

SUPPLEMENTAL MATERIAL

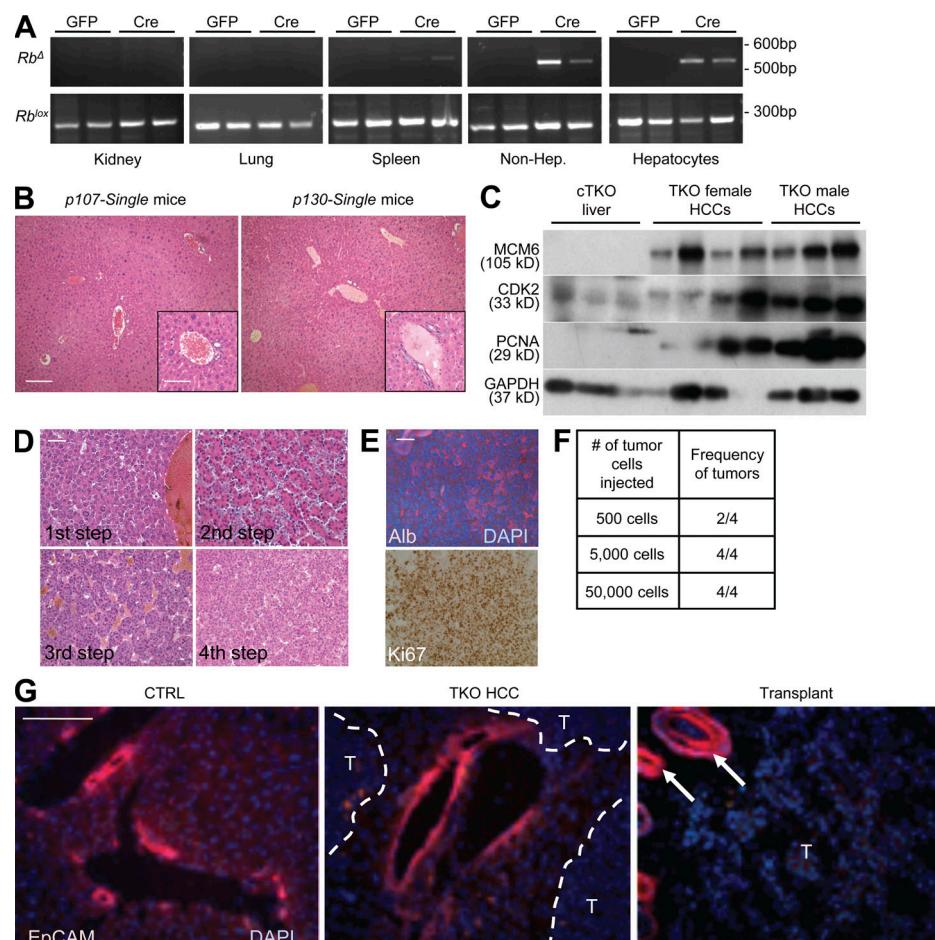
Viatour et al., <http://www.jem.org/cgi/content/full/jem.20110198/DC1>

Figure S1. Cellular and molecular features of TKO HCC tumors. This figure is related to Fig. 1. (A) Recombination efficiency of *Rb* floxed alleles in kidney, lung, spleen, hepatocytes, and nonparenchymal cells in the liver, as assessed by nonquantitative PCR. (top) Recombined allele (*Rb^A*). (bottom) Unrecombined conditional *Rb* allele (*Rb^{lox}*). (B) Representative H&E staining of liver sections from 8-mo-old *Mx1-Cre p107-Single* and *Mx1-Cre p130-Single* mice. A portal triad is shown at higher magnification for each genotype (insets). (C) Immunoblot analysis of several markers of cell cycle activity in control liver and TKO tumors. GAPDH serves as a loading control. (D) Serial transplantation of TKO HCC tumor cells into the flank of immunodeficient SCID mice. A high number of cells from a freshly dissected primary tumor was initially transplanted, and tumors were collected 3 mo after transplantation for another round of transplantation. To achieve serial transplantation, tumors were digested to obtain single cell suspension, and ~15–20% of the cells from the original tumor were retransplanted into SCID mice ($n = 4$). (E) Transplanted tumors (step 1) were stained with antibodies against Albumin (Alb; red; counterstained with DAPI in blue) and Ki67 (brown). (F) Limiting dilution of TKO cells transplanted into the flank of immunodeficient mice. Escalating amounts of TKO tumor cells were mixed with Matrigel and injected subcutaneously into the flank of *SCID//I2r^{-/-}* immunodeficient mice. Mice were inspected weekly up to 4 mo after transplantation for tumor development ($n = 4$ per group). (G) Sections from control and TKO HCCs were stained with an EpCAM antibody. (left) Control (CTRL) liver. The anti-EpCAM antibody only stains bile ducts. (middle) Tumor cells (T; circled with white dashed lines) do not express EpCAM. (right) Subcutaneously transplanted tumor cells do not express EpCAM. A positive control is provided by the skin epithelium of the transplanted mouse (white arrows). Bars: (B, D, E, and G) 50 μ m; (B, insets) 15 μ m.

