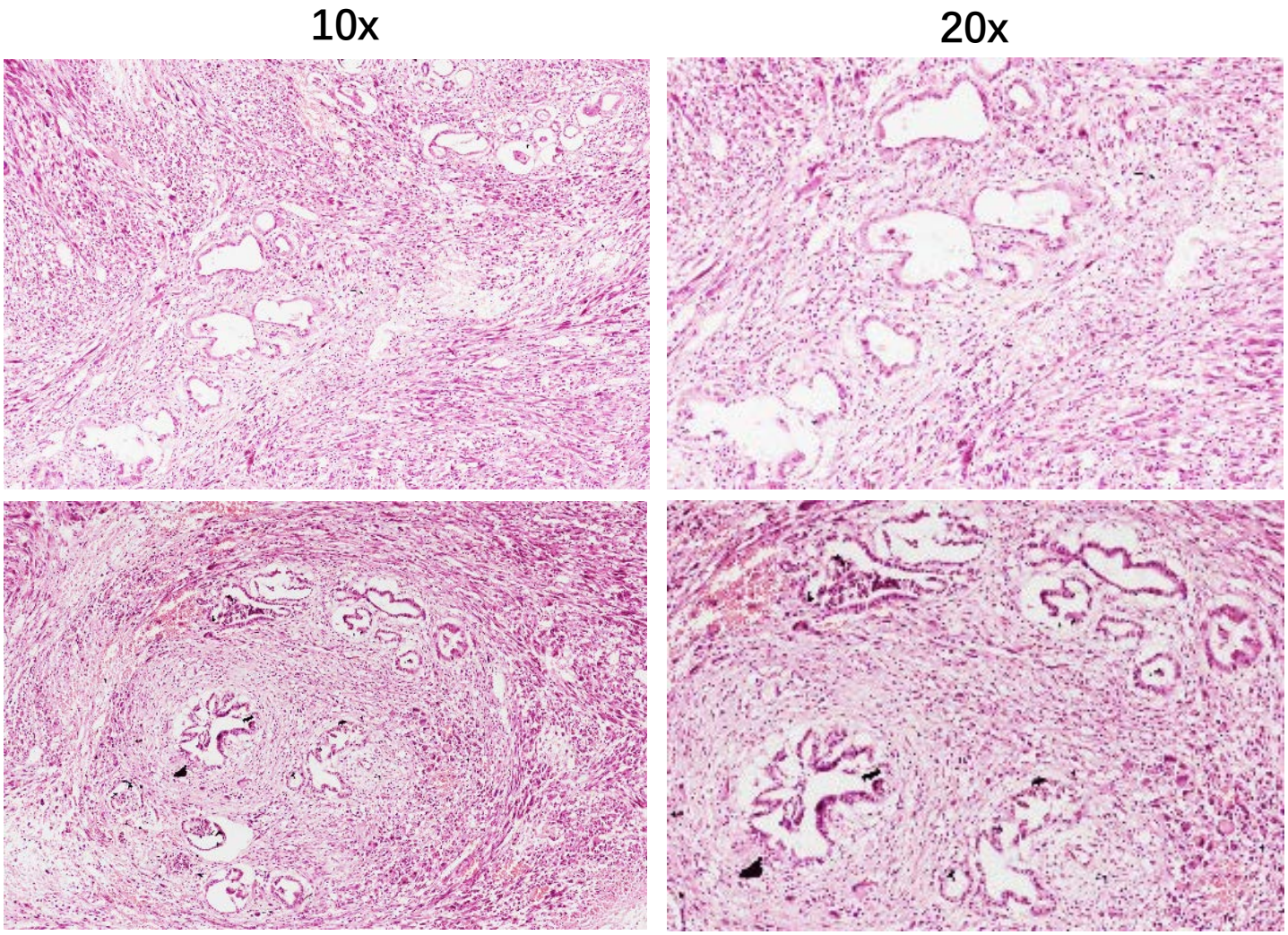




Supplementary Fig 6



Supplementary Fig 7



Supplementary Table 1. The quality of RNA-seq, reads mapping rate, and the correlation of 3 biological replicates.

Sample	Raw bases(G)	Clean bases(G)	Clean bases(%)	Clean Q20(%)	Clean Q30(%)	Overall read mapping rate*(%)	Mean correlation #(R)
newborn-1	11.99	11.8	0.9842	97.92	95.06	91.60	0.9823
newborn-2	10.06	9.91	0.9851	97.66	94.51	91.70	
newborn-3	10.61	10.45	0.9849	97.92	95.05	92.80	
9-wk-1	12.08	11.83	0.9793	97.84	94.91	91.10	0.9690
9-wk-2	10.42	10.22	0.9808	97.81	94.85	91.00	
9-wk-3	9.98	9.79	0.9810	97.84	94.88	91.40	
PDAC-1	9.36	9.15	0.9776	97.16	93.79	86.30	0.9108
PDAC-2	9.83	9.62	0.9786	97.22	93.82	88.20	
PDAC-3	10.95	10.72	0.9790	97.23	93.84	87.60	

* The reads were mapped to the mouse genome (GRCm38.p4).

Mean Perrson correlation of 3 biological replicates, and p-value < 2.2E-16 with cor.test and Pearson's product-moment correlation in all pairwise.

Supplementary Table 2. The enrichment of the core regulatory process or pathway in Fig3b.

Regulatory process or pathway *	Total genes**	The number of PDAC differential expression genes ***	Down-regulation genes	Up-regulation genes	p_value
Homophilic cell adhesion	2450	1043	Adam33,Adcy9,Adk,Adrb1,Adrb2,Alox12,Amigo1,Ang,Angpt1,Ap1ar,Ap3d1,Ap3s1,Apba1,Aph1c,Aplp1,Apol7a,Arhgap5,Arhgdig,Atf4,Atf6,Atp5e,Azgp1,Bmp7,Bmpr1b,Cacna1d,Cacnb2,Camsap3,Cckar,Cd24a,Cd36,Celsr2,Cgn,Cgref1,Chrm3,Chst2,Cldn10,Cldn3,Cldn8,Cldn9,Clstn1,Clstn3,Cml3,Cml5,Col7a1,Crb3,Creb3l1,Cuzd1,Cyfip2,Cytip,Dact2,Dgcr6,Dlg2,Dlgap3,Dmd,Dsg2,Dsp,Dtx1,Dusp22,Dusp26,Dvl3,Eda,Efemp1,Egf,Enpp2,Entpd1,Entpd2,Epb4.1,Epb4.1l5,Epha7,Faf1,Fat3,Fkbp2,Fndc3a,Foxa2,Foxa3,Foxp2,Fzd3,Fzd4,Gabra4,Gadd45g,Gata4,Gbf1,Gjb1,Gjb2,Glrx2,Gnai1,Gne,Gng7,Gp5,Gpam,Grb7,Grhl2,Grpr,Gsn,Gstp2,Habp2,Haplnl4,Hba_a1,Homer2,Igf1,Igfals,Igfbp6,Igsf11,Igsf5,Il11ra1,Il22ra1,Inadl,Ins1,Ins2,Itih2,Itpr2,Kdr,Kif13b,Kirrel2,Klk1b3,Lamc3,Lifr,Lpl,Lrfn3,Mapk19,Mapt,Mia,Mllt4,Mtss1,Muc1,Myh11,Myom1,Nat8,Nme2,Nphs1,Ntn1,Nuak1,Ocln,Onecut1,P2rx1,Pard6b,Pawr,Pcp4,Pde2a,Pde4a,Pde4c,Pdia6,Perp,Pip5k1b,Pkhd1,Pla2g12a,Plcb1,Plcb4,Plxna2,Plxnd1,Pnpla8,Prdx4,Prkce,Prkcz,Prss1,Prss3,Psen2,Psmb10,Ptger3,Ptprd,Rab27a,Rap1gap,Rora,Rorc,Rps6,Rtn4r,Serpini1,Serpini2,Setd6,Shank1,Slc7a11,Smarcc2,Smoc1,Spint2,Spock2,Sstr2,Ssx2ip,Stk11,Syp,Syt15,Syt3,Syt7,Syt9,Tek,Thra,Tinag,Tmem8,Tnxb,Try10,Tspan5,Tsta3,Ttyh1,Tuba4a,Umod,Unc13b,Unc5a,Vit,Vldlr,Vtn,Wbp1,Xbp1,Zbtb7b	Abi3bp,Acan,Acp5,Actb,Actg1,Actl6a,Actn1,Actn4,Actr3,Ada,Adam15,Adam23,Adam8,Adam9,Adamdec1,Adamts1,Adamts12,Adamts14,Adamts15,Adamts2,Adamts4,Adamts8,Adcy2,Adcy3,Adcy7,Adora2a,Adora2b,Adra2a,Aebp1,Ager,Agr2,Agrn,Aif1,Ajap1,Ajuba,Akt3,Alox15,Amica1,Angptl2,Ank3,Antxr1,Anxa1,Ap3m2,Apba2,Apbb1ip,Aplnr,Apoa1,Apoa4,Apob,Apoc3,Apod,Apoe,Apol6,Apol8,Arap3,Arhgap6,Arhgdia,Arhgdib,Arhgef1,Arhgef25,Arhgef6,Arpc1b,Arpc2,Arpc3,Arpc4,Arpc5,Arpc5l,Atp1b2,Atp7a,Avl,B2m,B4galnt2,B4galt1,Batf,Batf3,Bax,Bcar1,Bcl2l1,Bcl2l11,Bcl3,Bcl6,Bgn,Blm,Blnk,Bmp2,Btk,Btnl2,C3,C3ar1,C5ar1,Cacna1b,Cacna1c,Cacna1h,Cacna2d1,Cacnb3,Cacng7,Cadm1,Cadm3,Cadm4,Camk2d,Capn2,Capza1,Card11,Casp3,Casp8,Cav2,Cbl,Ccdc80,Ccl11,Ccl2,Ccl22,Ccl24,Ccl3,Ccl5,Ccl7,Ccl8,Ccnd1,Ccr1,Ccr2,Ccr5,Ccr7,Cd14,Cd1d1,Cd22,Cd274,Cd276,Cd300a,Cd33,Cd38,Cd3e,Cd3g,Cd4,Cd40,Cd44,Cd48,Cd53,Cd68,Cd74,Cd80,Cd81,Cd83,Cd84,Cd86,Cd9,Cd93,Cdh11,Cdh13,Cdh17,Cdh2,Cdh24,Cdh3,Cdh6,Cdhr2,Cdhr5,Cdx1,Cdx2,Cebpb,Cercam,Cfl1,Chd7,Chl1,Chrd,Chst1,Chst3,Chst7,Chst8,Clca2,Cldn15,Cldn2,Cldn4,Cldn5,Cldn6,Clec4a2,Clec4d,Clec4e,Clic1,Cntfr,Cntn6,Col11a1,Col12a1,Col14a1,Col15a1,Col16a1,Col18a1,Col27a1,Col4a1,Col4a2,Col4a6,Col5a1,Col5a2,Col5a3,Col6a1,Col6a2,Col6a3,Col8a1,Col8a2,Col9a3,Colec12,Coro1c,Cpxm1,Creb3l3,Creb5,Crlf2,Csf1,Csf1r,Csf2rb2,Csf3r,Csk,Csnk1e,Csnk1g3,Cspg4,Ctgf,Ctla2a,Ctnna1,Cttn,Cx3cl1,Cx3cr1,Cxcl5,Cxcl9,Cxcr3,Cyp1b1,Cyr61,Cyth3,Cyth4,Dab2,Dbn1,Dcbld2,Dchs1,Dhh,Dkk2,Dlg4,Dlgap4,Dll1,Dll4,Dmp1,Dnm1,Dock2,Dock8,Dst,Dusp1,Ecm1,Ednra,Efna4,Efna5