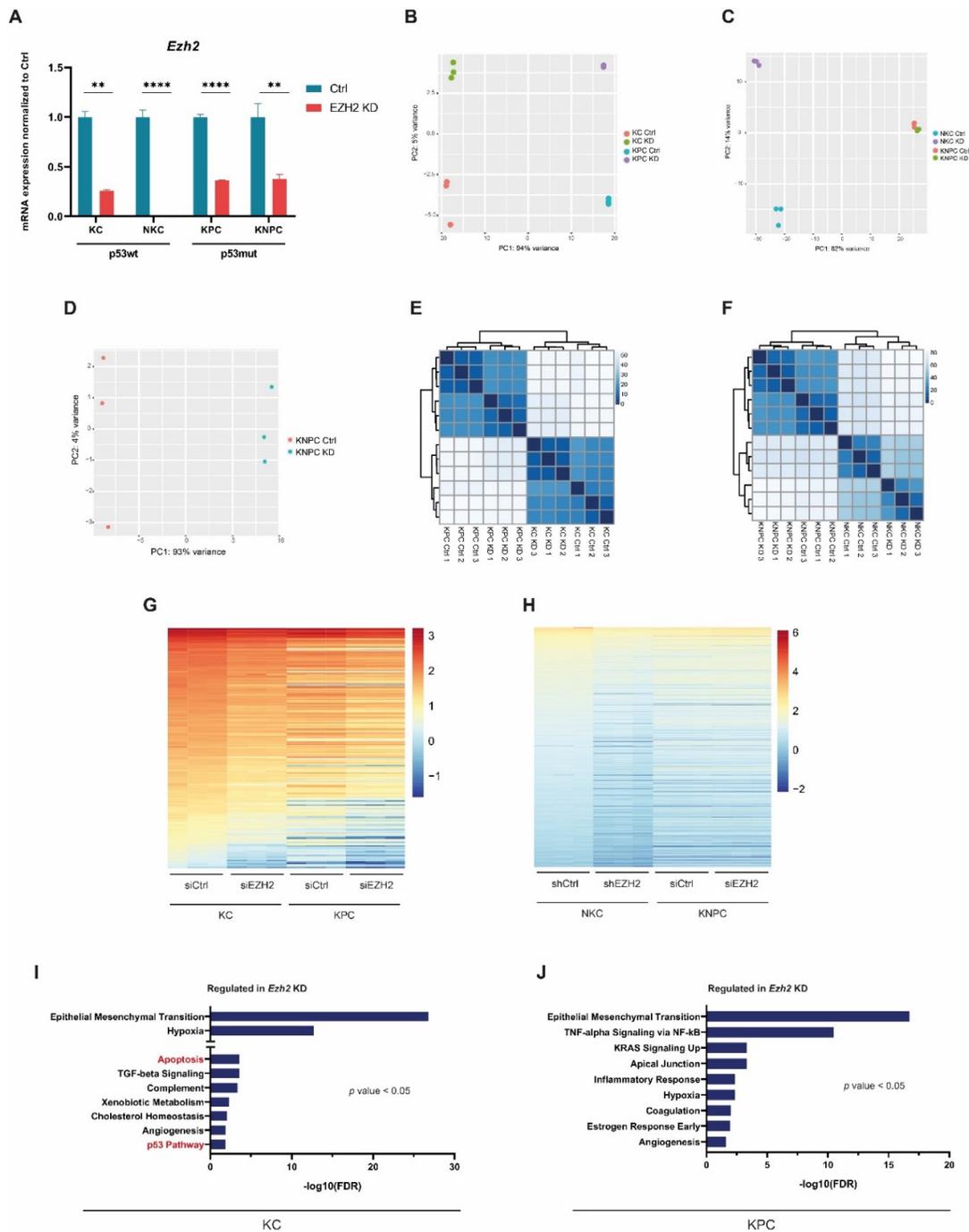
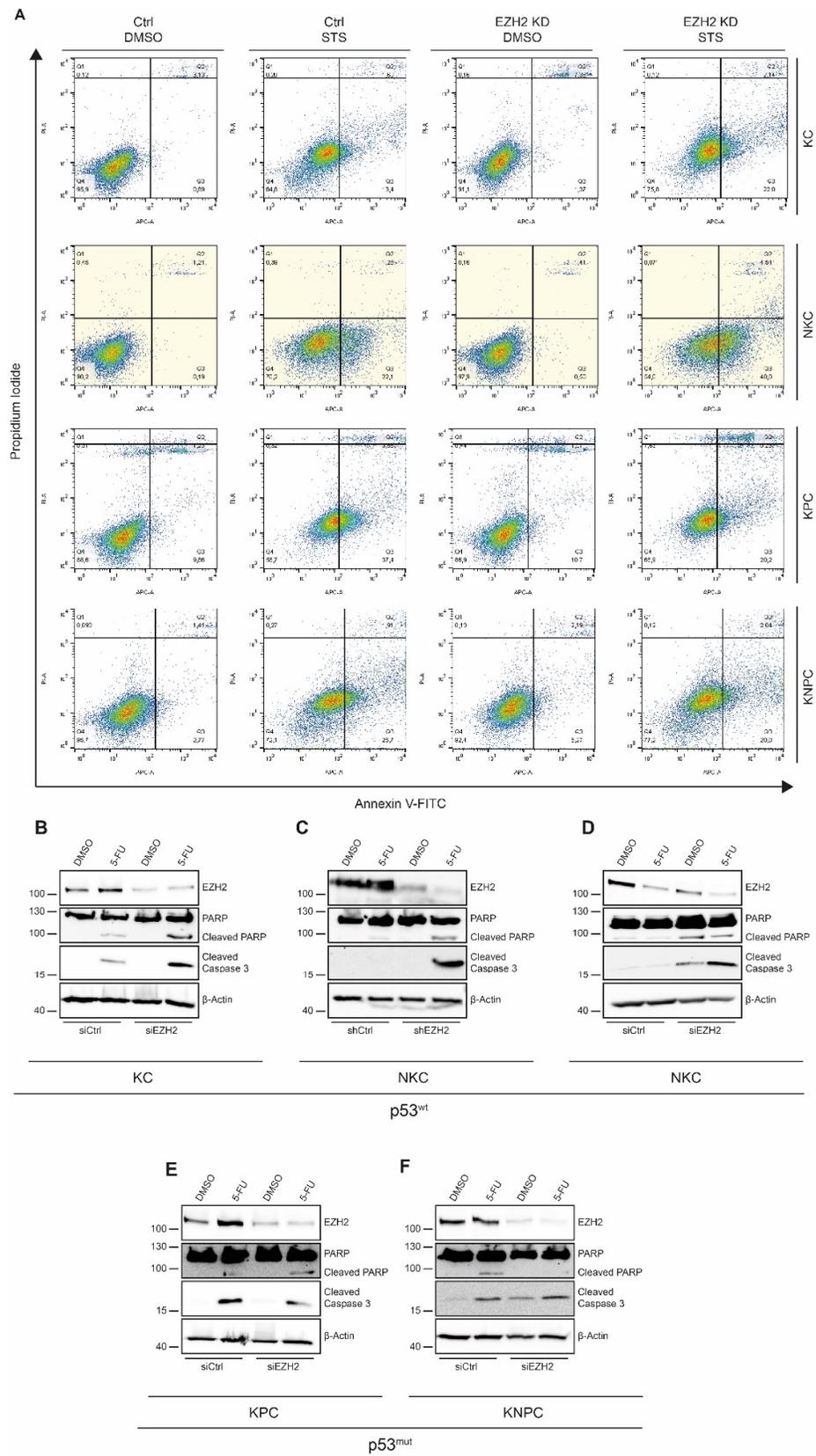