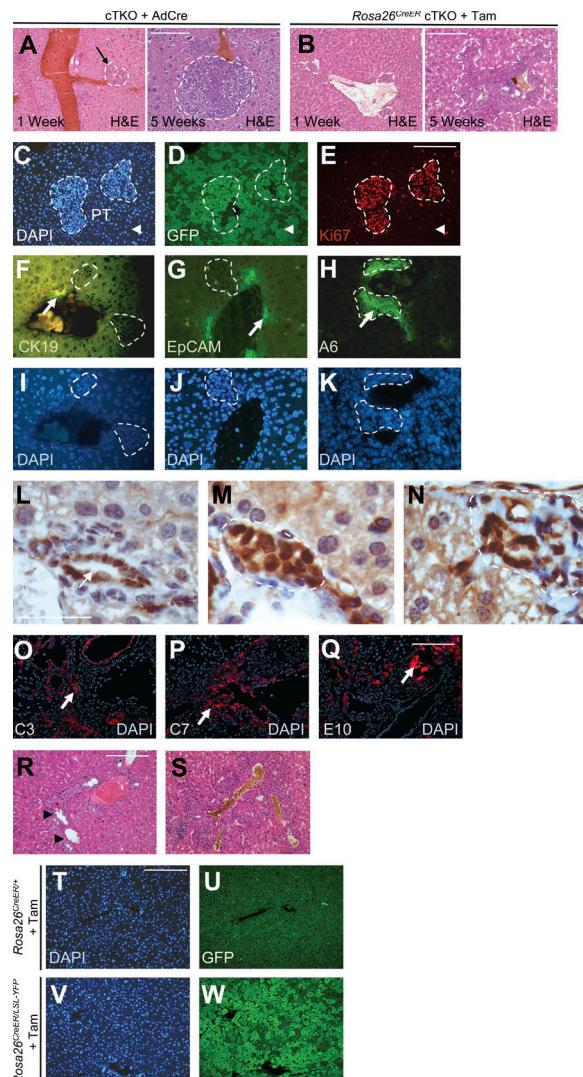


Figure S2. Characterization of TKO early liver lesions. This figure is related to Fig. 2. (A and B) Representative lesions ($n > 10$) at 1 wk (left) and 5 wk (right) in TKO mice + Ad-Cre (A) and *Rosa26^{CreER}* TKO mice treated with Tam (two injections; B). The white dashed lines circle foci of cells in early lesions. The black arrow further points to an early lesion. (C–E) GFP (D) and Ki67 (E) immunostaining of early lesions in cTKO;*Rosa26^{LSL-YFP}* mice infected with Ad-Cre. Arrowheads show one Ki67⁺ hepatocyte. DAPI stains nuclear DNA in blue (C). PT, portal triad. (F–K) CK19 (F), EpCAM (G), and A6 (H) immunostaining experiments show that early TKO lesions express A6 but not CK19 and EpCAM. Arrows indicate bile ducts that are positive for CK19 or EpCAM staining, whereas foci are negative. DAPI stains nuclear DNA in blue (I, J, and K). (L–N) White dashed lines circle foci of proliferative cells. (L–N) Immunohistochemistry for Sox9 (brown signal); slides were counterstained with hematoxylin (blue). (L) Bile duct in a normal liver (white arrow). (M and N) Two representative small TKO lesions are circled with a dashed line. (O–Q) Immunostaining for C3 (O), C7 (P), and E10 (Q; all red) on cryosections from the liver of mice treated with DDC, an inducer of oval cell expansion. Images were merged with DAPI images. Groups of positive cells are indicated by white arrows. (R and S) Representative H&E staining ($n \geq 3$) of liver from either WT mice treated for 3 wk with DDC (R) or *Rosa26^{CreER}* TKO mice 5 wk after Tam treatment (two injections; S). In R, black arrowheads point to atypical bile ducts. (T–W) Immunostaining with GFP antibodies on sections from cTKO mice crossed to *Rosa26^{CreER/LSL-YFP}* (bottom; W) or *Rosa26^{CreER/+}* (top; negative control for GFP staining; U) mice showing efficient Cre activation after Tam injection. DAPI stains nuclear DNA in blue (T and V). Bars, 50 μ m.