,Efnb1,Efnb2,Efs,Egflam,Egr1,Egr3,Elf4,Elk1,Elmo2,Eln,Emb,Emilin1,Emilin2,Eng,Epb4.1l2,Epcam,Epdr1,Epha2,Epha3,Epha4,Ephb2,Ephb3,Ephb6,Erbb2,Erbb3,Erf,Evl,Ezr,F10,F2r,F2rl1,F2rl3,F3,F5,Fap,Farp1,Fat1,Fblim1,Fbln1,Fbln2,Fbln7,Fbn1,Fbn2,Fcer1g,Fcgr1,Fcgr3,Fcgr4,Fermt3,Fes,Fez1,Fgb,Fgg,Fgr,Fhl2,Flna,Flnc,Flot1,Flrt3,Fmn1,Fn1,Fos,Fosb,Fosl2,Foxc1,Fpr1,Frem1,Fxyd5,Fyb,Fzd1,Fzd2,Fzd7,Gab2,Gabra3,Gabrp,Gata2,Gata5,Gbp3,Gcnt2,Git2,Gjc1,Glg1,Gli2,Gli3,Glrx,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gp1bb,Gpm6b,Gpnmb,Gpr37l1,Grem1,Gria3,Grik2,Grik3,Grin2d,Gzmb,Hapln1,Has2,Hbegf,Hck,Hes1,Hgf,Hlx,Hmmr,Homer3,Hp,Hpse,Hsd17b12,Hspg2,Hyal2,Icam1,Icosl,Ido1,Ifnar1,Igfbp2,Igfbp3,Igfbp4,Igfbp7,Iglon5,Igsf9,Igsf9b,Ikzf1,Il13ra1,Il18,Il18r1,Il1rl2,Il20rb,Il21r,Il2rb,Il2rg,Il3ra,Il4ra,Ilk,Iqgap1,Irf1,Irs1,Islr,Itga11,Itga2,Itga3,Itga4,Itga5,Itga8,Itga9,Itgae,Itgal,Itgam,Itgav,Itgax,Itgb1,Itgb2,Itgb3,Itgb5,Itgb7,Itk,Itpr3,Itsn1,Jak3,Jam3,Jdp2,Jun,Junb,Kif26b,Kif3c,Kifap3,Kirrel,Klra4,Kng2,Krt18,L1cam,Lag3,Lama1,Lama3,Lama4,Lama5,Lamb1,Lamb2,Lamc1,Lamc2,Lat,Layn,Lcp2,Ldlr,Lef1,Lgals1,Lgals3,Lgals3bp,Lgals4,Lgals7,Lgals8,Lgals9,Limk1,Lims1,Loxl2,Lpar1,Lpar4,Lpp,Lpxn,Lrp1,Lrp5,Lrrc32,Lrrn2,Ltb4r1,Lum,Ly6d,Ly9,Lyn,Lyve1,Mad1l1,Madcam1,Mafb,Map2k1,Map3k8,Map4k4,Mapk11,Mapk7,Marcks,Mast2,Mcam,Megf10,Mertk,Mex3b,Mfap2,Mfap4,Mfge8,Mical1,Mical2,Mmp10,Mmp12,Mmp13,Mmp14,Mmp16,Mmp17,Mmp19,Mmp2,Mmp3,Mmp7,Mmp9,Mmrn1,Mpdz,Mpzl1,Mpzl2,Msln,Msn,Msr1,Myadm,Myh10,Myh9,Myo1e,Myo1f,Myo1g,Ncam1,Ncapd2,Ncapg,Ncapg2,Ncaph,Nck2,Nckap1l,Net1,Nfatc4,Nfkb2,Ngef,Ngf,Ngfr,Nid1,Nid2,Nkx2-3,Nlgn2,Nlgn3,Nnmt,Notch2,Notch4,Npnt,Nptn,Npy,Nrcam,Nrg1,Nrp2,Nt5e,Ntrk1,Olr1,Onecut2,Osmr,P2rx7,P2ry1,P2ry2,P2ry6,Pak1,Pak3,Pard6g,Parvb,Parvg,Patz1,Pcdh18,Pcdh19,Pcdh20,Pcdh7,Pcdha1,Pcdha11,Pcdha12,Pcdha2,Pcdha3,Pcdha4,Pcdha5,Pcdha6,Pcdha7,Pcdha8,Pcdha9,Pcdhac1,Pde10a,Pde1a,Pde1b,Pde3a,Pde4b,Pde7b,Pdgfa,Pdgfc,Pdgfra,Pdgfrb,Pdp1,Pdpn,Peg12,Pf4,Pfn1,Pfn2,Phc2,Phip,Phldb2,Pik3cd,Pik3cg,Pik3r3,Pik3r5,Pik3r6,Pla2g4a,Pla2g7,Plat,Plau,Plaur,Plcb2,Plcg2,Plek,Plekha2,Plxna4,Plxnb2,Plxnb3,Podxl2,Pop1,Postn,Ppap2a,Ppfibp1,Prdx1,Prdx2,Prkacb,Prkar1a,Prkar1b,Prkar2b,Prkcb,Prkcd,Prkcg,Prkg2,Prnp,Prokr1,Pros1,Prx,Psma5,Psmb8,Psmb9,Pspc1,Pstpip1,Ptafr,Ptgir,Ptgis,Ptgs1,Ptn,Ptpn1,Ptpn13,Ptpn22,Ptpn23,Ptpn6,Ptprc,Ptprg,P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Integrin signaling	771	353	Adam33,Ang,Aph1c,Apol7a,Arhgdig,Cd24a,Cib2,Col7a1,Cytip,Dvl3,Egf,Eif4ebp1,Epha7,Fzd3,Fzd4,Gata4,Gnai1,Gng7,Inpp5b,Itpr2,Kdr,Lamc3,Mapt,Muc1,Myh11,Nme2,Ntn4,Pde2a,Pde4a,Pde4c,Pip5k1b,Plcb1,Plcb4,Plxna2,Prkce,Prkcz,Psen2,Setd6,Syp,Tinag,Tspan5,Ttr,Tuba4a,Vtn	Actb,Actg1,Actn1,Actn4,Actr3,Ada,Adam15,Adam23,Adam8,Adam9,Adamts1,Adamts14,Adamts15,Adamts2,Adm,Ager,Akt3,Apbb1ip,Apoa1,Apoa4,Apoc3,Apod,Apoe,Apol6,Apol8,Arhgdia,Arhgef6,Arpc1b,Arpc2,Arpc3,Arpc4,Arpc5,Bcar1,Btk,C3,Camk2d,Capn1,Capn2,Cav2,Ccl5,Ccnd1,Ccr7,Cd3e,Cd3g,Cd44,Cd53,Cd81,Cd9,Cfl1,Col14a1,Col16a1,Col18a1,Col4a1,Col4a2,Col4a6,Col5a1,Col5a2,Col5a3,Col6a1,Col6a2,Col6a3,Col8a1,Col8a2,Col9a3,Csk,Ctgf,Ctnna1,Cyp1b1,Cyr61,Cyth3,Dab2,Ddr2,Diap3,Dll1,Dll4,Dst,Efna4,Efna5,Epha2,Epha3,Epha4,Erbb2,Erbb3,Ezr,F2r,F2rl3,Farp1,Fblim1,Fbln1,Fbln2,Fbn1,Fcer1g,Fcgr1,Fermt3,Fes,Fgb,Fgg,Fgr,Flna,Flnc,Flot1,Fn1,Fos,Foxc1,Fpr1,Fyb,Fzd1,Fzd2,Fzd7,Gab2,Git2,Gjc1,Gli2,Gli3,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gsg2,Hand2,Hck,Hes1,Hgf,Hhex,Hp,Hspg2,Icam1,Id3,Igfbp7,Ilk,Irs1,Isl1,Itga11,Itga2,Itga3,Itga4,Itga5,Itga8,Itga9,Itgae,Itgal,Itgam,Itgav,Itgax,Itgb1,Itgb2,Itgb3,Itgb5,Itgb7,Itk,Itpr3,Jak3,Jam3,Jun,Klhl13,L1cam,Lama1,Lama3,Lama4,Lama5,Lamb1,Lamb2,Lamc1,Lamc2,Lat,Lcp2,Lef1,Lgals1,Lgals8,Limk1,Lims1,Lpxn,Ltb4r1,Lum,Lyn,Madcam1,Map2k1,Mapk11,Mef2a,Mef2c,Mkl1,Mmrn1,Msn,Mst1r,Myh10,Myh9,Mzb1,Ncf1,Ncf4,Nck2,Nckap1l,Nfatc4,Npnt,Nrg1,Nrp2,Pak1,Pak3,Parvb,Pde10a,Pde1a,Pde1b,Pde3a,Pde4b,Pde7b,Pdgfa,Pdp1,Pfn1,Pfn2,Phk3cd,Pik3cg,Pik3r3,Pik3r5,Plau,Plcb2,Plcg2,Plec,Plek,Plp1,Plxna4,Postn,Prkacb,Prkcb,Prkcd,Prkcg,Prkg2,Ptafr,Ptgir,Ptpn1,Ptpn6,Pxn,Rac2,Rac3,Rasgrf1,Rasgrp1,Rassf5,Rbpj,Rcn1,Ret,Rhob,Rnd3,Rock2,Ras,S100a9,Sct,Sdc1,Sdc2,Sdc3,Sell,Selp,Selplg,Sema3a,Sema7a,Serpine1,Sfrp2,Snai1,Snai2,Sparc,Sphk1,Spp1,Swap70,Syk,Tbx2,Tbx3,Tcf7,Tec,Tgfb1,Tgfb1i1,Tgfb2,Tgfb3,Tgm2,Thbs1,Tln1,Tnc,Tnfaip1,Trio,Tspan32,Tspan4,Tspan7,Tspan8,Tuba1a,Tuba1b,Tuba1c,Tubb2a,Tubb2b,Tubb4a,Tubb5,Tubb6,Tyrobp,Vangl2,Vasp,Vav1,Vav3,Vcam1,Vcan,Vcl,Vwf,Was,Wasf1,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Wwtr1,Ywhag,Zyx	<1.00E-26