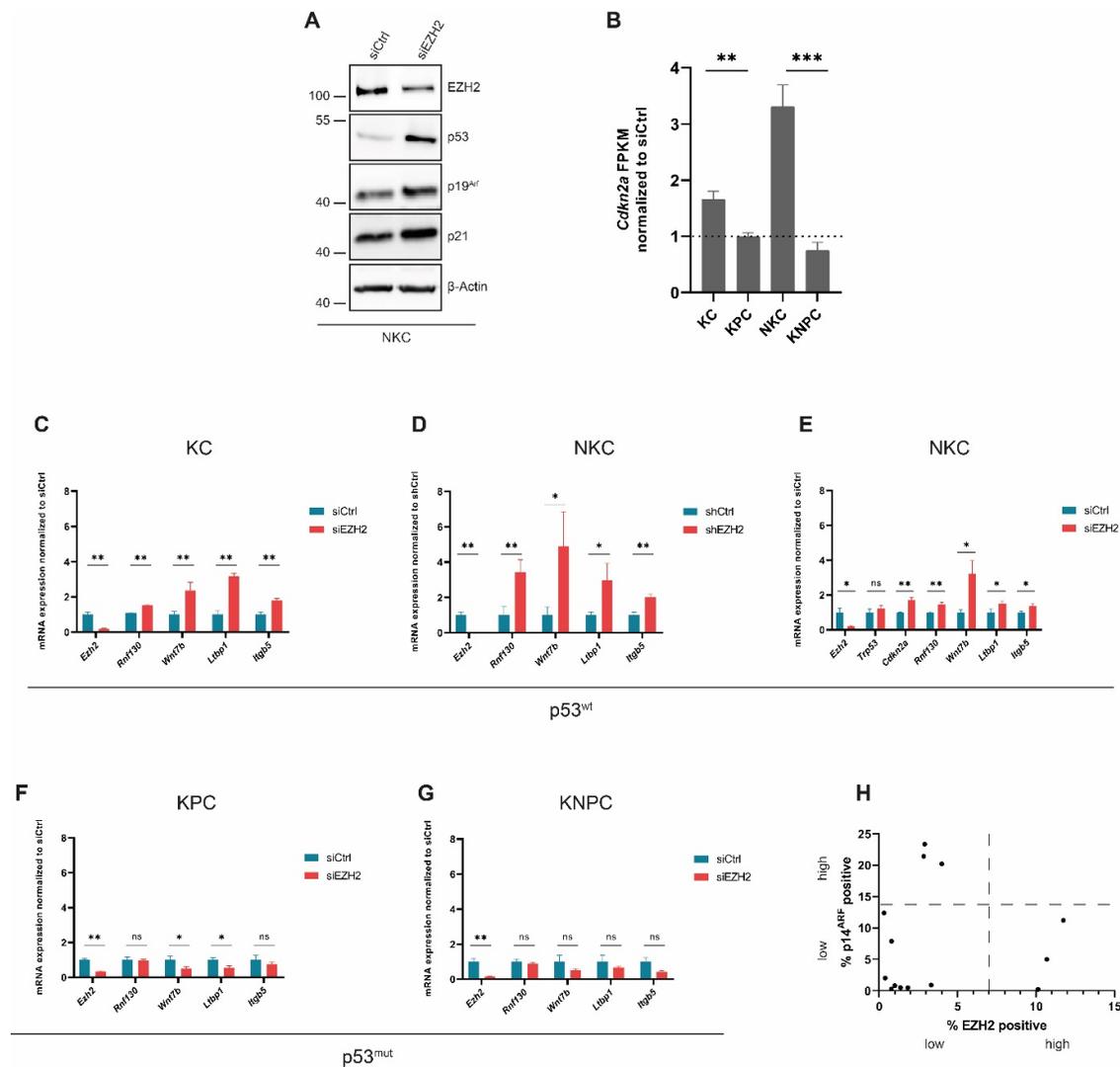
Supplementary Figure S1. Quantification of (immuno-) histological stainings depicted in Figure 1G. **A-C** Quantification of Ki-67 positive staining (**A**), Masson's Trichrome staining (**B**), and αSMA expression (**C**) of PDAC from orthotopically transplanted Panc1 cells (upper panel) and KrasG12D;Trp53R172H/+ (KPC) cells (lower panel). **D** Calculation of the activated stroma index by dividing the αSMA positive area by Masson's Trichrome blue area (collagen). For Masson's Trichrome and αSMA staining percentage of positively stained area of ten representative images of each tumor and for Ki-67 staining percentage of Ki-67 positive cells of ten representative images were measured using ImageJ Fiji. Each dot represents one mouse. Values represent mean ± SD. Significance was determined by two-tailed unpaired Student's t test; **, $p \leq 0.01$; ns, non-significant.



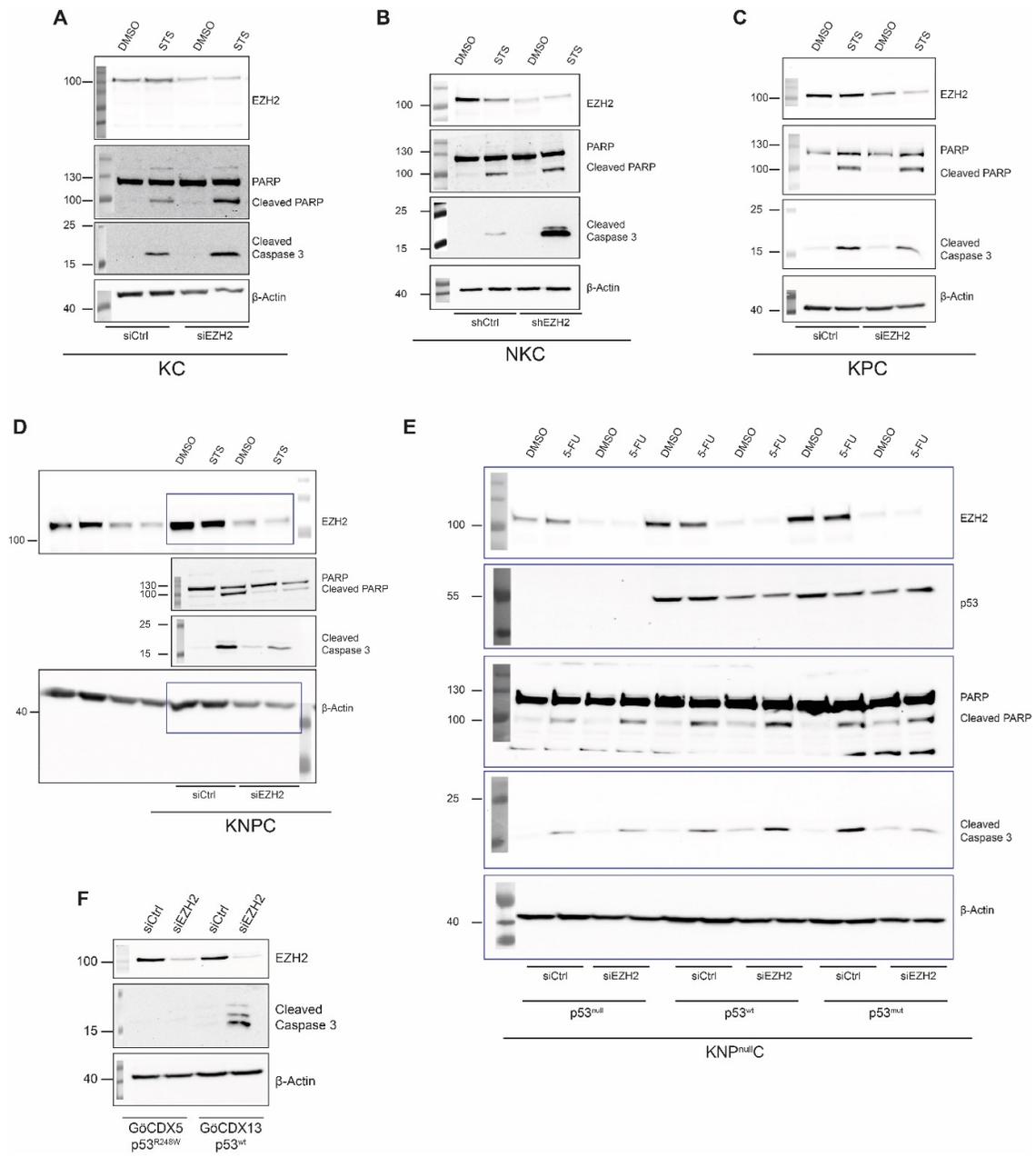
Supplementary Figure S2. TP53-status dependent EZH2 target gene regulation. **A** qRT-PCR analysis in the indicated p53wt and p53mut PDAC cells confirming knockdown of EZH2 ($n = 3$). Values represent mean \pm SD. Significance was determined by Student's t test; **, $p \leq 0.01$; ****, $p \leq 0.0001$. **B–D** Principal component analysis (PCA) upon RNA-sequencing of KC and KPC cells (**B**) and NKC and KNPC cells (**C, D**) after EZH2 knockdown displaying distinct clusters of triplicates. **E, F** Sample-to-sample distances upon RNA-seq analysis of KC and KPC cells (**E**) and NKC and KNPC cells (**F**) upon EZH2 knockdown. **G, H** Heatmap illustrating genes being significantly downregulated (FPKM > 0.01, $\log_2FC < -0.5$, $q < 0.05$) upon knockdown of EZH2 in the indicated p53wt cells (KC: 188 genes, NKC: 964 genes) and its consequences on the expression of these genes in the respective p53mut cells. **I, J** Gene ontology (GO) analysis to reveal significantly upregulated pathways upon EZH2 depletion in the indicated PDAC cells ($p < 0.05$).