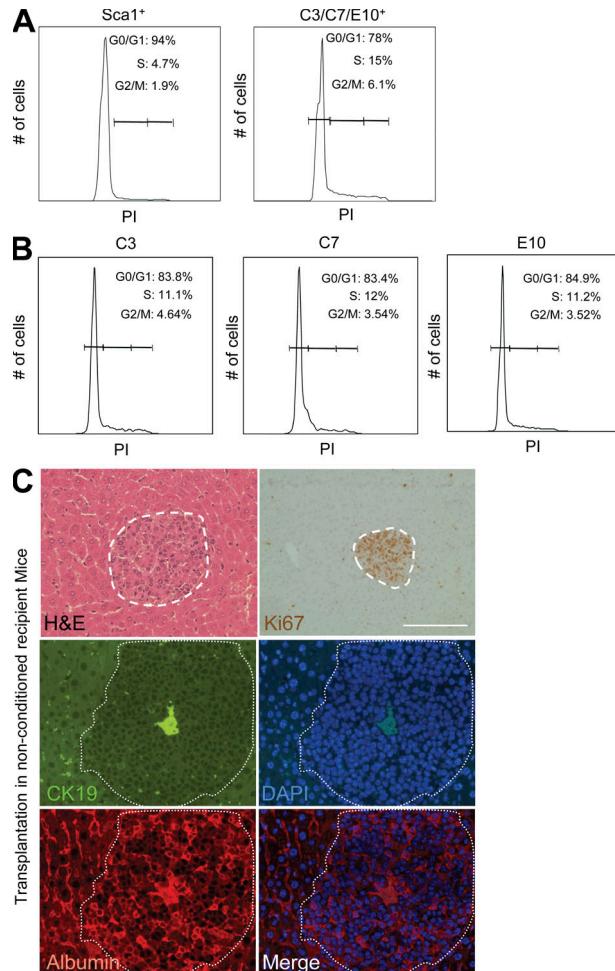


Figure S3. Proliferation of TKO liver stem/progenitor populations. This figure is related to Fig. 3. (A) Sca1⁺ and C3/C7/E10⁺ populations were FACS sorted, and their DNA content was analyzed by propidium iodide incorporation. (B) Progenitor cell populations were independently sorted using the C3, C7, and E10 antibodies. DNA content was analyzed by propidium iodide incorporation. (A and B) Representative graphs out of three independent experiments each are shown. (C) Nonparenchymal cells were isolated from *Rosa26*^{CreER} TKO mice 3 wk after Tam treatment and transplanted into the liver of SCID/*Il2r^{-/-}* mice (without preconditioning). (top left) Representative H&E staining of a lesion observed in a recipient mouse 2 mo after transplantation of TKO cells. (top right) Ki67 staining of a recipient liver. The proliferative lesion is circled with a white dashed line. Staining of a representative lesion with lineage markers ($n \geq 3$) is shown: CK19 (middle left), Albumin (bottom left), and DAPI to stain DNA (middle right). The merge is displayed in the bottom right panel. The lesion is circled with a white dashed line ($n = 6$). Bar, 50 μ m.

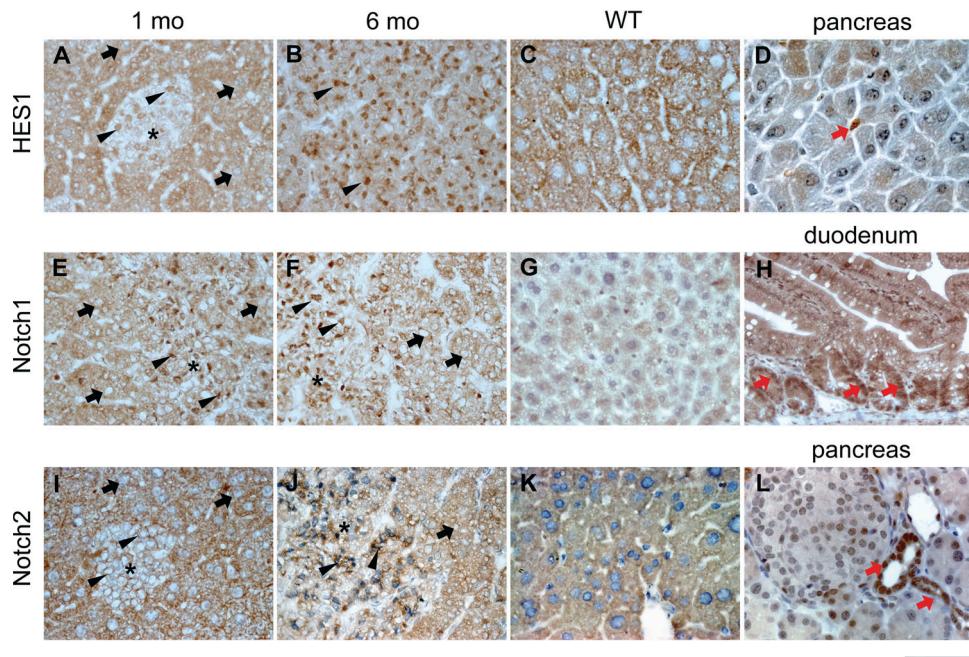


Figure S4. Immunohistochemical staining of Notch1, Notch2, and Hes1 in early TKO liver lesions, TKO HCC, WT liver, and control tissues. This figure is related to Figs. 5 and 6. (A–D) HES1 immunostaining. (A) Early TKO lesions show nuclear expression of HES1 (brown signal, black arrowheads) compared with the adjacent normal hepatocytes (black arrows). (B) TKO HCC cells also display HES1 expression (black arrowheads), suggesting activation of the Notch signaling pathway. (C) Normal liver cells (hepatocytes) are negative for Hes1 immunostaining. (D) Centroacinar cells of the pancreas serve as a positive control (red arrow). (E–H) Notch1 immunostaining: early lesions (E) and HCC (F) show nuclear localization of Notch1, a sign of Notch1 activation (black arrowheads); adjacent normal hepatocytes and WT liver (G) are largely negative for active Notch1 (black arrows); intestinal crypt cells (H) provide a positive control (red arrows). (I–L) Notch2 immunostaining: early neoplastic lesions (I) and advanced HCC (J) show only very weak membrane staining of Notch2 (black arrowheads) and negative nuclear Notch2 expression similar to normal tissue (K; black arrows); pancreatic duct cells (L) serve as a positive control for nuclear active Notch2 (red arrows). Asterisks depict tumors/lesions. Bar, 50 μ m.