Small GTPase–dependent signaling	1077	424	Adap2,Adrb1,Adrb2,Anapc13,Apol7a,Arfgap3,Arfgef2,Arhgap24,Arhgap26,Arhgap28,Arhgap44,Arhgap5,Arhgdig,Arhgef16,Arhgef19,Arhgef26,Arhgef28,Arhgef37,Arhgef4,Arl1,Arl3,Arl4a,Arl5b,Arl8b,Asap3,Cckar,Cdc25a,Cdc42ep1,Chrm3,Clip1,Cox16,Cyfip2,Cytip,Dgkg,Dvl3,Egf,Eps8l2,Fam13a,Fbxo8,Gbf1,Gng7,Grpr,Grtp1,Hist2h3c1,Hist2h3c2,Igf1,Inpp5b,Iqgap2,Kdm4c,Klk1b24,Klk1b3,Klk1b4,Mapk9,Mcf2l,Mpp2,Myh11,Plk2,Rab25,Rab26,Rab27a,Rab27b,Rab39b,Rab3a,Rab3d,Rab40b,Rab6b,Rabl6,Ralgapa2,Rap1gap,Rap1gap2,Rapgef5,Rapgefl1,Rasef,Rasgef1a,Rhobtb1,Rhoq,Rhot2,Rhov,Rhpn2,Sec23b,Sec31b,Setd6,Sgsm1,Sgsm3,Smarcc2,Srprb,Ssx2ip,Stard13,Stradb,Tbc1d15,Tbc1d16,Tbc1d22b,Tbc1d30,Tbc1d4,Ulk1	A2m,Aatk,Abr,Acap1,Acap3,Actb,Actg1,Actl6a,Actr3,Adap1,Adra2a,Agap2,Agfg1,Aif1,Akap13,Amot,Apitd1,Aplnr,Apoa1,Apoa4,Apob,Apoc3,Apod,Apoe,Apol6,Apol8,Arap1,Arap3,Arf2,Arhgap11a,Arhgap15,Arhgap19,Arhgap22,Arhgap23,Arhgap25,Arhgap27,Arhgap30,Arhgap31,Arhgap43,Arhgap4,Arhgap6,Arhgdia,Arhgdib,Arhgef1,Arhgef10,Arhgef17,Arhgef25,Arhgef3,Arhgef39,Arhgef40,Arhgef6,Arhgef7,Arhgef9,Arl11,Arl4c,Arl8a,Arpc1b,Arpc2,Arpc3,Arpc4,Arpc5,Asap1,Aurkb,B9d2,Bcar3,Bcl6,Birc5,Bnip2,Bub1,Bub1b,Bub3,C5ar1,Camk2d,Capza1,Cbl,Ccna2,Ccr2,Ccr5,Cdc20,Cdc23,Cdc25b,Cdc25c,Cdca8,Cdh13,Cdh2,Cdk1,Cdk2,Cdkn1a,Cenpa,Cenpe,Cenpf,Cenph,Cenpl,Cenpm,Cenpo,Cenpt,Cfl1,Cftr,Chn1,Cit,Ckap5,Csf1,Ctnna1,Cttn,Cxcr3,Cybb,Cyth3,Cyth4,Dbnl,Dennd4b,Depdc1b,Dhcr24,Diap3,Dlg4,Dnajc27,Dnm1,Dock10,Dock11,Dock2,Dock6,Dock8,Dok1,Dok2,Dok3,Dsn1,Ect2,Ednra,Elk1,Elmo1,Eps8,Erbb2,Ercc6l,Evl,F2r,F2rl1,Farp1,Fgd1,Fgd2,Fgd3,Fgd5,Fgd6,Flna,Flot1,Fmnl1,Fmnl2,Fmnl3,Fos,Fpr1,Garnl3,Gem,Git2,Gmip,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gpr37l1,Hdac1,Hmgn3,Hmha1,Hmox1,Hp,Incenp,Iqgap1,Iqgap3,Itga11,Itga2,Itga3,Itga4,Itga5,Itga8,Itga9,Itgav,Itgb1,Itsn1,Kif18a,Kif2c,Kifap3,Klhl13,Klk10,Klk8,Kntc1,Kras,Ksr1,Lat,Limk1,Lpar1,Lpar2,Lrrk1,Lrrk2,Mad1l1,Mad2l1,Map2k1,Mapk11,Mapre1,Mkl1,Mras,Myh10,Myh9,Myo9a,Myo9b,Ncf1,Ncf2,Ncf4,Ndc80,Net1,Ngef,Ngf,Ngfr,Notch2,Notch4,Noxo1,Nras,Nrg1,Nsl1,Ntrk1,Nuf2,Nup107,Nup37,Pak1,Pak3,Pik3cd,Pik3r3,Plekhg1,Plekhg2,Plk1,Plxnb2,Pmf1,Por,Ppp1r8,Prc1,Prokr1,Rab12,Rab13,Rab15,Rab19,Rab20,Rab21,Rab31,Rab32,Rab34,Rab38,Rab3b,Rab44,Rab8b,Rac2,Rac3,Racgap1,Rad51,Ralb,Ralgds,Ran,Rap1b,Rap2a,Rap2b,Rasa2,Rasa3,Rasa4,Rasal3,Rasgef1c,Rasgrf1,Rasgrp1,Rasl11a,Rasl11b,Rassf1,Reln,Rem1,Rem2,Rerg,Rgl1,Rgs19,Rhebl1,Rhob,Rhobtb3,Rhoc,Rhod,Rhog,Rhoh,Rhoj,Rin2,Rnd3,Rock2,Rrad,Rras,S1pr2,S1pr3,Sec23a,Sfn,Sgol1,Sh2b2,Shc2,Sipa1,Sipa1l1,Sipa1l2,Ska1,Ska2,Slit2,Smarcb1,Smarcd1,Smc2,Spc25,Spdl1,Spry1,Spry2,Srgap1,Stard8,Svle1,Tax1bp3,Tbc1d10c,Tiam2,Timp2,Tnfaip1,Trf,Trio,Trp53,Vangl2,Vav1,Vav2,Vav3,Wasf1,Ywhab,Ywhaq,Ywhah,Ywhaz,Zc3h12a	1.30E-09
Apoptosis	1517	553	Acvr1c,Acvr2a,Adcy9,Adora1,Adrb2,Agtr1a,Aifm3,Aktip,Aldh1a1,Alox12,Anapc13,Aph1c,Apip,Aplp1,Asah2,Atf4,Atf5,Atf6,Aven,Bcl2l2,Bmp7,Cacna1a,Camk1d,Cckar,Cd24a,Cd36,Cecr2,Clptm1l,Creb3l1,Cyfip2,Dap,Dapk2,Ddx20,Dedd2,Derl3,Dnajc3,Dsg2,Dsp,Dynll2,Ebag9,Edem1,Eif2ak3,Eif2b1,Eif2b2,Eif2b4,Eif2b5,Eif3k,Eif3m,Eif4ebp1,Elmo3,Endog,Epha7,Ern1,Faf1,Fastkd1,Fbxl4,Fbxo3,Fbxo8,Fgfr3,Foxo4,Fzd3,Fzd4,Gadd45g,Gal,Gcg,Gclm,Ghrl,Glrx2,Gnai1,Gng7,Grpr,Gsn,H13,H1f0,Herpud1,Hist1h1c,Hist1h1d,Hist1h1e,Hist1h2be,Htra2,Ig1,Ins2,Insr,Irak1,Itpr2,Lgals12,Map3k5,Mapk8ip1,Mapk9,Mapt,Metap2,Mgmt,Napa,Ndufa1,Ndufa13,Ndufa6,Ndufa9,Ndufb11,Ndufb2,Ndufb4,Ndufb5,Ndufb6,Ndufb8,Ndufb9,Ndufc1,Ndufs5,Ndufs6,Ndufs7,Ndufv3,Nme2,Nmnat3,Nr3c1,Ntn1,Nupr1,Ocln,P2rx1,Pawr,Pdcd4,Pdia6,Pdk2,Perp,Pim2,Plcb1,Plekhf1,Ppib,Ppp2r5a,Prdx4,Prkce,Prkcz,Psen2,Rab27a,Rec8,Rffl,Rfk,Rhot2,Rps6,Rps6kb1,Sarm1,Serinc3,Sgk1,Sirt2,Sirt5,Stradb,Syp,Syt7,Syvn1,Thop1,Trd52l1,Tnt1,Triap1,Tuba4a,Ube4b,Unc5a	