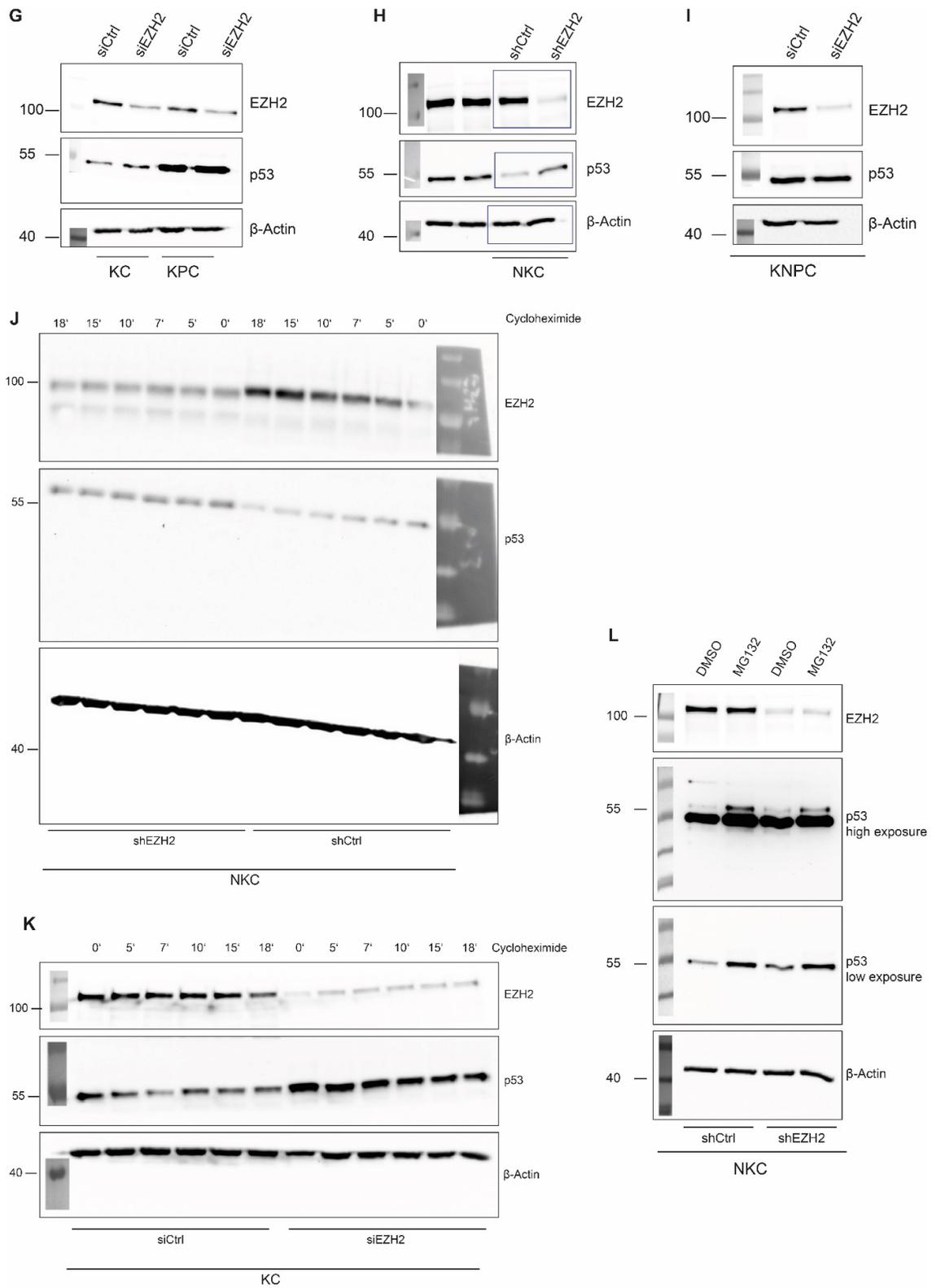


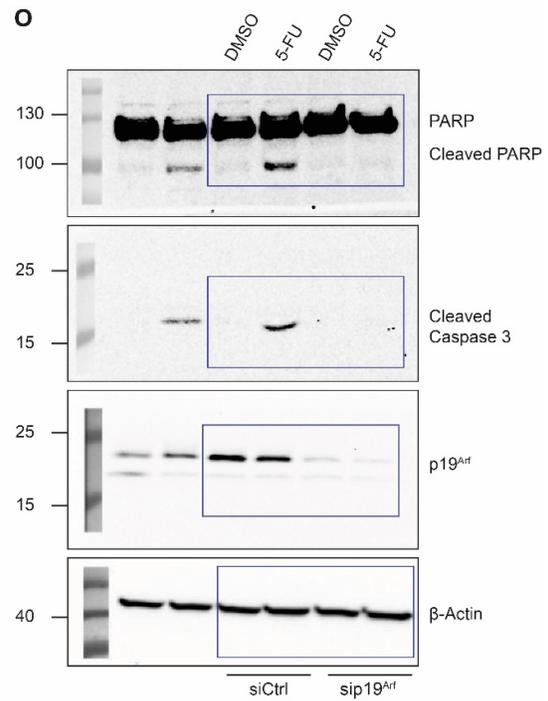
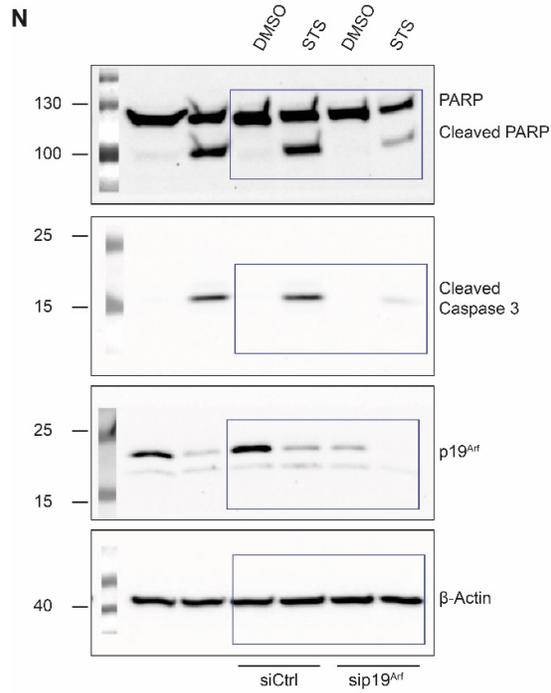
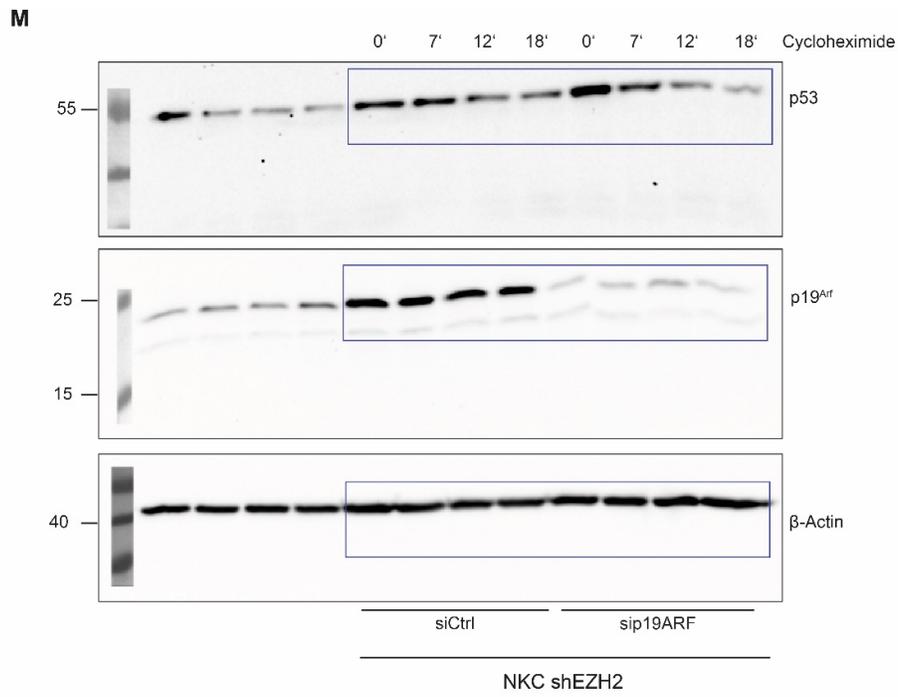
p53wt (KC, NKC) and p53mut (KPC, KNPC) expression and simultaneous treatment with staurosporine (STS). Representative flow cytometry results with the respective gating strategy upon Annexin-V/propidium iodide staining for each cell line referring to Figure 3. **B-F** Western blot analysis of apoptosis-related proteins upon knockdown of EZH2 and simultaneous treatment with 5-FU in the indicated p53wt and p53mut PDAC cells.



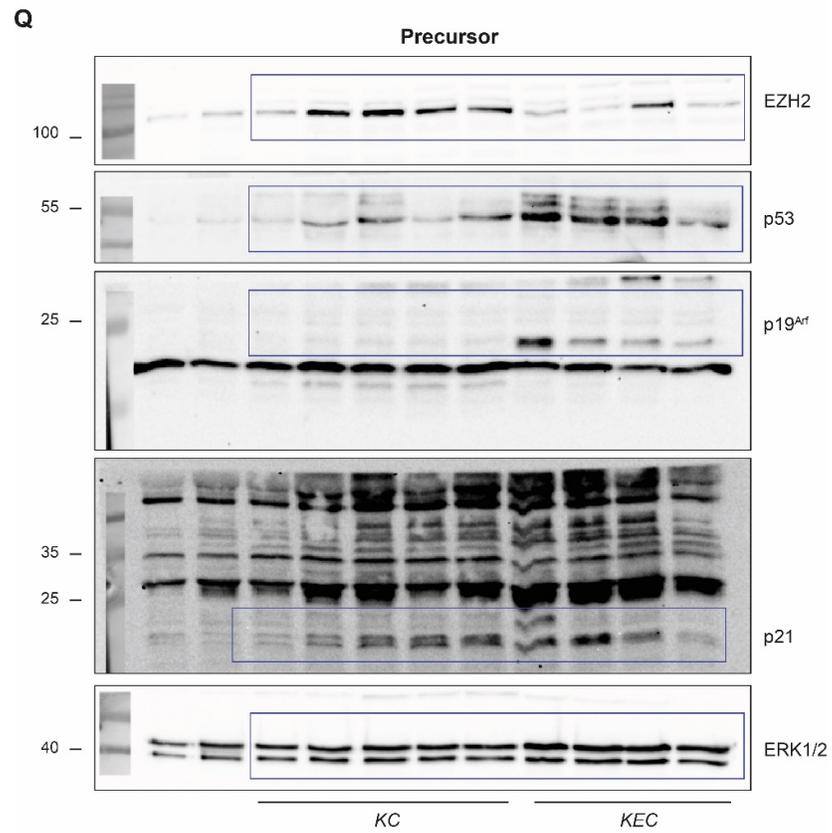
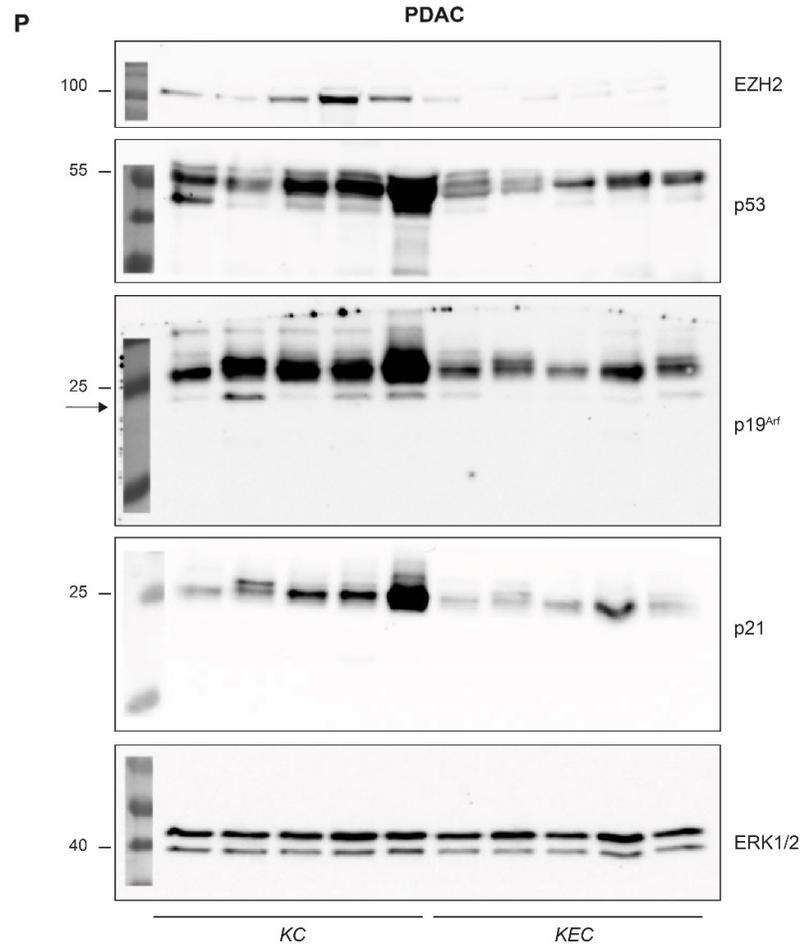
Supplementary Figure S4. EZH2-dependent target gene regulation differs in p53wt and p53mut PDAC. **A** Knockdown of EZH2 in p53wt NKC cells using siRNA following western blot analysis to investigate the consequences of EZH2 KD on the indicated proteins. **B** Normalized FPKM values of Cdkn2a expression after knockdown of EZH2 as revealed by RNA-seq in the indicated cell lines. Values represent mean ± SD. Significance was determined by Student’s t test; **, p ≤ 0.01; ***, p ≤ 0.001. **C-G** QRT-PCR analysis in the indicated PDAC cells upon knockdown of EZH2 validating the upregulation of these genes in p53wt cells (n = 3). Values represent mean ± SD. Significance was determined by Student’s t test; *, p ≤ 0.05; **, p ≤ 0.01; ns, non-significant. **H** Table displaying number of patients in the indicated EZH2low/high and p14ARF low/high groups based on IHC staining.