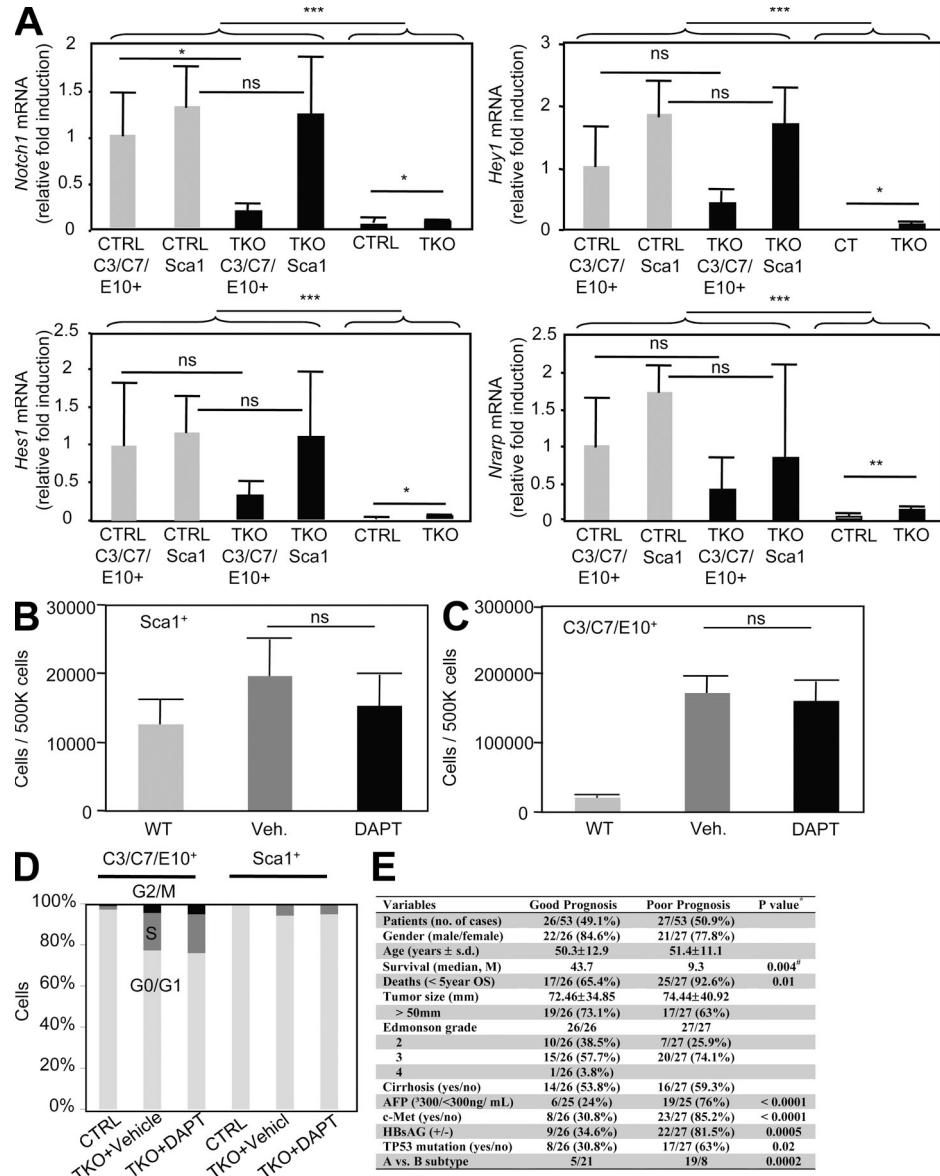


Figure S5. Lack of Notch signaling activity and function in TKO liver progenitor cells in early lesions. This figure is related to Fig. 6. (A) The expression of *Notch1*, *Hes1*, *Hey1*, and *Nrarp* was assessed by RT-qPCR in Sca1⁺ and C3/C7/E10⁺ cells from control (CTRL; $n = 4$) and *Rosa26*^{CreER} cTKO (TKO; $n = 6$) mice 2 wk after Cre-mediated recombination, control liver (CT; $n = 4$), and TKO HCC tumors (TKO; $n = 4$). Statistical differences (p -values) were tested between control and TKO C3/C7/E10⁺, between control and TKO Sca1⁺, and between progenitor populations (first four bars) and mature populations (last two bars). (B-D) Cell numbers (B, Sca1⁺; and C, C3/C7/E10⁺) and cell cycle profile (D) of cells sorted from control (WT or CTRL) and TKO mice 2 wk after Cre-mediated recombination were assessed by propidium iodide incorporation. 3 d before sacrifice, mice were injected daily with DAPT or vehicle ($n = 3$). (E) Variations of clinical features between patients with high Notch and low Notch signatures. Only significant p -values ($P < 0.05$) are presented in the table. Univariate p -values were calculated by χ^2 tests (*). #, Log-Rank survival test. Error bars indicate SEM. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ns, not significant.