Aatk,Actn4,Ada,Adamtsl4,Adcy2,Adcy3,Adcy7,Add1,Add2,Adora2a,Agap2,Ahr,Akt3,Aldh1a3,Angptl4,Apaf1,Aplnr,Apoe,Arhgdib,Arhgef7,Atp7a,B4galt1,Bag3,Bak1,Bax,Bcap29,Bcar1,Bcl2a1a,Bcl2a1b,Bcl2l1,Bcl2l11,Bcl3,Bcl6,Bcl7c,Bid,Birc5,Blcap,Blm,Bnip2,Brca1,Btc,Btk,Bub1b,C5ar1,Cadm1,Calm2,Capn1,Capn2,Card11,Card9,Casp1,Casp12,Casp3,Casp4,Casp7,Casp8,Cbl,Ccnb1,Ccnb2,Ccne1,Ccr2,Ccr5,Cd3e,Cd3g,Cd4,Cd40,Cd74,Cdc20,Cdc23,Cdk1,Cdk5rap2,Cdkn1a,Cebpb,Cenpf,Cfr,Chek1,Chrnb1,Chst11,Ckap2,Clca2,Clip3,Clspn,Col18a1,Creb3l3,Csf2,Csf2rb,Csf2rb2,Csn3,Csnp1,Csrnp2,Ctnna1,Ctnnbl1,Ctsb,Ctsc,Ctsh,Ctso,Ctss,Cx3cl1,Cx3cr1,Cxcr3,Cybb,Dbnl,Dhcr24,Dlg4,Dnase1l3,Dok1,Dynll1,E2f1,Ednra,Egln3,Egr1,Egr3,Elk1,Elmo1,Elmo2,Endod1,Erap1,Erbb2,Erbb3,Ercc1,Espl1,Eya2,F2r,F2rl1,Fap,Fbxo5,Fcer1g,Fcgr1,Fcgr3,Fos,Foxc1,Fpr1,Fzd1,Fzd2,Fzd7,G2e3,Gadd45a,Gapdh,Gas2,Gdnf,Ggct,Gli2,Gli3,Glrx,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gpr37l1,Gpr65,Grik2,Grin2d,Gsr,Gulp1,Gzmb,H1fx,H2afx,Hand2,Hbegf,Hdac1,Hells,Hgf,Hif1a,Hip1,Hist1h2bj,Hmgb2,Hmox1,Hp,Hspa14,Hspa1b,Hspa2,Hspa8,Id3,Ido1,Ier3,Ifi204,Ifih1,Ifnar1,Ifngr1,Ifngr2,Igfbp3,Il18,Il1r1,Il1rap,Il2rb,Il3ra,Ilk,Inhba,Inpp5d,Irf1,Irf5,Irs1,Itgb1,Itpr3,Itsn1,Jak3,Jun,Klf10,Kras,Krt18,Krt20,Ksr1,Leprot,Lgals3,Lgals7,Lmna,Lmnb1,Lmnb2,Lrp1,Lrrk2,Lsp1,Lst1,Ltb,Map1s,Map2k1,Map3k3,Map4k4,Mapk11,Mapk7,Mef2a,Mef2c,Mfsd10,Mkl1,Mmp9,Mnt,Msx1,Muc2,Mybl2,Myd88,Myo5a,Naip5,Nbl1,Ncf1,Ncf2,Ncf4,Nefl,Nek6,Nfkb2,Nfya,Ngf,Ngfr,Nlrc4,Nmt2,Notch2,Nr4a1,Nras,Nrg1,Ntrk1,Nuak2,P2rx7,Pak1,Pcsk9,Pdia3,Pdp1,Pea15a,Peg10,Pglyrp1,Phlda1,Phlda3,Pik3cd,Pik3cg,Pik3r3,Pik3r5,Pim1,Pla2g4a,Plec,Plscr1,Pmaip1,Ppp2r2a,Ppp2r2b,Prdx1,Prdx2,Prkacb,Prkar1a,Prkar1b,Prkar2b,Prkcb,Prkcd,Prkcg,Prnd,Prnp,Prokr1,Prtn3,Prune2,Psap,Ptgis,Ptpn6,Ptprc,Rac2,Rad51,Rarb,Rarg,Rassf5,Rel,Relb,Rhob,Ripk3,Rock2,Rps6ka4,Rtn4,Runx3,Sept4,Serpina3g,Serpinb9,Sfn,Sgpl1,Shf,Shisa5,Shkbp1,Skil,Skp2,Slc25a4,Slc9a1,Smo,Snai2,Sp110,Sphk1,Spn,Spp1,Sptan1,Srgn,Stat3,Steap3,Stil,Stk17b,Sulf1,Tbx3,Tcf7,Tgfb1,Tgfb2,Tgfb3,Tgfbr1,Tgfbr2,Tgm2,Thbs1,Ticam2,Timp3,Tinagl1,Tlr3,Tlr4,Tmem173,Tnfaip3,Tnfrsf10b,Tnfrsf11a,Tnfrsf11b,Tnfrsf12a,Tnfrsf14,Tnfrsf19,Tnfrsf1a,Tnfrsf1b,Tnfrsf21,Tnfrsf4,Tnfsf11,Tnfsf13,Tnfsf13b,Tnfsf8,Tnfsf9,Top2a,Traf1,Traf5,Traf7,Traip,Trex1,Trim35,Trp53,Trpm2,Tuba1a,Tuba1b,Tuba1c,Twist1,Ube2c,Ube2n,Unc13d,Unc5b,Uox,Usp18,Vav1,Vcam1,Vdr,Vim,Vip,Xaf1,Xdh,Xrcc4,Ywhab,Ywhag,Ywhah,Ywhaz,Zc3h12a	1.54E-06
Ras signaling	874	330	Adap2,Adrb1,Adrb2,Akap9,Angpt1,Apol7a,Arfgap3,Arfgef2,Arhgap24,Arhgap5,Arhgdig,Arhgef16,Arhgef19,Arhgef26,Arhgef28,Arhgef37,Arhgef4,Asap3,Cckar,Cdc42ep1,Chrm3,Cox16,Cytip,Dgkg,Egf,Eps8l2,Fbxo8,Fgfr3,Foxo4,Gbf1,Gng7,Grpr,Grtp1,Hnf1a,Igf1,Itpr2,Kit,Klb,Lamtor2,Mapk9,Mcf2l,Mpp2,Plk2,Ppp2r5a,Psmb10,Psmd6,Psme4,Rab25,Rab26,Rab27a,Rab27b,Rab39b,Rab3a,Rab3d,Rab40b,Rab6b,Ralgapa2,Rapgef5,Rasef,Rasgef1a,Rps27a,Rps6ka6,Rps6kb1,Setd6,Sgsm1,Sgsm3,Sptbn2,Ssx2ip,Stradb,Tbc1d15,Tbc1d16,Tbc1d22b,Tbc1d30,Tbc1d4,Tek,Toh1,Uba52,Ulk1	Aatk,Abr,Acap1,Acap3,Adap1,Adra2a,Agap2,Agfg1,Aif1,Akap13,Akt3,Aplnr,Apoa1,Apoa4,Apob,Apoc3,Apod,Apoe,Apol6,Apol8,Arap1,Arap3,Arhgap27,Arhgap4,Arhgap6,Arhgdia,Arhgdib,Arhgef1,Arhgef10,Arhgef17,Arhgef25,Arhgef3,Arhgef39,Arhgef40,Arhgef6,Arhgef7,Arhgef9,Artn,Asap1,B2m,Bax,Bcar1,Bcl2l1,Bcl6,Btc,C5ar1,Calm2,Camk2d,Ccna2,Ccnd1,Ccne1,Ccr2,Ccr5,Cd3e,Cd3g,Cd4,Cdh13,Cdk1,Cdk2,Cdk4,Cdkn1a,Cebpb,Cfl1,Csf1,Csf2,Csf2ra,Csf2rb,Csf2rb2,Cxcr3,Cyth3,Cyth4,Dbnl,Dennd4b,Dhcr24,Dlg4,Dnajc27,Dnm1,Dock2,Dok1,Dok2,Dok3,Dusp5,Dusp6,Dusp7,Dusp9,E2f1,Ect2,Ednra,Elk1,Elmo1,Elmo2,Eps8,Erbb2,Erbb3,Ereg,F2r,F2rl1,Farp1,Fgd1,Fgd2,Fgd3,Fgd5,Fgd6,Fgfr4,Flot1,Fos,Fpr1,Gdnf,Gfra1,Gfra2,Git2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gpr37l1,Grin2d,Hbegf,Hp,Il18,Il2rb,Il2rg,Il3ra,Iqgap3,Irs1,Itga11,Itga2,Itga3,Itga4,Itga5,Itga8,Itga9,Itgav,Itgb1,Itpr3,Itsn1,Jak3,Jun,Kifap3,Klhl13,Kras,Ksr1,Lat,Limk1,Lpar1,Lpar2,Map2k1,Mapk11,Mapkapk2,Mras,Myo9b,Ncam1,Nefl,Net1,Ngef,Ngf,Ngfr,Notch2,Notch4,Nras,Nrg1,Ntrk1,Pak1,Pak3,Pdgfa,Pdgfra,Pdgfrb,Pea15a,Pik3cd,Pik3r3,Plau,Plekhg1,Plekhg2,Prokr1,Psma5,Psmb8,Psmb9,Psmd11,Psmd14,Psme1,Psme2,Ptpn6,Pxn,Rab12,Rab13,Rab15,Rab19,Rab20,Rab21,Rab31,Rab32,Rab38,Rab3b,Rab44,Rab8b,Ralb,Ralgds,Rap1b,Rap2a,Rap2b,Rasa2,Rasa3,Rasa4,Rasal3,Rasgrf1,Rasgrp1,Rassf1,Ret,Rgl1,Rgs19,Rhob,Rhod,Rhog,Rhoj,Rin2,Rock2,Rras,S1pr2,S1pr3,Sfn,Sh2b2,Shc2,Skp2,Slc2a1,Smc2,Snai1,Spred1,Spry1,Spry2,Sptan1,Srgap1,Stat3,Syde1,Tax1bp3,Tbc1d10c,Thbs1,Tiam2,Timp2,Tnfaip1,Trio,Trp53,Vangl2,Vav1,Vav2,Vav3,Wasf1,Ywhab,Ywhag,Ywhah,Ywhaz	7.92E-06

Regulation of invasion	2204	763	Acrbp,Acvr1c,Adam33,Adi1,Adrb1,Adrb2,Aga,Agtpbp1,Aifm3,Alox12,Anapc13,Ang,Anpep,Ap1g2,Ap1m2,Ap1s3,Aph1c,Apol7a,Apopt1,Appl2,Asb11,Asb13,Asb16,Asb8,Asrgl1,Atg4c,Atg4d,Aup1,Aurkaip1,Bckdha,Bckdhb,Brcc3,C1rl,C7,Capn13,Capn9,Cckar,Cdc34,Cdk5rap3,Cfd,Chac1,Chmp4c,Chrm3,Chst2,Cish,Clec3b,Clock,Clpx,Col7a1,Cpa2,Cpn1,Crbn,Cryab,Cst3,Cuzd1,Cyfip2,Dap,Dbt,Ddrgk1,Derl3,Dnajb9,Dnajc1,Dnajc3,Dnpep,Dpp7,Dpp9,Dtx1,Dvl3,Ece2,Edem1,Edem2,Edem3,Egf,Egln2,Eif2ak3,Eif3k,Eif3m,Epha7,Erlec1,Ero1lb,Faf1,Fbxl16,Fbxl4,Fbxo16,Fbxo3,Fbxo36,Fbxo8,Fbxo9,Fem1a,Fgl2,Fhl1,Foxred2,Fxn,Gabarapl2,Gca,Ggt1,Ggta1,Glrx2,Gm10334,Gm15800,Gpld1,Grpr,Gsn,H13,Habp2,Hba_a1,Hdac10,Hdac5,Herpud1,Hgfac,Hpn,Htra2,Igf1,Immp1l,Immp2l,Inpp5b,Ins1,Ins2,Itih2,Itih4,Kcmf1,Klhl3,Klhl8,Klk1,Klk1b11,Klk1b24,Klk1b3,Klk1b4,Klk1b5,Klk1b8,Lnx2,Lonrf2,Lrp4,Map3k5,Mapk9,March2,March5,March8,March9,Mbp,Metap1d,Metap2,Mgmt,Mpc2,Mpnd,Mvb12a,Myh11,Myrf,Ndufa1,Ndufa13,Ndufa6,Ndufa9,Ndufb11,Ndufb2,Ndufb4,Ndufb5,Ndufb6,Ndufb8,Ndufb9,Ndufc1,Ndufs5,Ndufs6,Ndufs7,Ndufv3,Nhlrc1,Nr1h3,Nr3c1,Nrd1,Oma1,Os9,Osbp2,Osbpl1a,Osgepl1,Otub2,Otud3,P2rx1,P4hb,Pawr,Pcsk1,Pcsk1n,Pcsk2,Pcsk6,Perp,Pgc,Pgpep1,Pias2,Pink1,Plk2,Pm20d1,Pm20d2,Pmpcb,Ppara,Ppp2r5a,Prdx4,Prkce,Prkcz,Prss1,Prss3,Prss36,Prss53,Prss8,Psen2,Psmb10,Psmd6,Psme4,Ptpn3,Qpctl,Rab40b,Rad23a,Rchy1,Rec8,Rffl,Rgn,Rhbdd1,Rhbdl1,Rilp,Rnf125,Rnf128,Rnf167,Rnf185,Rnf187,Rnf43,Rnf5,Rnpepl1,Rps27l,Scg5,Scrn2,Scrn3,Sdf2l1,Sec11c,Sec61b,Sec61g,Sel1l,Serpina10,Serpinb1a,Serpini1,Serpini2,Sirt2,Sirt5,Smarcc2,Snurf,Socs7,Spcs1,Spcs2,Spcs3,Spint1,Spint2,Svip,Syp,Syvn1,Taf9b,Tasp1,Thop1,Tinag,Tmem208,Tmem27,Tom1,Tom1l1,Tpd52l1,Triap1,Trim50,Try10,Tuba4a,Uba5,Uba52,Ube2cbp,Ube2f,Ube2h,Ube4a,Ube4b,Ubxn2a,Uchl5,Ufc1,Ufl1,Ufm1,Ufsp1,Ufs	A2m,Acan,Ace,Actb,Actl6a,Adam15,Adam23,Adam8,Adam9,Adamdec1,Adamts1,Adamts12,Adamts14,Adamts15,Adamts16,Adamts2,Adamts4,Adamts6,Adamts7,Adamts8,Adamtsl1,Adamtsl2,Adamtsl4,Adora2a,Adora2b,Adra2a,Aebp1,Aim2,Akt3,Amz1,Anxa8,Ap1m1,Ap1s2,Apaf1,Aplnr,Apoa1,Apoa4,Apob,Apoc3,Apod,Apoe,Apol6,Apol8,Arrb2,Asph,Aurka,Aurkb,Bak1,Bax,Bcl2l1,Bcl2l11,Bid,Birc5,Brca1,Bst2,Bub1,Bub1b,Bub3,C1qa,C1qb,C1qc,C1ra,C2,C3,C4b,C5ar1,C6,Camp,Capn1,Capn2,Capn6,Capns1,Card11,Casp1,Casp12,Casp3,Casp4,Casp7,Casp8,Cast,Cbl,Cblc,Ccbe1,Ccnb1,Ccnb2,Ccne1,Ccnf,Ccr2,Ccr5,Cd109,Cd14,Cd44,Cdc20,Cdc23,Cdc6,Cdca3,Cdk1,Cdk2,Cdkn2d,Cebpb,Cenpe,Cenpf,Cfb,Cfh,Cfi,Cfp,Chd7,Chst1,Chst3,Chst7,Chst8,Cit,Clca2,Clec4a3,Cma2,Cndp2,Col14a1,Col16a1,Col18a1,Col4a1,Col4a2,Col4a6,Col6a1,Col6a2,Col6a3,Cpne1,Cpxm1,Cpz,Csn3,Csnk1e,Csnk1g3,Ctgf,Ctla2a,Ctla2b,Ctsb,Ctsc,Ctse,Ctsh,Ctsk,Ctso,Ctss,Ctsw,Ctsz,Cuedc2,Cxcr3,Cyr61,Dab2,Dcaf15,Dhcr24,Dhh,Dlgap5,Dll1,Dnajc10,Dtl,Dtx3,Dtx3l,Dzip3,Ecm1,Ednra,Egln3,Eln,Epha2,Epha3,Epha4,Erap1,Ermp1,Espl1,Ezr,F10,F2r,F2rl1,F3,F5,F7,Fabp7,Fap,Fbln1,Fbxl19,Fbxl7,Fbxl8,Fbxo4,Fbxo5,Fgb,Fgfr4,Fgg,Fmod,Fn1,Fpr1,G2e3,Ggt7,Glg1,Gli3,Glrx,Gm2663,Gpr37l1,Grn,Gzmb,Hdac1,Hdac7,Hfe,Hgf,Hip1,Hp,Hspa14,Hspa1b,Hspa2,Hspa8,Htra1,Igfbp7,Il33,Irf9,Isg15,Itgb5,Itih5,Jun,Kctd10,Kirrel3,Klhl13,Klk10,Klk8,Kng2,Lama1,Lama3,Lamb1,Lamc1,Lamc2,Lef1,Lgals9,Lgmn,Lpar4,Lrp1,Lrp8,Lrrk2,Ltf,Lum,Mad1l1,Mad2l1,Mafg,Mapk11,March1,Masp1,Mcpt1,Mcpt2,Mcpt8,Mep1b,Mical1,Mkl1,Mmp10,Mmp11