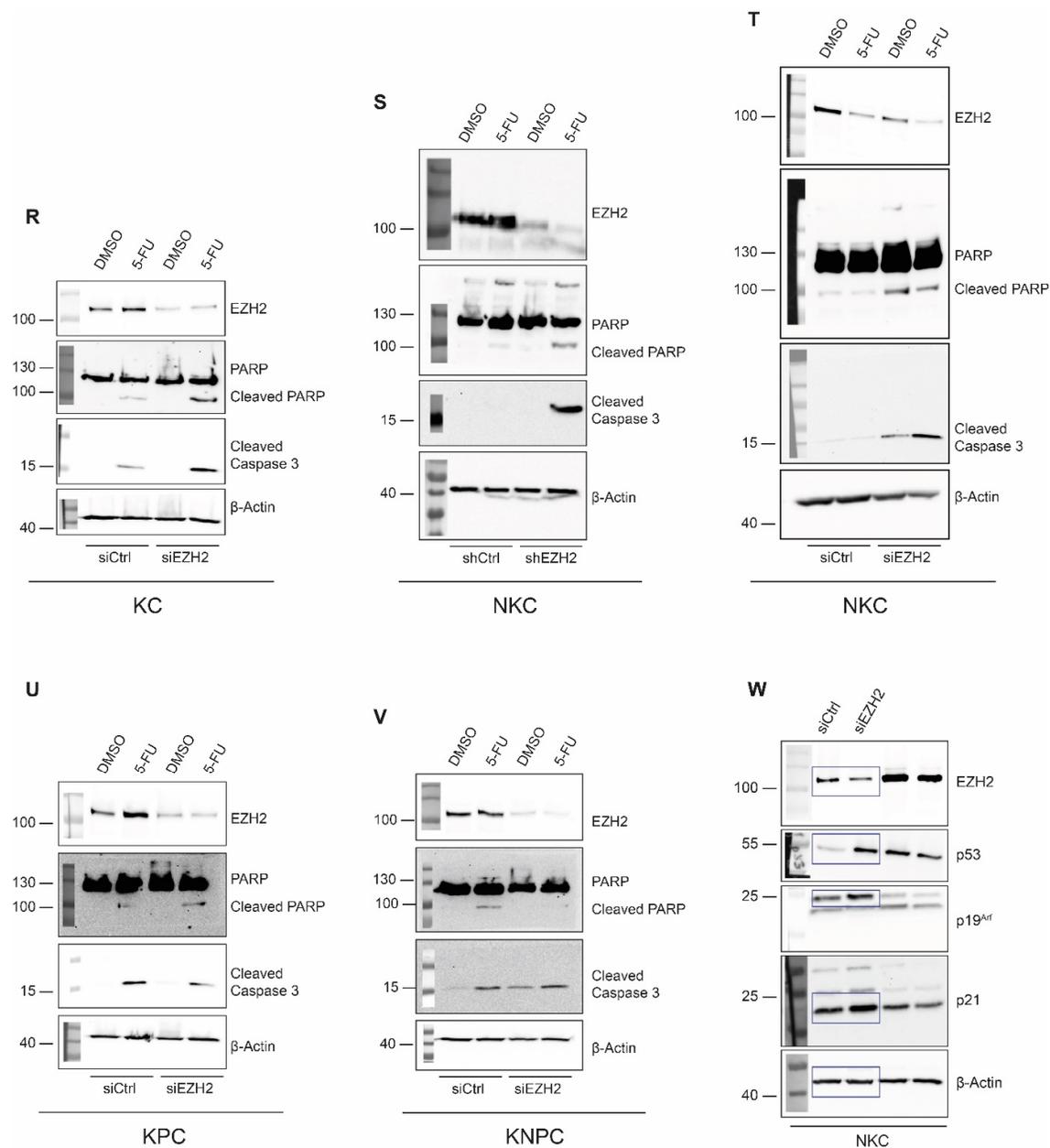






NKC shEZH2





Supplementary Figure S5. Un-cut original Western Blot images. Original western blot images from those western blots shown throughout the manuscript. We used the PageRule Prestained Protein Ladder, 10 bis 180 kDa from Thermo Scientific (26616) having bands at 180, 130, 100, 70, 55, 40, 35, 25, 15, and 10 kDa. We did not label all bands of the molecular weight marker but only the most relevant. However, the other molecular weight sizes can be identified accordingly. For protein visualization, we used the Western Lightning Plus (NEL103E001EA) or Ultra (NEL111001EA) chemiluminescent substrate from PerkinElmer. However, the marker cannot be visualized with the chemiluminescent solution and was imaged separately. Subsequently, we added the marker from the raw colorimetric image onto the enhanced chemiluminescent image to compare the molecular weight of the protein of interest with the standard. Please note, that we pre-cut the membranes before antibody incubation around the expected molecular weight of the protein of interest in order to stain different proteins of distinct molecular weight on one membrane. Blue boxes indicate excerpt of protein lanes depicted in the respective Figures. **A** Un-cut western blot images referring to Fig. 3C. **B** Un-cut western blot images referring to Fig. 3E. **C** Un-cut western blot images referring to Fig. 3G. **D** Un-cut western blot images referring to Fig. 3I. **E** Un-cut western blot images referring to Fig. 3K. **F** Un-cut western blot images referring to Fig. 3L. **G** Un-cut western blot images referring to Fig. 4A

and 4C. **H** Un-cut western blot images referring to Fig. 4B. **I** Un-cut western blot images referring to Fig. 4D. **J** Un-cut western blot images referring to Fig. 4F. **K** Un-cut western blot images referring to Fig. 4G. **L** Un-cut western blot images referring to Fig. 4H. **M** Un-cut western blot images referring to Fig. 5E. **N** Un-cut western blot images referring to Fig. 5F. **O** Un-cut western blot images referring to Fig. 5G. **P** Un-cut western blot images referring to Fig. 6B. **Q** Un-cut western blot images referring to Fig. 6H. **R** Un-cut western blot images referring to Supplementary Fig. 3B. **S** Un-cut western blot images referring to Supplementary Fig. 3C. **T** Un-cut western blot images referring to Supplementary Fig. 3D. **U** Un-cut western blot images referring to Supplementary Fig. 3E. **V** Un-cut western blot images referring to Supplementary Fig. 3F. **W** Un-cut western blot images referring to Supplementary Fig. 4A.