Table S1. Selected genes from the SAM analysis

| Biological analysis | Genes/enriched GO terms |
|---|---|
| SAM analysis | |
| <i>Genes with increased expression in TKO tumors vs. control livers</i> | |
| Cell cycle | <i>Rad1/18/21/23a/51c, Cyclin E1, Cyclin B1, Cyclin B2, Cyclin A2, Cyclin T1, Mcm2/4/5/6/7/8, p18, Cdkn3, Cdkn1b, Cdk2, Cdk4, Plk1/4, PcnA, and Ki67</i> |
| Chromosomes/DNA damage/modifications | <i>Brca1, Suv39h1, Dnmt1, Thymidine kinase1, Thymidylate Synthase 1, Chek1/2, Hdac2, Aurora Kinase A/B, and Hurp</i> |
| Apoptosis | <i>Siva-1</i> |
| Extracellular communication | <i>HDGF, Sca2, Itgb5, Itga5, CD276, EphrinB4, EphrinB2, Icam1, Bmpr1a, LaminB receptor, and LTbR</i> |
| Signaling pathways | <i>p53, Pou2af1, Smad1/3, Map4k4, Kras, Traf4, E2F1, E2F7, Stat5a, β-catenin, Dvl2, GSK3-β, Racgap1, Rangap1, and Gps2Arghef1/7</i> |
| Ligase/phosphatase activity | <i>Skp2, Myst2, Smyd5, and HAT1</i> |
| Others | <i>Ect-2, Terf1, Pbx3, FoxM1, Fip111, Gata6, Ets2, and Timeless</i> |
| <i>Genes with decreased expression in TKO tumors vs. control livers</i> | |
| Receptor | <i>Ahr, Pth1R, Ghr, TgfbR3, Bmpr2, and gp130</i> |
| Extracellular communication | <i>Igf1, Il18, Sdf4, Cathepsin H and L, CD55, Fgf1, CD59a, and Neuropilin1</i> |
| Signaling pathways | <i>CDK6 and 7, Wnt2, HoxA5, Bmp2&5, Hdac11, Braf, Maf, PTEN, and Sox6</i> |
| Others | <i>Ceacam1, Tbx3, Axin2, Glu12, Rnf43, Npr2, Cyp2e1, Slc1a2, Skp1a, Sirt4, and Pdk1</i> |
| <i>Genes with increased expression in TKO tumors vs. E2F1 tumors</i> | |
| Cell cycle | <i>Aurora kinase B, Mcm2/4/5/6/7, Ki67, Cyclin A2, Cyclin B1, Cyclin E1, p21, Cdk4, Skp2, and Plk1</i> |
| DNA modification | <i>Hdac2/3, Dnmt1, Dnmt3b, Chek1/2, Brca1/2, Hat1, Ncor1, Tk1, and Ttk</i> |
| Others | <i>Ect2, Timeless, Pbx3, p53, Terf1, Notch1, Hdgf, Stat5a, Pou2af1, Gata6, and Ets2</i> |
| <i>Genes with decreased expression in TKO tumors vs. E2F1 tumors</i> | |
| Others | <i>CyclinD1, Bmp5, Maf, CD59a, Ceacam1, Socs2, Il18, and TCF7</i> |
| DAVID analysis | |
| <i>Enriched GO terms</i> | |
| Genes up-regulated in TKO tumors | Nucleus 10^{-130} , Chromosome 10^{-54} , Cell Cycle 10^{-56} , DNA Repair 10^{-31} , DNA Binding 10^{-22} , and Chromosome Organization 10^{-18} |
| Genes down-regulated in TKO tumors | Mitochondria 10^{-54} , Cytoplasm 10^{-52} , and Carboxylic Acid Metabolism Process 10^{-17} |

Selected genes whose expression significantly varies in TKO tumors compared with control liver and liver tumors driven by overexpression of E2F1 are shown. The complete list is in Table S2. DAVID analysis was performed on the genes obtained by the SAM analysis. The most significant GO enrichments are displayed for the genes up- and down-regulated in TKO HCC versus control livers. P-values for the enrichment are shown.

Table S2, included as a separate Excel file, shows the complete gene list resulting from the SAM analysis performed on preprocessed WT and TKO datasets.

Table S3, included as a separate Excel file, shows the GSEA of the TKO dataset.

SUPPLEMENTAL TEXT

List of genes included in the "gene sets of interest" from the GSEA (see pathways in Fig. 4 D)

Lin_Wnt_up (Lin_APc_up). ABCC1, ACAP1, ACTN4, ADRA2C, AES, AGRN, ALG3, ARHGDIA, ATP6V0A1, BCAP31, CAPN1, CCND1, CD99, CTDSPL, CYB5R3, DOK1, EIF5A, ETS1, FLOT2, GIPC1, GJB1, HDAC3, HDGF, HMG20B, HNRNPA0, HSPE1, KRT5, KRT7, L1CAM, LMNA, LY6E, MAP3K11, MMP14, MTA1, PCNA, PDAP1, PFN1, POLR2A, POLR2E, PRKCSH, RPL39L, SCAP, SCN5A, SF3A1, SH2B2, SLC1A5, SNRNP70, SORBS3, SYK, TELO2, TGM2, and UBA1.

Kenny_Wnt_up (Kenny_Ctnnb_up). ABI1, ARCN1, ARGEF2, BAD, BTRC, CAPN3, CASKIN2, CCNB1, CCR5, CD14, CSE1L, CTSC, CYR61, EBNA1BP2, ECT2, EXOSC2, GAN, GNA11, HAT1, HMGB2, IGFBP5, KIAA0195, KRT7, LOXL2, MMP2, NCOR1, PKN1, PLK4, PTPN22, RAMP3, RPA2, S100A8, SEPHS2, SERPIND1, SFRS7, SORBS1, SPP1, SQRD, SYNE1, TACC3, TFDP1, TK1, TM4SF1, TNFAIP2, and UPP1.

E2F1 target genes (REN_bound_by_E2F). BARD1, BRD2, BUB3, CBX5, CCNA2, CDC25A, CDC6, CDK2, CENPA, CENPE, CHEK1, CSTF1, DUT, E2F2, E2F3, FEN1, H2AFX, H2AFZ, MAD2L1, MCM3, MCM5, MCM6, MLH1, MSH2, NAP1L4, ORC1L, PCNA, POLA2, POLD1, PRKDC, PTTG1, RAD51, RAD54L, RB1, RBL1, RFC2, RFC3, RFC4, RPA3, RRM1, SUPT4H1, TK1, TOP2A, TP53, TTK, UMPs, and UNG.

YU_MYC_TARGETS_UP. ANLN, ASPM, AURKA, BIRC5, BRCA2, BUB1, CCNB1, CCNB2, CDC2A, CDKN3, CKS1B, CKS2, CLIC4, CSDA, DCTPP1, DTL, E2F8, ECT2, FDPS, GMNN, HMGB2 /// OTTMUSG000, HMGN2, HNRPLL, IDI1, KIF20A, KPNA2, MKI67, NUDCD2, NUP54, PCNA, PLK1, RACGAP1, RRM1, STRAP, TFDP1, TOP2A, TSPAN4, TXN1, UBE2S, and UCHL5.

MYB_UP. *ADRB2*, *ARHGAP24*, *CCL20*, *CCNA1*, *CDC42SE2*, *CHSY1*, *CLEC5A*, *CMAH*, *COL4A2*, *CSDA*, *CSF2*, *CSGALNACT1*, *DALR3D*, *EAF2*, *EHD1*, *FAM107B*, *FAM117A*, *FAM45A*, *GATA3*, *GNG2*, *GPR18*, *IL12B*, *IL23A*, *IL6*, *KCNA3*, *KLF5*, *LASS6*, *LOC100288442* /// LOC, *MAPKAPK2*, *NKG7*, *NRIP3*, *OXTR*, *PALLD*, *PTPRJ*, *PXK*, *S1PR3*, *SLC38A1*, *TFPI2*, *TM4SF1*, *TPSAB1*, *TSC22D3*, *USP31*, and *VCAN*.

E2F3 oncogenic signature. ABCB10, ABCC10, ABCG2, ABHD15, ACPL2, ADCY3, AK3L1, AKR1B1, AKT1, ALDH5A1, ANKH, ANKRD18A, ANKRD18A /// ANKRD18, AP1S2, ARHGAP8 /// LOC55315, ATAD2, ATP5O /// DONSON, ATRNL1, B4GALT6, BAI2, BCL2L11, BCOR, BRI3BP, C12ORF34, C20ORF112, C20ORF199, C22:CTA-250D10.9, C5ORF30, C6ORF136, C6ORF168, CAMK2N1, CAMKK2, CCND3, CCNE1, CCNE2, CCNO, CD83, CDC20B, CDC2L6, CDKN1C, CDKN2A, CDKN2C, CEBPA, CEP78, CHD7, CHML, CHST1, CHST2, CHST7, CIZ1, CMPK2, CP110, CRELD2, CRY1, CSPG5, CXXC5, D4S234E, DCK, DCLRE1B, DDAH1, DGKQ, DIS3L, DKFPZP686Q24166, DNAJC9, DPY19L1, DSCR6, DTL, DVL3, DYM, E2F7, EEF1A2, EIF4A1, EML6, ENO2, EPB41L4A, EPB41L4B, EPHA2, EPHX4, EZH2, FAM119A, FAM134B, FAM171A1, FAM46A, FAM57A, FAM92A1, FANCA, FBXO21, FEN1, FERMT1, FGF9, FGFR3, FLJ25076, FLJ34077, FOXQ1, FRAT1, FZD1, GAS5, GCH1, GINS1, GKAP1, GLRB, GNAL, GNAS, GPR137B, HACE1, HECA, HEY1, IL17RB, IL1B, INHBB, INO80C, INSR, JPH1, KANK2, KCTD15, KCTD6, KDM2B, KDM4B, KHDRBS3, KIAA0020, KIAA0182, KIAA1804, KISS1R, LIN7B, LOC202451, LOC400931, LOC646762, LOC729046 /// RPL17, LRIG1, LRP4, LYPD6, MANEAL, MBOAT1, MDN1, MFHAS1, MMP15, MRAS, MYB, NASP, NAT9, NCK-IPSD, NEFL, NETO2, NIN, NIPA1, NR2F1, NUP155, PCNA, PCOLCE2, PDE8A, PEG10, PFKFB3, PHF10, PHF2, PHTF2, PIN1, PKN3, PLCL2, PLXND1, PMS2L1, POLE, POLE2, PPP2B, PRRG4, PSIP1, PTCH1, PTGS1, PWP1, PXMP2, RAB15, RAB26, RASEF, RAVER2, RBM25, RDH13, RECQL4, REEP1, RPA1, RRAGD, RTN4R, RUNX3, SAC3D1, SAMD1, SBK1, SCN8A, SCNN1A, SDCCAG1, SFMBT1, SFRS6, SFRS7, SH3BGR, SHANK3, SHROOM1, SIN3B, SIX5, SLC16A6, SLC25A12, SLC27A3, SLC9A3R1, SMAD6, SOBP, SOX12, SREBF1, SSX2IP, STRA13, STXBP1, SYNM, TAF1D, TAF4, TBC1D9, TEAD4, TFDP1, TIAM1, TLCD1, TM6SF1, TMEM106C, TMEM155, TMEM158, TMEM200B, TMEM214, TMEM43, TMEM97, TMOD2, TNC, TNFAIP3, TPPP, TRIM3, TRIM7, TSHZ1, TSPAN5, UGT8, USPL1, WIP12, WNT5A, ZBTB42, ZDHHC23, ZNF195, ZNF275, ZNF367, ZNF703, and ZWINT.