,Mmp12,Mmp13,Mmp14,Mmp16,Mmp17,Mmp19,Mmp2,Mmp23,Mmp3,Mmp7,Mmp9,Mnda,Mpdz,Msn,Mtbp,Myh10,Myh9,Naalad2,Napsa,Nek2,Nek6,Neurl3,Nfe2l2,Nfkb2,Ngf,Ngfr,Ngp,Nid1,Nkd2,Nlrc4,Nmt2,Notch2,Notch4,Nr4a1,Olr1,Osbpl11,P2rx7,P2ry1,P2ry2,P2ry6,P4ha1,P4ha2,P4ha3,Pam,Pappa,Pbk,Pcolce,Pcsk5,Pcsk9,Pdia3,Pdp1,Peg10,Pi15,Pik3r3,Pim1,Plat,Plau,Plaur,Plk1,Plk3,Pmaip1,Por,Ppp1r8,Ppp2r2a,Ppp2r2b,Prcp,Prdx1,Prdx2,Prep,Prkacb,Prkcb,Prkcd,Prkcg,Prokr1,Pros1,Prss12,Prss27,Prss32,Prss35,Prtn3,Psap,Psma5,Psmb8,Psmb9,Psmd14,Psme1,Psme2,Ptch2,Pthlh,Ptpn23,Pwp2,Qpct,Rbbp7,Rbmxl1,Rbp1,Rbpj,Reck,Rel,Relb,Reln,Renbp,Rest,Ret,Rgs19,Rin2,Rnf217,Robo1,Ruvbl2,S100a9,Sae1,Scpep1,Sec61a2,Sept5,Serpina3g,Serpinb2,Serpinb5,Serpinb6b,Serpinb9,Serpinb9b,Serpine1,Serpinf1,Serping1,Serpinh1,Sfn,Sfrp1,Sfrp2,Sh3rf1,Sin3b,Skp2,Smarcb1,Smarcd1,Smc5,Smurf1,Socs1,Socs3,Socs5,Sox2,Sp100,Sparc,Spink4,Spp1,Sppl3,Spsb1,Spsb4,Srgn,Stat1,Stat2,Stil,Sufu,Tcf7,Tec,Tenm3,Tenm4,Tfap2c,Tfpi,Tfpi2,Tgfb1i1,Thbs1,Ticam2,Timp2,Timp3,Tinagl1,Tll1,Tlr3,Tlr4,Tmprss4,Tmprss5,Tnc,Tnfaip1,Tnfaip3,Tnfrsf10b,Tnfrsf1b,Top2a,Tpsb2,Trabd2b,Traf7,Trf,Trib1,Trib2,Trim21,Trp53,Trpm2,Ttc3,Ttk,Tuba1a,Tuba1b,Tuba1c,Tubb2a,Tubb2b,Tubb4a,Tubb5,Tubb6,Tubg1,Uba7,Ube2c,Ube2d1,Ube2e2,Ube2l6,Ube2n,Ube2ql1,Ube2s,Ube2t,Uchl1,Uhrf1,Unc5cl,Urm1,Usp11,Usp13,Usp18,Usp35,Vps37d,Wfdc2,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Wsb1,Wwtr1,Xdh,Ywhab,Ywhag,Ywhah,Ywhaz,Zfand2a,Znrf1	7.55E-05
Hedgehog signaling	666	249	Adcy9,Adrb1,Adrb2,Aldh1a7,Aldh2,Aph1c,Apol7a,Bmp6,Bmp7,Bmpr1b,Cyp2c65,Dvl3,Dync2h1,Epha7,Erlec1,Fktn,Foxa2,Fzd3,Fzd4,Gata4,Gbgt1,Gnai1,Gng7,Hnf1a,Hnf1b,Htra2,Igfbp6,Lefty1,Lifr,Ltk,Map7,Mapk8ip1,Mpp2,Mtss1,Muc1,Muc5ac,Mycn,Ncoa1,Ndufa1,Ndufa13,Ndufa6,Ndufa9,Ndufb11,Ndufb2,Ndufb4,Ndufb5,Ndufb6,Ndufb8,Ndufb9,Ndufc1,Ndufs5,Ndufs6,Ndufs7,Ndufv3,Nkx2-2,Nkx6-1,Nr1h3,Nr1h4,Os9,P4hb,Plcb1,Plcb4,Ppara,Psen2,Psmb10,Psmd6,Psme4,Rora,Rpl36al,Rps27a,Sel1l,Slc6a4,Sst,Syvn1,Tead2,Tek,Thra,Thrb,Tuba4a,Uba52	Acvr1,Adcy2,Adcy3,Adcy7,Add1,Add2,Apoa1,Apoa4,Apob,Apoc3,Apod,Apoe,Apol6,Apol8,Arrb2,Bmp2,Ccl2,Ccna2,Ccnb1,Ccnd1,Cd38,Cdc25c,Cdk1,Cdk19,Cdkn1a,Cdkn2d,Chd7,Cntfr,Col11a1,Csnk1e,Csnk1g3,Ctgf,Ctsh,Dab2,Dhh,Disp2,Dusp1,Dzip1,Egr1,Eln,Epha2,Epha3,Epha4,Evc,Evc2,Eya2,Ezh2,Flna,Fos,Foxc1,Fzd1,Fzd2,Fzd7,Gata2,Gata5,Gli1,Gli2,Gli3,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Grem1,Hand2,Hdac1,Hes1,Hhat,Hoxa2,Id3,Igfbp2,Igfbp3,Igfbp4,Igfbp7,Inhba,Irf1,Itgb3,Kif7,Lef1,Lyn,Map2k1,Mapk11,Mdk,Mef2a,Mef2c,Mest,Mmp13,Mmp2,Mmp9,Msx1,Nab2,Nr2f2,Osr1,Pdgfa,Pdgfra,Pdgfrb,Phc2,Pik3cg,Pik3r5,Plcb2,Prkacb,Prkar1a,Prkar1b,Prkar2b,Psma5,Psmb8,Psmb9,Psmd1,Psmd14,Psme1,Psme2,Ptch2,Ptges,Pth1r,Pthlh,Rara,Rarb,Rarg,Rbbp7,Rbp1,Rbp4,Rbpj,Ret,Ripk3,Rock2,Runx1,Runx2,Serpinf1,Sin3b,Skp2,Smo,Smurf1,Snai1,Sox2,Sp100,Spp1,Sufu,Tbx2,Tcf3,Tead1,Tgfb1,Tgfb2,Tgfb3,Tlr4,Tnc,Tnfsf11,Trp53,Ttf2,Tuba1a,Tuba1b,Tuba1c,Tubb2a,Tubb2b,Tubb4a,Tubb6,Tulp3,Twf2,Vdr,Wdr19,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Xpo1,Zeb1,Zfp105	1.92E-04
c-Jun N-terminal kinase signaling	460	175	Arhgef16,Arhgef4,Cbs,Cckar,Dixdc1,Dusp22,Dvl3,Epha7,Ern1,Fktn,Fzd3,Fzd4,Gadd45g,Gnai1,Gng7,Grpr,Gstp2,Ins2,Irak1,Magi3,Map3k13,Map3k5,Map3k9,Mapk8ip1,Mapk9,Marveld3,Mcf2l,Mecom,Nphs1,Pdcd4,Pink1,Plcb1,Plcb4,Prkce,Sstr2,Stradb,Tnxb,Tpd52l1,Uba52	Abr,Adora2a,Adora2b,Ager,Akap13,Akt3,Aplnr,Arhgap4,Arhgef1,Arhgef17,Arhgef3,Arhgef6,Arhgef7,Arhgef9,Bcl2l11,Blnk,Btk,C3ar1,C5ar1,Calm2,Card11,Card9,Ccr2,Ccr5,Ccr7,Csn3,Ctgf,Cx3cr1,Cxcr3,Dab2,Dact1,Dbnl,Dusp10,Dusp9,Ect2,Eda2r,Ednra,Elk1,Epha2,Epha3,Epha4,Ephb2,Ephb3,Ephb6,F2r,F2rl1,Fcer1g,Fgd1,Fgd2,Fgd3,Flt4,Fpr1,Fzd1,Fzd2,Fzd7,Gab2,Gadd45a,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gpr37l1,Gria3,Grik2,Grik3,Hdac1,Igfbp7,Itsn1,Jun,Lmnb1,Lmnb2,Lpar4,Map2k1,Map3k3,Map3k6,Map3k8,Map4k1,Map4k4,Mapk11,Mdfi,Mdfic,Mef2a,Mef2c,Myd88,Net1,Ngef,Ngf,Ngfr,P2ry1,P2ry2,P2ry6,Pak1,Pik3cg,Pik3r5,Plcb2,Plekhg2,Prkcb,Prokr1,Ptgir,Ptpn1,Ptpn22,Rap2a,Rasgrp1,Sfrp1,Sfrp2,Sfrp4,Sh3rf1,Syk,Tiam2,Tlr3,Tlr4,Tlr6,Tlr9,Tnfrsf11a,Tnfrsf19,Tnfrsf1a,Tnfsf11,Tnik,Trf,Trib1,Trio,Trp53,Unc5cl,Vangl2,Vav1,Vav2,Vav3,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Zeb2	5.83E-04