Supplementary tables

Supplementary Table S1. sgRNA sequences and validation primers for CRISPR/Cas9-mediated *EZH2* knockout.

| | Murine <i>Ezh2</i> | Human <i>EZH2</i> |
|--|----------------------|------------------------|
| sgRNA sequence | GTGGTGGATGCAACCCGAAA | GTGGTGGATGCAACCCGCAA |
| Forward primers for knockout validation | CCTGTGTAAGTGGGTGTGCT | TGCCTATTCGTGATGTTTGAAG |
| Reverse primers for knockout validation | GTTTGCTGTCACTTGGCTGG | TGTCAACAGCAGGGTGAGAAA |

Supplementary Table S2. siRNA sequences.

| | Sense | Antisense |
|----------------------------|-----------------------|-----------------------|
| siEZH2 | GGAUACAGCCUGUGCACAUU | AUGUGCACAGGCUGUAUCCTC |
| siP19^{Arf} | GGCUAGAGAGGAUCUUGAGTT | CUCAAGAUCUCUCUAGCCTC |

Supplementary Table S3. Primer for qRT-PCR.

| Target | Direction | Sequence |
|---------------|-----------|----------------------------|
| <i>Cdkn2a</i> | forward | CGCAGGTTCTTGGTCACTGT |
| <i>Cdkn2a</i> | reverse | TGTTACGAAAGCCAGAGCG |
| <i>Ezh2</i> | forward | CAACCCGAAAGGGCAACAAA |
| <i>Ezh2</i> | reverse | ACC AGT CTG GAT AGC CCT CT |
| <i>Itgb5</i> | forward | GAAGTGCCACCTCGTGTGAA |
| <i>Itgb5</i> | reverse | GGACCGTGGATTGCCAAAGT |
| <i>Ltbp1</i> | forward | GGTCGCATCAAGGTGGTCTTT |
| <i>Ltbp1</i> | reverse | GTGGTGGTATTCCCCTTCTGG |
| <i>Rnf130</i> | forward | CTGCCCATCCACGGAGTTG |
| <i>Rnf130</i> | reverse | CAAGCCGATCCACTGTTTGA |
| <i>Rplp0</i> | forward | TGGCAAGAACACCATGATG |
| <i>Rplp0</i> | reverse | AGTTTCTCCAGAGCTGGGTTGT |
| <i>Trp53</i> | forward | AGGTGTGCGTAGCACC |
| <i>Trp53</i> | reverse | CCCCACAACACCAGTG |
| <i>Wnt7b</i> | forward | CTTACCTATGCCATCACGG |
| <i>Wnt7b</i> | reverse | TGGTTGTAGTAGCCTTGCTTCT |

Supplementary Table S4. Antibodies used for western blotting.

| Antibody | Company | Number | Dilution |
|-----------------------|----------------|--------|----------|
| Actin-HRP | Sigma | A3854 | 1:40000 |
| Cleaved caspase 3 | Cell Signaling | 9661 | 1:500 |
| Erk (1/2) | Cell Signaling | 9102 | 1:1000 |
| EZH2 | Cell Signaling | 5246 | 1:1000 |
| p19 ^{Arf} | Abcam | Ab80 | 1:1000 |
| p19 ^{Arf} | Santa Cruz | 32748 | 1:250 |
| p53 | Cell Signaling | 2524 | 1:1000 |
| PARP | Cell Signaling | 9542 | 1:1000 |
| Anti-mouse (IgG) HRP | Cell Signaling | 7076 | 1:6500 |
| Anti-rabbit (IgG) HRP | Cell Signaling | 7074 | 1:6500 |
| Anti-rat (IgG) HRP | Santa Cruz | 2006 | 1:5000 |

Supplementary Table S5. Antibodies used for immunohistochemistry and immunofluorescence.

| Antibody | Company | Number | Dilution |
|---------------------------------|------------------|------------|----------|
| EZH2 (mouse) | Cell Signaling | 5246 | 1:100 |
| EZH2 (human) | Leica Biosystems | NCL-L-EZH2 | 1:50 |
| Ki-67 | Thermo Fisher | RM9106 | 1:600 |
| α SMA | Agilent Dako | M0851 | 1:100 |
| p14 | Cell Signaling | 2407 | 1:400 |
| p19 ^{Arf} | Santa Cruz | 32748 | 1:100 |
| Alexa Fluor 488 donkey anti-rat | Invitrogen | A21208 | 1:500 |

Supplementary Table S6. Antibodies used for ChIP experiments.

| Antibody | Company | Number | Amount |
|------------|----------------|-------------------|-----------|
| EZH2 | Diagenode | C15410039-classic | 2 μ g |
| H3K4me3 | Cell Signaling | 9751 | 2 μ g |
| Rabbit IgG | Diagenode | C15410206 | 2 μ g |

Supplementary Table S7. Primer for qRT-PCR following ChIP experiments.

| Target | Direction | Sequence |
|-------------------|-----------|------------------|
| <i>Cdkn2a</i> TSS | forward | GACCGTGAAGTTCAGC |
| <i>Cdkn2a</i> TSS | reverse | GGGGTCGCTTCTTCGG |

Supplementary Table S8. Favorable prognosis genes depicted in Figure 2C/D.