Kegg Notch signaling pathway. ADAM17, APH1A, CIR1, CREBBP, CTBP1, CTBP2, DLL1, DLL3, DLL4, DTX1, DTX2, DTX3, DTX3L, DTX4, DVL1, DVL2, DVL3, EP300, HDAC1, HDAC2, HES1, HES5, JAG1, JAG2, KAT2A, KAT2B, LFNG, MAML1, MAML2, MAML3, MFNG, NCOR2, NCSTN, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NUMB, NUMBL, PSEN1, PSEN2, PSENEN, PTCRA, RBPJ, RBPJL, RFNG, and SNW1.

SWEET_KRAS_TARGETS_DN. *ACLY, ATP1B1, BSG, BTG1, CDKN1A, FCGR2A, FKBP2, GABPB1, GADD45A, GLRX, GNS, IL18, LAMC1, LGALS3, MANF, MAPK1, NPC2, PON2, PSEN1, RABGGTB, SHC1, SIRPA, TGFB1, TGOLN2, TSTA3, and VASP*.

P38 MAPK pathway. AKT1, ATF1, CDC42, CREB1, CREB3, CREB5, DUSP1, DUSP10, EEF2K, EIF4E, ELK1, GADD45A, HSPB1, IL1R1, MAP2K3, MAP2K4, MAP2K6, MAP3K10, MAP3K4, MAP3K5, MAP3K7, MAPK1, MAPK11, MAPK12, MAPK13, MAPK14, MAPKAPK2, MAPKAPK5, MKNK1, MKNK2, MYEF2, NFKB1, NR2C2, SRF, and TRAF6.

JNK MAPK pathway. *AKT1, ATF2, CDC42, DLD, DUSP10, DUSP4, DUSP8, GAB1, GADD45A, GCK, IL1R1, JUN, MAP2K4, MAP2K5, MAP2K7, MAP3K1, MAP3K10, MAP3K11, MAP3K12, MAP3K13, MAP3K2, MAP3K3, MAP3K4, MAP3K5, MAP3K7, MAP3K9, MAPK10, MAPK7, MAPK8, MAPK9, MYEF2, NFATC3, NR2C2, PAPPA, SHC1, TP53, TRAF6, and ZAK.*

Genes identified in cluster M (Fig. 4 A)