TGF-b signaling	332	127	Acvr1c,Acvr2a,Bmp6,Bmp7,Bmpr1b,Cdk8,Cgn,Fkbp2,Igf1,Irak1,Lefty1,Mapk9,Mecom,Ocln,Plcb1,Plcb4,Prkce,Prkcz,Rps27a,Rps6kb1,Taz,Tfdp2,Tob1,Uba52,Zfyve9	Actb,Actg1,Acvr1,Akt3,Arrb2,Bmp2,Cbl,Cdh2,Cdk2,Cdk4,Cdkn1a,Cdkn2b,Cfl1,Cltr,Chrd,Dab2,Dok1,Egr1,Elk1,Eng,Erbb2,Ets1,Etv1,Fkbp1a,Fn1,Fos,Fosb,Fosl2,Fst,Hdac1,Hgf,Hif1a,Hmga2,Id3,Id4,Ilk,Inhba,Inhbb,Irf7,Irs1,Itgal,Itgam,Itgav,Itgax,Itgb1,Itgb2,Itgb3,Jun,Junb,Klf10,Lef1,Lims1,Ltbp1,Map2k1,Mkl1,Mmp2,Mmp9,Nfkb2,Notch4,Nox4,Pdgfa,Pdgfra,Pdgfrb,Plcb2,Pmepa1,Prkcb,Prkcd,Prkcg,Ptges,Rbl1,Rel,Relb,Rock2,Runx2,Serpine1,Skil,Smurf1,Snai1,Snai2,Star,Tcf3,Tgfb1,Tgfb1i1,Tgfb2,Tgfb3,Tgfbr1,Tgfbr2,Tgif1,Tgif2,Thbs1,Thbs2,Thbs3,Thbs4,Tpm1,Trp53,Twist1,Ube2d1,Vav1,Vcl,Vim,Wwtr1,Zeb1	2.21E-03
Wnt/Notch signaling	1234	420	Adcy9,Adrb1,Adrb2,Aes,Alg3,Amer1,Amotl2,Aph1c,Atf4,Atf6,Atp6v0b,Bmp7,Ccdc88c,Cd24a,Cdk8,Celsr2,Cfd,Chac1,Chrm3,Creb3l1,Cryab,Cux1,Cxxc4,Dact2,Dixdc1,Dtx1,Dvl3,Eda,Egf,Eif4ebp1,Fgfr3,Fhl1,Foxa2,Foxa3,Fzd3,Fzd4,Gata4,Gdpd5,Gnai1,Gnat2,Gng7,Hba_a1,Hdac10,Hdac5,Hes7,Hist1h4h,Hnf1a,Hnf1b,Ift20,Il11ra1,Ins2,Irak1,Itpr2,Kat2b,Kdr,Lfng,Lgr4,Lifr,Lnx2,Lrp4,Map2,Mapk9,Mcc,Mknk1,Myh11,Nr0b2,Nr1h4,Onecut1,Ovol2,Perp,Pip5k1b,Plcb1,Plcb4,Ppp2r5a,Prkaa2,Psen2,Psmb10,Psmd6,Psme4,Ptp4a3,Rfng,Rilp,Rnf43,Rps27a,Rps6,Rps6kb1,Rspo1,Sel1l,Slc35c2,Smarcc2,Sostdc1,Sstr2,Stk11,Syp,Tfdp2,Tle2,Tmed2,Tspan5,Uba52,Uty,Vit,Vtn,Wwox,Zbtb33,Zfyve9	Actb,Actg1,Actl6a,Actn1,Actn4,Actr3,Adcy2,Adcy3,Adcy7,Adm,Adra2a,Akap12,Akt3,Angpt4,Apcdd1,Aplnr,Areg,Arnt2,Arpc1b,Arpc2,Arpc3,Arpc4,Arpc5,Arrb2,Aspm,Atp6v0a4,Atp6v0d2,Atp6v0e2,Batf,Batf3,Bcar1,Bcl6,Bend6,Bicc1,Birc5,Bmp2,C3ar1,C5ar1,Calm2,Camk2d,Car9,Ccna2,Ccnb1,Ccnd1,Ccne1,Ccr7,Cd4,Cd44,Cdh2,Cdh3,Cdh6,Cdk14,Cdkn1a,Cdkn2b,Cebpb,Cfl1,Chd7,Cntfr,Cntn6,Col4a1,Col4a2,Col4a6,Cpz,Creb3l3,Creb5,Csnk1e,Csnk1g3,Cthrc1,Cx3cr1,Daam2,Dab2,Dact1,Dact3,Depdc1b,Dhh,Dkk2,Dkk3,Dlk1,Dll1,Dll4,Dok2,Dtx3,Dtx3l,E2f1,E2f3,Efnb1,Efnb2,Egr1,Epn2,Erbb2,Erbb3,Ereg,Erh,F3,Fbn1,Fbxo4,Flna,Fn1,Fos,Foxc1,Foxs1,Fpr1,Frzb,Fzd1,Fzd2,Fzd7,Gata2,Gata5,Gjc1,Gli1,Gli2,Gli3,Gnai2,Gnb1,Gnb4,Gng10,Gng11,Gng2,Gprc5b,Grem1,Grk5,Gzmb,Hand2,Havcr2,Hbegf,Hdac1,Hdac7,Hes1,Heyl,Hhex,Hic1,Hif1a,Hp,Id3,Il1r1,Il2rb,Il2rg,Ilk,Isl1,Itga3,Itga4,Itga5,Itgb1,Itpr3,Jdp2,Jun,Klhl13,Kremen1,Krt19,Lama1,Lamb1,Lamc1,Lef1,Lgr6,Limk1,Lpar1,Lrp1,Lrp5,Maml2,Map2k1,Mapk11,Mapk6,Mark1,Mdfi,Mdfic,Mdk,Mef2a,Mef2c,Mfap5,Mfng,Mkl1,Mmp13,Mmp2,Mmp7,Mov10,Mpdz,Myh10,Myh9,Neurl3,Nfatc4,Nfkb2,Nkd2,Notch2,Notch4,Nphp3,Nrcam,Nrg1,Nrp2,Numbl,Osmr,Pak1,Pcna,Pdgfa,Pdgfc,Pdgfra,Pdgfrb,Pdp1,Peg12,Pfn1,Pik3cd,Pik3r3,Plat,Plau,Plaur,Plcb2,Plcg2,Postn,Ppap2a,Ppp2r2a,Ppp2r2b,Prickle1,Prkacb,Prkar1a,Prkar1b,Prkar2b,Prkcb,Prkcg,Prkg2,Psma5,Psmb8,Psmb9,Psmd1,Psmd14,Psme1,Psme2,Ptpn6,Ptpro,Pxn,Pygo1,Rac2,Rac3,Rara,Rarb,Rarg,Rbbp7,Rbp1,Rbpj,Rcn1,Rcn2,Reck,Rel,Relb,Rest,Rock2,Rspo4,Ruvbl2,S1pr2,S1pr3,Sdc1,Serpine1,Serping1,Sfrp1,Sfrp2,Sfrp4,Sin3b,Skp2,Slc2a1,Smarcb1,Smarcd1,Smo,Smurf1,Snai1,Snai2,Sox2,Sox4,Stat3,Sulf1,Sulf2,Tax1bp3,Tbx2,Tbx3,Tcf12,Tcf3,Tcf4,Tcf7,Tcirg1,Tgfb1,Tgfb1i1,Tgfb2,Tgfb3,Tgfbr1,Tgfbr2,Thbs1,Tle3,Tle4,Tln1,Tlr2,Tmem100,Tmem237,Tnfaip1,Tnik,Trabd2b,Trp53,Tsku,Tspan14,Vangl1,Vangl2,Vav1,Vcan,Vcl,Vim,Wif1,Wisp1,Wisp2,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Wwtr1,Xpo1	1.05E-02