| | | | | | | |
|-----------------|------------------|----------------|-----------------|----------------|-----------------|-----------------|
| <i>CAMTA2</i> | <i>ABHD8</i> | <i>HCFC1</i> | <i>VPS54</i> | <i>SNAI3</i> | <i>GSE1</i> | <i>TBPL1</i> |
| <i>TSPYL2</i> | <i>SEMA6C</i> | <i>PPP1R10</i> | <i>MCM3AP</i> | <i>DOHH</i> | <i>LRRC29</i> | <i>ARIH2</i> |
| <i>ANAPC2</i> | <i>TMEM74B</i> | <i>SAFB</i> | <i>PMM1</i> | <i>RFX6</i> | <i>UAP1L1</i> | <i>RFX2</i> |
| <i>DEF8</i> | <i>GALT</i> | <i>KLHL36</i> | <i>ATP6V0A1</i> | <i>HERC1</i> | <i>KIF5A</i> | <i>SLC22A5</i> |
| <i>USP20</i> | <i>COG8</i> | <i>TMEM175</i> | <i>COQ10A</i> | <i>PRPSAP2</i> | <i>SLC27A3</i> | <i>DOPEY1</i> |
| <i>MICAL1</i> | <i>RAB11FIP3</i> | <i>ABCA5</i> | <i>RAB4B</i> | <i>UNC13B</i> | <i>DYNLL2</i> | <i>BAHCC1</i> |
| <i>SOCS2</i> | <i>EPOR</i> | <i>SSBP4</i> | <i>NEIL1</i> | <i>GNG7</i> | <i>PNISR</i> | <i>ASPHD1</i> |
| <i>SLC43A2</i> | <i>DENND4B</i> | <i>BRSK1</i> | <i>RBM4B</i> | <i>SNTA1</i> | <i>NCALD</i> | <i>MPDZ</i> |
| <i>ARNT2</i> | <i>NECAB3</i> | <i>BBS5</i> | <i>QTRT1</i> | <i>TACO1</i> | <i>INPP5B</i> | <i>MLLT6</i> |
| <i>WDR37</i> | <i>NAT9</i> | <i>TYK2</i> | <i>SPATC1L</i> | <i>NCDN</i> | <i>RAD51C</i> | <i>SMPD1</i> |
| <i>INPP5K</i> | <i>NFASC</i> | <i>CBX7</i> | <i>ZBTB46</i> | <i>HNRNPA0</i> | <i>TRMT10B</i> | <i>ULK3</i> |
| <i>PITPNA</i> | <i>PKD1</i> | <i>RNF166</i> | <i>CXXC4</i> | <i>ALKBH5</i> | <i>TAPT1</i> | <i>XAB2</i> |
| <i>PPP1R3F</i> | <i>ARMCX2</i> | <i>RBM14</i> | <i>IPO13</i> | <i>PSPH</i> | <i>TSPYL1</i> | <i>PPP6R2</i> |
| <i>MAMDC4</i> | <i>PNPLA6</i> | <i>ATP1B2</i> | <i>BTBD6</i> | <i>MAVS</i> | <i>POLR3H</i> | <i>MAP2K6</i> |
| <i>ARMC5</i> | <i>TMEM91</i> | <i>APH1B</i> | <i>WHRN</i> | <i>DVL2</i> | <i>NAP1L2</i> | <i>ANKRD13B</i> |
| <i>RNF167</i> | <i>B4GAT1</i> | <i>PLD6</i> | <i>PIP5K1C</i> | <i>CD81</i> | <i>INTS3</i> | <i>RBM5</i> |
| <i>CCDC106</i> | <i>IRGQ</i> | <i>PTPRS</i> | <i>IRF2BP1</i> | <i>GOLGA3</i> | <i>WDR83</i> | <i>RMND5B</i> |
| <i>MUM1</i> | <i>INCA1</i> | <i>ZFP3</i> | <i>ST3GAL2</i> | <i>FRS3</i> | <i>PFDN5</i> | <i>GAS8</i> |
| <i>SFXN5</i> | <i>RNASEH2C</i> | <i>GDF11</i> | <i>EFHC1</i> | <i>DIDO1</i> | <i>ANGEL1</i> | <i>PHKA2</i> |
| <i>TLE2</i> | <i>ACSF3</i> | <i>NCOA5</i> | <i>SDR39U1</i> | <i>IQCD</i> | <i>SYT5</i> | <i>GPX4</i> |
| <i>CBX6</i> | <i>GADD45G</i> | <i>NICN1</i> | <i>FOXA2</i> | <i>IGIP</i> | <i>NELL2</i> | <i>FKBP8</i> |
| <i>KCND1</i> | <i>CBX8</i> | <i>HDAC4</i> | <i>CCDC130</i> | <i>ADD1</i> | <i>REC8</i> | <i>RNPC3</i> |
| <i>RBM10</i> | <i>POMT1</i> | <i>KLHDC4</i> | <i>CERK</i> | <i>MAGEE1</i> | <i>HEXDC</i> | <i>ATP6AP1</i> |
| <i>TBC1D13</i> | <i>ARGLU1</i> | <i>ADGRL1</i> | <i>FN3K</i> | <i>HDAC3</i> | <i>SCG2</i> | <i>MC1R</i> |
| <i>RAD51D</i> | <i>PELP1</i> | <i>LIPE</i> | <i>SYNGR1</i> | <i>HIRA</i> | <i>STK40</i> | <i>MVB12B</i> |
| <i>FXR2</i> | <i>OAZ1</i> | <i>CCM2</i> | <i>FAM219A</i> | <i>FASTK</i> | <i>KCNH2</i> | <i>PDE3B</i> |
| <i>VAMP2</i> | <i>PPP1R12C</i> | <i>MBLAC1</i> | <i>NUDT18</i> | <i>TBC1D17</i> | <i>CALM1</i> | <i>SPECC1L</i> |
| <i>KLHL22</i> | <i>ZBTB40</i> | <i>DNMT3A</i> | <i>DCLK2</i> | <i>PRKAR2B</i> | <i>NEK9</i> | <i>MZF1</i> |
| <i>RAB6B</i> | <i>SPATA7</i> | <i>GRK6</i> | <i>RCAN2</i> | <i>SOWAHA</i> | <i>B4GALT6</i> | <i>DCAF15</i> |
| <i>EVL</i> | <i>MED9</i> | <i>SALL2</i> | <i>NPR1</i> | <i>ENPP5</i> | <i>TEX264</i> | <i>MIS12</i> |
| <i>TMEM203</i> | <i>KCTD17</i> | <i>RGS11</i> | <i>SLC25A44</i> | <i>NXF1</i> | <i>TMEM150C</i> | <i>TSC1</i> |
| <i>PRAF2</i> | <i>GPR162</i> | <i>MKS1</i> | <i>ID4</i> | <i>RAB17</i> | <i>CLEC3B</i> | <i>PHKG2</i> |
| <i>CYB561D1</i> | <i>MCF2L</i> | <i>UNC119B</i> | <i>TRIM39</i> | <i>RANBP3</i> | <i>JMJD6</i> | <i>AKAP8L</i> |
| <i>ZBTB48</i> | <i>SNAPC4</i> | <i>LUC7L</i> | <i>PIGT</i> | <i>RFXAP</i> | <i>TUBGCP6</i> | <i>PPP1R21</i> |
| <i>ELMOD3</i> | <i>SNRNP70</i> | <i>RAPGEF4</i> | <i>THEM4</i> | <i>MRPL38</i> | <i>ITGAE</i> | <i>CERS4</i> |
| <i>PHLDB3</i> | <i>TTC13</i> | <i>TBL1X</i> | <i>CHPF2</i> | <i>DEXI</i> | <i>ATP6VOE2</i> | <i>CUL9</i> |
| <i>SLC25A11</i> | <i>CCDC92</i> | <i>SPPL2B</i> | <i>TMEM240</i> | <i>ACCS</i> | <i>SFI1</i> | <i>FBXO46</i> |
| <i>VASH1</i> | <i>MTHFR</i> | <i>RGS9</i> | <i>CCND2</i> | <i>HAP1</i> | <i>SMDT1</i> | <i>TECPR1</i> |