Actg1, *Adam11*, *Adam8*, *Add1*, *Adsl*, *Aes*, *Akap1*, *Akap10*, *Alcam*, *Amn*, *Ankrd32*, *Anln*, *Ap1m1*, *Ap3s2*, *Apba3*, *Apobec3*, *Aprt*, *Arf2*, *Armc6*, *Arpp19*, *Arsa*, *Asxl1*, *Atf4*, *Aurkb*, *B230120H23Rik*, *B4galtn5*, *BC022623*, *BC023882*, *BC038286*, *BC049807*, *BC057552*, *Bak1*, *Barf1*, *Bap1*, *Bat1a*, *Bat3*, *Bcas2*, *Bckdk*, *Bclf1*, *Bex2*, *Bid*, *Birc5*, *Birc6*, *Bok*, *Bra1*, *Bra2*, *Brd2*, *Bub3*, *Calu*, *Camk1*, *Capn7*, *Capza1*, *Car2*, *Casp8ap2*, *Cbx1*, *Ccna2*, *Ccnb1*, *Cne1*, *Cnrf*, *Cng1*, *Cng2*, *Cd164*, *Cd200*, *Cdc25a*, *Cdc25c*, *Cdc2a*, *Cdc2l1*, *Cdc45l*, *Cdt5l*, *Cdca3*, *Cdkn1a*, *Celsr1*, *Cenpa*, *Cenpe*, *Cenpf*, *Cfdp1*, *Chaf1b*, *Chd1l*, *Chd4*, *Chek1*, *Chek2*, *Cited2*, *Cldn7*, *Clock*, *Clpx*, *Cln1*, *Cops3*, *Cops7b*, *C79407*, *Coro1b*, *Cpb1*, *Cpsf1*, *Crebl1*, *Crym*, *Cs*, *Csad*, *Csrp1*, *Csrp2*, *Cxxc1*, *Dapk3*, *Dapp1*, *Dck*, *Dct*, *Dctn1*, *Ddb2*, *Ddc*, *Ddost*, *Ddx24*, *Dedd*, *Dgat1*, *Dhx8*, *Diap1*, *Diap3*, *Dnm1t*, *Dpm2*, *Dtymk*, *Dyrk1a*, *E130303B06Rik*, *E2f1*, *Ect2*, *Eef2*, *Efna1*, *Elf2*, *Endog*, *Enpp4*, *Epb4.115*, *Epha3*, *Ephb4*, *Ephx1*, *Eprs*, *Erc3*, *Erp29*, *Ewsr1*, *Exo1*, *Ext1*, *Ezh1*, *Ezh2*, *F2h1*, *F730047E07Rik*, *Fastk*, *Fen1*, *Fgd1*, *Fkbp4*, *Flot2*, *Foxa2*, *Frk*, *Fzd5*, *Galns*, *Galnt2*, *Gart*, *Gas2*, *Gcat*, *Gmnn*, *Gna11*, *Gtse1*, *Gtpbp1*, *Gusb*, *Gdf15*, *Glis2*, *Gorasp2*, *Gpx2*, *Gsg2*, *Gsn*, *Gsp1*, *Gtf3c*, *H2afz*, *Hat1*, *Hdgf*, *Hells*, *Hira*, *Hmgb3*, *Hmmu*, *Hn1*, *Homer3*, *Hspa14*, *Hif9c*, *Ier3*, *Ifi2*, *Ifid1*, *Igf2*, *Igfbp3*, *Ilk*, *Incnip*, *Ipo4*, *Ipo9*, *Irx3*, *Khdbs1*, *Kif11*, *Kif20a*, *Kif4*, *Klb1a*, *Krtcap2*, *Lamb2*, *Land2*, *Lasp1*, *Lbr*, *Leng8*, *Litaf*, *Lmna*, *Lmn1b*, *Lsm2*, *Lta4*, *Luc7l*, *Lztr1*, *Mad2l1*, *Mafg*, *Magoh*, *Mapk1*, *Mapk13*, *Mat2a*, *Mat2b*, *Maz*, *Mbc2*, *Mbd4*, *Mcm2*, *Mcm4*, *Mcm5*, *Mcm6*, *Mcm7*, *Mrs1*, *Mdk*, *Mdm4*, *Me2*, *Melk*, *Mki67*, *Mkln1*, *Mlt3*, *Mmp14*, *Mmp2*, *Mre11a*, *Mns1*, *Mrpl13*, *Msh2*, *Msh6*, *Mta2*, *Mtbp*, *Mthfd2*, *Mtm1*, *Mybl2*, *Myg1*, *Myst2*, *Nap1l4*, *Ncbp2*, *Nek2*, *Nek4*, *Nfatc2ip*, *Njkbil1*, *Nfy4*, *Nfyfc*, *Ngfrap1*, *Nid2*, *Nol5*, *Nolc1*, *Notch1*, *Notch2*, *Notch3*, *Notch4*, *Npd1*, *Nrarp*, *Nsbp1*, *Nucb2*, *Nude*, *Nup107*, *Nup155*, *Nup160*, *Nup50*, *Nup11*, *Nusap1*, *Nxf1*, *ORF61*, *Oas1a*, *Oas1l2*, *Ogfr*, *P2rx4*, *Pa2q4*, *Pabpn1*, *Pafah1b1*, *Pafah1b3*, *Pask*, *Pbx3*, *Pcolce*, *Pdgfb*, *Pdlim7*, *Peli1*, *Phc2*, *Phf10*, *Phf5a*, *Pkp1*, *Plek2*, *Plekhh1*, *Plk1*, *Pmfn1*, *Pmm2*, *Pnn*, *Pofut2*, *Pold1*, *Pold2*, *Pold3*, *Pole*, *Pole2*, *Pou2f1*, *Ppic*, *Ppig*, *Ppil2*, *Ppm1g*, *Ppox*, *Ppp1ca*, *Ppp1c1*, *Ppp1r14b*, *Ppp2r1a*, *Ppp2r3a*, *Ppp5c*, *Prim1*, *Prim2*, *Prkebp1*, *Prkcsb*, *Prkdc*, *Prpf8*, *Psat1*, *Psen1*, *Psmc3ip*, *Psm3d*, *Psm7d*, *Pspb*, *Ptp4a3*, *Ptpn2*, *Purb*, *Pvrl3*, *Pycr2*, *Rab34*, *Ragap1*, *Rad1*, *Rad18*, *Rad21*, *Rad23a*, *Rad51ap1*, *Rai12*, *Rangap1*, *Rara*, *Rbm17*, *Rbp7*, *Rela*, *Rfc5*, *Rnaseh1*, *Rnf6*, *Rock1*, *Rp2a*, *Rp3a*, *Rpm2*, *Rrm1*, *Rrm2*, *Rwvbl2*, *Rybp*, *Safb2*, *Sart3*, *Senp2*, *Senp3*, *Serpib1b*, *Serpind1*, *Sf3a2*, *Sfrs2*, *Sfrs9*, *Sgo1*, *Sh3bp1*, *Shcbp1*, *Skp2*, *Slbp*, *Slc12a4*, *Slc16a1*, *Slc25a4*, *Slc26a2*, *Slc27a3*, *Slc42a*, *Slc6a8*, *Smarcc1*, *Smpd13b*, *Smtn*, *Smyd5*, *Snrpd1*, *Snrpd3*, *Sntb1*, *Snx4*, *Socs7*, *Son*, *Sor1l*, *Spag5*, *Spard1*, *Ssrp1*, *St5*, *St7*, *Stat5a*, *Stk11*, *Stk16*, *Stk35*, *Str13*, *Tacc3*, *Taf6*, *Terbp2*, *Tcfcb*, *Tcof1*, *Tfrc*, *Thoc4*, *Thop1*, *Timeless*, *Tjp3*, *Tk1*, *Tlk2*, *Timp*, *Tnfrsf1a*, *Tob1*, *Tomm22*, *Top2a*, *Tpr*, *Tpst1*, *Tpx2*, *Tradd*, *Traf4*, *Traip*, *Trim30*, *Tripl3*, *Trp53*, *Tsn*, *Ttk*, *Ttl1*, *Tubgcp2*, *Txnl1*, *Tacstd1*, *Tbrg1*, *Tcf6e2a*, *Tff3*, *Thap7*, *Ubap2*, *Ube2c*, *Ubn1*, *Ubf*, *Uchl5*, *Uhrf1*, *Upp1*, *Usp10*, *Usp22*, *Vamp2*, *Vegfb*, *Vil1*, *Vps4a*, *Vrk1*, *Wars*, *Wbscr16*, *Wee1*, *Xpo1*, *Xpo4*, *Xrc5*, *Yvhag*, *Yvhaz*, *Zbed4*, *Zdhhc2*, *Zfp101*, *Zfp142*, *Zfp238*, *Zfp36l2*, *Zfp395*, and *Zmym1*.