Regulation of G1/S phase transition	513	177	Anapc13,Cables1,Cdc25a,Cdc34,Cryab,Ctdspl,Dgkg,Eif4ebp1,Fhl1,Gfi1,Lin37,Muc1,Myo16,Pim2,Plcb1,Plcb4,Plk2,Ppp2r5a,Psmb10,Psmd6,Psme4,Rps27l,Rps6,Rps6kb1,Smarcc2,Susd2,Taf9b,Tfdp2,Tob1,Tram1,Triap1,Uba52,Zfyve9	Actb,Actl6a,Acvr1,Aif1,Akt3,Anapc15,Anxa1,Atrip,Bcat1,Bid,Bim,Bmyc,Brca1,Bub1b,Bub3,Camk2d,Ccna2,Ccnb1,Ccnb2,Ccnd1,Ccne1,Cdc20,Cdc23,Cdc25b,Cdc25c,Cdc45,Cdc6,Cdc7,Cdca5,Cdk1,Cdk2,Cdk4,Cdkn1a,Cdkn2b,Cdkn2c,Cdkn2d,Cdkn3,Chek1,Cks1b,Clspn,Crlf3,Dact1,Dbf4,E2f1,E2f3,E2f7,Ezh2,Fbxo4,Fbxo5,Fos,Gadd45a,Gpr132,Gsg2,Gtse1,Hdac1,Id4,Inhba,Inhbb,Iqgap3,Itga11,Itga2,Itga3,Itga4,Itga5,Itga8,Itga9,Itgav,Itgb1,Jun,Junb,Klf10,Klhl13,Larp7,Lin9,Map2k1,Mcm10,Mcm2,Mcm3,Mcm4,Mcm5,Mcm6,Mcm7,Mtbp,Mybl2,Nfatc4,Nfkb2,Orc1,Orc6,Pak1,Pcna,Pdpn,Pid1,Pik3cd,Pik3r3,Pim1,Pkmyt1,Plcb2,Plk1,Plk3,Pola1,Pola2,Pole,Pole2,Ppp2r2a,Ppp2r2b,Prim1,Prim2,Psma5,Psmb8,Psmb9,Psmd14,Psme1,Psme2,Ptpn6,Rbbp7,Rbl1,Rcc1,Rel,Relb,Rock2,Rpa2,Rpa3,Rrm1,Rrm2,Skp2,Slfn1,Smarcb1,Smarcd1,Sox4,Stat3,Stxbp4,Tcf3,Tgfb1,Tgfb2,Tgfbr1,Tgfbr2,Tnfaip1,Top2a,Trp53,Ube2c,Ube2d1,Ube2e2,Xpo1,Zfp385a	4.31E-02
DNA damage control	1177	327	Alkbh7,Anapc13,Ap1g2,Ap1m2,Ap1s3,Aph1c,Atf4,Atf6,Bcl2l2,Brcc3,Brsk2,Cdc25a,Cdk5rap3,Clock,Creb3l1,Cryab,Dgkg,Egln2,Eme2,Epha7,Fign,Fnip2,Foxn3,Foxo4,Foxo6,Gadd45g,Helq,Hist1h2be,Hist1h4h,Htra2,Immp2l,Macrod1,Mapk9,Mgmt,Mpp2,Mpp7,Muc1,Ndrg1,Nuak1,Nup210,Nupr1,Pias2,Poli,Poll,Polr3k,Ppp2r5a,Prkce,Prkcz,Psen2,Psmb10,Psmd6,Psme4,Rad23a,Rad51d,Rchy1,Rec8,Rev3l,Rint1,Rps27l,Rps6ka6,Sesn1,Sgk1,Sirt2,Sirt5,Smarcc2,Stk11,Stra13,Syp,Taf9b,Tpt1,Triap1,Uba52,Uchl5	Actb,Actl6a,Akt3,Alyref,Ankrd1,Ap1m1,Ap1s2,Apaf1,Apex2,Aptd1,Asf1b,Atad5,Atrip,Bak1,Batf,Batf3,Bax,Bcat1,Bcl2l1,Bcl2l11,Bcl3,Bcl6,Bid,Blm,Brca1,Brsk1,Casp3,Ccna2,Ccnb1,Ccnb2,Ccnd1,Ccne1,Ccng2,Cd44,Cd74,Cdc20,Cdc23,Cdc25b,Cdc25c,Cdc45,Cdc7,Cdca5,Cdk1,Cdk2,Cdk4,Cdk5rap2,Cdkn1a,Cdkn2d,Cebpb,Chaf1a,Chaf1b,Chd7,Chek1,Clspn,Creb3l3,Creb5,Crip1,Csn3,Csnk1e,Csnk1g3,Ctc1,Ddx39,Dek,Dna2,Dtl,Dtx3l,E2f1,E2f7,Egln3,Epha2,Epha3,Epha4,Ercc1,Esco2,Espl1,Exo5,Eya2,Fbxo4,Fignl1,Fignl2,Fos,Fosb,Fosl2,Fsbp,Gadd45a,Gen1,Gtse1,H2afx,Hdac1,Hdac7,Hic1,Hist1h2ai,Hist1h2bj,Hmga1,Hmga2,Hmgb2,Hmgn1,Hmox1,Hspa14,Hspa1b,Hspa2,Hspa8,Ier3,Ifi204,Ikbke,Ino80c,Irf7,Isg15,Jdp2,Jun,Junb,Kif22,Klhl13,Lig1,Lrp1,Lyn,Map2k1,Mapk11,Mastl,Mcm4,Mcm6,Mcm7,Mms22l,Mnda,Mre11a,Msx1,Mtr,Nabp1,Ncapd2,Ncapg,Ncapg2,Ncaph,Nek6,Nfatc4,Nfkb2,Nfya,Nup107,Nup155,Nup188,Nup205,Nup37,Nup93,Parp3,Parp9,Pcna,Pdp1,Pea15a,Phc2,Phlda3,Pif1,Pik3r3,Pkmyt1,Plk1,Plk3,Plscr1,Pmaip1,Pola1,Pola2,Pold1,Pold4,Pole,Pole2,Poln,Polr2h,Ppp1r8,Ppp2r2a,Ppp2r2b,Prim1,Prim2,Prkcb,Prkcd,Prkcg,Psma5,Psmb8,Psmb9,Psmd14,Psme1,Psme2,Rad51,Rad51ap1,Rad54b,Rassf1,Rbbp7,Rbl1,Rbp4,Rel,Relb,Rfc3,Rfc5,Rhno1,Rnaseh2b,Rpa2,Rpa3,Rrm1,Rrm2,Ruvbl2,Sae1,Sfn,Sfpq,Sfrp2,Shisa5,Skil,Skp2,Slx4,Smarcb1,Smarcd1,Smc2,Smc4,Smc5,Snai1,Snai2,Sox4,Sp100,Spred1,Spred2,Stat1,Steap3,Stxbp4,Suv39h1,Tdg,Tdp1,Timeless,Tipin,Tnfaip1,Tnfrsf1a,Tnfrsf1b,Top2a,Topbp1,Trex1,Trip13,Trp53,Trpm2,Twist1,Uba7,Ube2e2,Ube2l6,Ube2n,Ube2t,Uhrf1,Vav3,Whsc1,Wnt11,Wnt2,Wnt4,Wnt5a,Wnt7a,Wnt7b,Xrcc4,Ywhab,Ywhag,Ywhah,Ywhaz,Zfp385a,Zswim7	9.95E-01
* The gene sets are from integrating Metacore,KEGG,Reactome,and DAVID.					
** The number of expressed protein coding genes.					
*** The PDAC differential expression genes are |log2(PDAC/9-week)| >1 and p<0.05.					

Supplementary Table 3. Sequence of primers used in this study and target sequence of shRNA.

primer name	sequence(5'-3')
TP53 RT-Forward	CTC TCC CCC GCA AAA GAA AAA
TP53 RT-Reverse	CGG AAC ATC TCG AAG CGT TTA
CDKN2A RT-Forward	ACA TCA AGA CAT CGT GCG ATA TT
CDKN2A RT-Reverse	CCA GCG GTA CAC AAA GAC CA
CDKN2B RT-Forward	CCC TGC CAC CCT TAC CAG A
CDKN2B RT-Reverse	CAG ATA CCT CGC AAT GTC ACG
Xba I-*KRAS* ^{G12D}-Forward	TAG CTC TAG AGC CAC CAT GAC TGA ATA TAA ACT TGT GGT AGT TGG AGC TGA TGG CGT AGG C
Sal I-*Age* I-*KRAS* ^{G12D}-Reverse	CAG CAT TTA AGG TAA AAG CT
Cla I-sh*Tp53* -Forward	CCA TCG ATG CGG AAT TCG AAC GCT GAC GTC
Cla I-sh*Tp53* -Reverse	CCA TCG ATG CAA AAA GTA CAT GTG TAA T
Kpn 2I-shCdkn2b-Forward	ATC GTC CGG AGA GGG CCT ATT TCC CAT GAT
Sal I-shCdkn2b-Reverse	ACG TGT CGA CAT GAA TAC TGC CAT TTG TCT
Sal I-shCdkn2a-Forward	ATC GGT CGA CGA GGG CCT ATT TCC CAT GAT
Sal I-shCdkn2a-Reverse	ACG TGT CGA CAT GAA TAC TGC CAT TTG TCT
target sequences of sh*Tp53*	GTA CAT GTG TAA TAG CTC CTT
target sequences of sh*Cdcn2a*	CGG GCA TAG CTT CAG CTC AAC
target sequences of sh*Cdcn2b*	CAC CTC CAG CTC GAC AAG GAA ATA GTG AT