| | | | | | | |
|----------|----------|----------|----------|---------|----------|----------|
| LRSAM1 | LPCAT1 | MRPL53 | SAFB2 | POMGNT1 | DXO | LENG1 |
| CBFA2T2 | PKIG | SCN1B | ZBTB4 | NAA60 | GPANK1 | SRR |
| FAM53B | USF2 | RWDD2A | CLDN15 | CACNA1A | DNAJC18 | OTUD5 |
| BRF1 | RNF146 | TOP3A | EID2B | RECQL5 | IGHMBP2 | FZD8 |
| NUAK2 | MAP1LC3A | GCH1 | MAGEH1 | IKZF4 | GNAO1 | EFNB3 |
| TBKBP1 | STRADA | RBM6 | CXXC1 | SIN3B | CEP164 | WRAP53 |
| DLG4 | TRIM3 | CCDC159 | ENGASE | SH2B1 | GFOD2 | MRPL57 |
| ATOH8 | CCDC57 | DTX3 | ELP5 | CRY2 | FXYD6 | CHD3 |
| SGSM2 | MCOLN1 | PCGF3 | FBXO44 | EMC10 | NEU3 | CNPY2 |
| NCAM1 | PRR3 | RABL6 | PBXIP1 | RANGRF | ZDHHC1 | FIZ1 |
| CEP250 | DCUN1D2 | TERF2IP | MAP1S | UCKL1 | GBA2 | KATNB1 |
| B3GNT8 | SCAMP5 | NINL | CAMKK1 | SIRT3 | SLC30A4 | STARD3NL |
| SLC2A8 | MADD | SLC16A13 | NT5C3B | FLCN | EPC1 | SHC2 |
| TMEM86B | PTCH2 | APBA3 | ASPSR1 | SLC29A4 | PLEKHB1 | SDSL |
| NAIF1 | VPS16 | MAP3K12 | CIRBP | TMOD2 | MEGF8 | KDM2B |
| SEC61A2 | PCED1A | PEBP1 | CDK10 | ALDH9A1 | LUC7L3 | PAF1 |
| CCDC28B | LLGL2 | EXOC3 | FAM120B | AP2A2 | ZZEF1 | R3HCC1 |
| PHF10 | SAT2 | ASB1 | MIF4GD | ARFGAP1 | ELMO2 | VPS18 |
| CLSTN3 | MOCS1 | ATP8B2 | WDR19 | ATP5D | RGL2 | TMEM59L |
| ATP6VOD1 | ANKRD39 | ING5 | METTL3 | ELMO1 | SLC25A27 | TPGS1 |
| BCAS3 | ATP1A3 | MYBBP1A | KRBA1 | ACBD4 | ANKRD54 | IRX2 |
| PI4KB | SENP3 | STK11IP | RAI2 | TATDN2 | GPR137 | TSPAN33 |
| KCTD2 | RNF216 | STAT5B | MINK1 | FBXW4 | SUOX | FKRP |
| CHST12 | MTG2 | LIN37 | MAGED2 | DCXR | LRRC56 | NPM2 |
| GIGYF1 | CTNS | IZUMO4 | SLC25A45 | DCAF8 | GPATCH3 | SREBF1 |
| MXD4 | CTC1 | TSPAN7 | FAAP20 | PLCG1 | RABEP1 | KCTD13 |
| SLC26A11 | IFFO1 | DPY19L3 | SLC25A29 | ASCL2 | PLD3 | IQSEC1 |
| SLC16A11 | TNRC6C | PGPEP1 | SLC38A10 | TFEB | MED22 | HELQ |
| SOBP | UNK | GTPBP6 | PACS2 | TAOK2 | PRKACA | KLHDC3 |
| VPS53 | PPP3CB | TNS2 | CENPT | FYN | POLR3F | TRAPPC12 |
| ZMAT1 | GKAP1 | ARHGEF11 | TANGO2 | DIRAS1 | CLPP | PTOV1 |
| ABHD17A | UPF3A | TMEM220 | SMARCA1 | MAN1C1 | DPH7 | HDAC10 |
| MBD3 | SLC23A2 | SLC22A17 | METTL16 | FAM193A | PAPSS2 | SPHK2 |
| GPRASP1 | NMNAT3 | KDM8 | SGSH | EGLN2 | AXIN2 | USP27X |
| DPH1 | ARMCX1 | ITGA7 | PPP1R9B | RFNG | AKT1S1 | TDRP |
| CRTC1 | PGS1 | TAF1C | TBCB | FAM222A | POU6F1 | ZFAND2B |
| UBOX5 | FBXL16 | ZBTB49 | SEPHS1 | INTS1 | KBTD7 | FAM83F |
| APBB1 | LRRC75A | ZSWIM1 | TFPT | GGA1 | SSTR2 | RASIP1 |
| FLYWCH2 | GPS2 | ZSWIM7 | TMEM8B | NCKAP5L | PKNOX1 | LYRM9 |
| EXOG | AH1 | CFD | NPDC1 | MRPL34 | IMMP1L | GTF3C1 |
| ARID3A | RAB11B | SLC25A14 | ATP6V0B | CCDC96 | KLC1 | ATOX1 |
| TMEM104 | CYB5D2 | LRRC14 | PIN1 | SORBS3 | PGBD1 | AGFG2 |
| ARAP1 | CAPN10 | CTDNEP1 | KCTD7 | LSM10 | APBB3 | SGK3 |
| SAP30L | PMPCA | FAM117A | ERCC2 | NAAA | WBP1 | CISH |
| ENPP2 | RUFY3 | INPP5E | MON1A | WNT4 | IP6K1 | NDUFA3 |
| VPS37D | UNC119 | FBXO9 | WDR81 | P3H3 | TRMU | PABPN1 |
| CDIP1 | IQCC | CPT1C | ABCB8 | SPG7 | ACADV1 | EFCC1 |
| TRAF1 | DPP7 | DUSP28 | TRIM25 | RFX1 | TMEM198 | ROGDI |
| MARK1 | TSPYL4 | UQCR11 | CSAD | PDZRN3 | NAGLU | TIMM13 |
| PNPLA7 | ORAI2 | CYB561D2 | ACADSB | DISP1 | PPP1R26 | WIPI2 |
| GPR173 | U2AF1L4 | YIF1B | MAP6 | SMIM4 | ZDHHC14 | STXBP1 |
| NEURL4 | TXLNA | NISCH | RGAG4 | STIM2 | UBXN6 | PALM |
| TRAF3 | NRIP2 | RNASEK | AGER | RSAD1 | MAST3 | ATG4D |
| EBF4 | LRWD1 | TOM1L2 | SLC25A4 | CPLX1 | RXRA | CHGB |
| CASKIN2 | FBXO31 | TRO | TIMM22 | TSC2 | PIAS4 | CHMP6 |
| GABBR1 | DMPK | ZCWPW1 | MTERF4 | MTG1 | ATG16L2 | SMPD2 |
| TSEN54 | FAM69B | ACACB | LMBR1L | MTMR4 | SCAP | |
| CD99L2 | MTA1 | KLHDC1 | ZSCAN2 | IFT88 | MST1 | |
| HSD17B14 | GABARAP | ZFP57 | CALY | CLCN5 | TBXA2R | |
| PDZD4 | CSNK1D | ANKRD16 | KAT2A | RPAIN | GRIK5 | |

Supplementary Table S9. Genes being significantly upregulated in p53wt but not in p53mut cells upon EZH2 knockdown.

| | | | | | | |
|---------------|---------------|----------------|-----------------|-----------------|----------------|------------------|
| <i>Anxa6</i> | <i>Dtna</i> | <i>Igf2bp3</i> | <i>Maged2</i> | <i>Pbbp</i> | <i>Sfn2</i> | <i>Tpm2</i> |
| <i>Camk2b</i> | <i>Efemp2</i> | <i>Igf2r</i> | <i>Map1lc3a</i> | <i>Rdh10</i> | <i>Spon2</i> | <i>Trp53inp2</i> |
| <i>Cdkn2a</i> | <i>Fhdc1</i> | <i>Itgb5</i> | <i>Masp1</i> | <i>Rnf130</i> | <i>Sprr1a</i> | <i>Tuft1</i> |
| <i>Ddah2</i> | <i>Foxg1</i> | <i>Ltbp1</i> | <i>Neat1</i> | <i>Serpib6b</i> | <i>Tbc1d16</i> | <i>Wnt7b</i> |
| <i>Dnaaf9</i> | <i>Fzd6</i> | <i>Ltbp3</i> | <i>Palld</i> | <i>Slc44a2</i> | <i>Tcf24</i> | <i>Zfp62</i> |