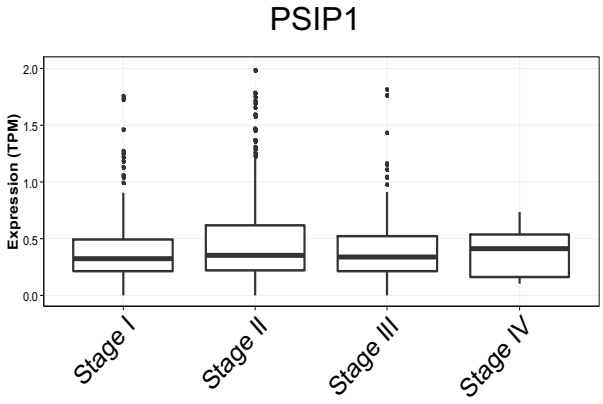
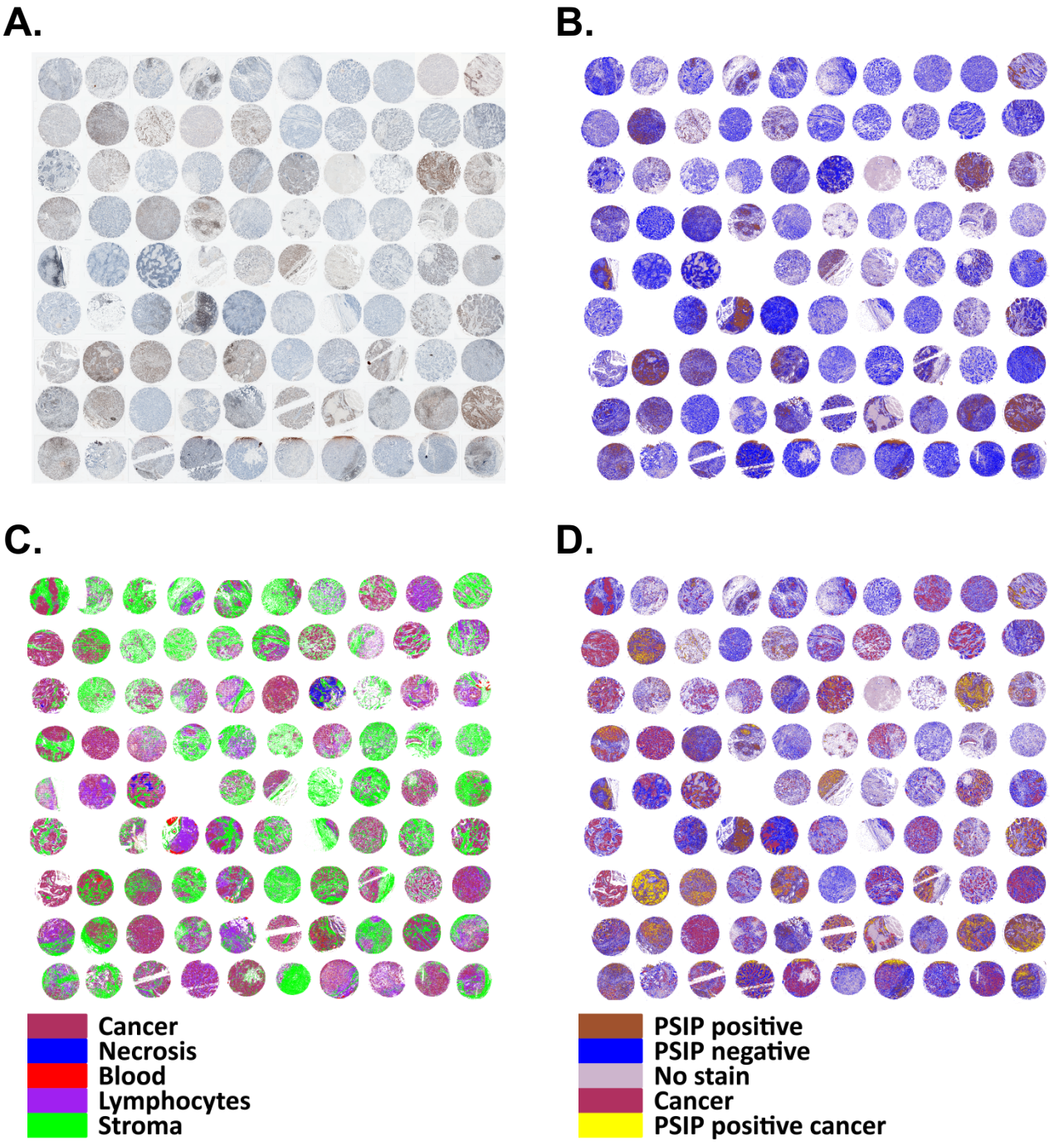
Supplementary Figure 1



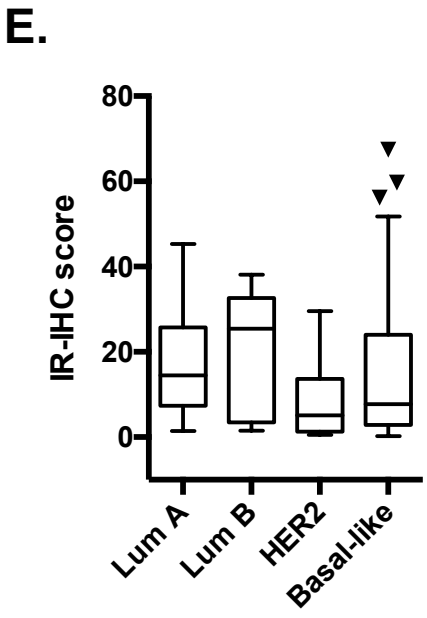
Supplementary Figure 1. Stage specific expression of PSIP1 mRNA in the BC patient samples (p-value > 0.1; Kruskal-Wallis Test). Data is extracted from TCGA RNA-seq.

Supplementary Figure 2



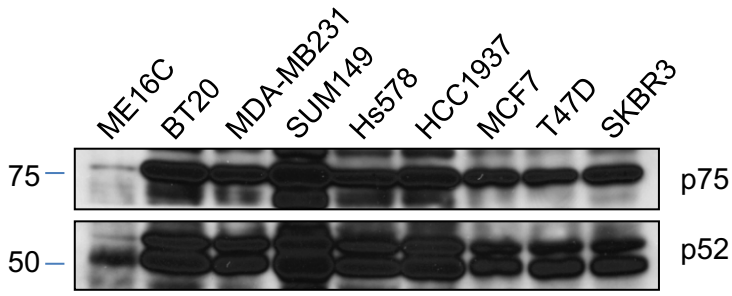
Supplementary Figure 2. Digital pathology of BR10010d to identify cancerous regions stained positive for PSIP1 antibody in patient TMA samples. **(A)** IHC staining of PSIP antibody in cancerous epithelium and lymphocytes **(B)** Digital IHC stain of PSIP1 antibody in cancerous epithelium and lymphocytes obtained by supervised classification based on RGB color values of IHC stain. **(C)** Digital pathology of IR image to identify cancer, necrosis, blood, lymphocytes and stroma in the TMA. **(D)** Digital IHC image with cancer regions identified from IR image overlaid on top. The overlaid images show PSIP1 positive cancer and PSIP1 negative cancer cores

Supplementary Figure 2



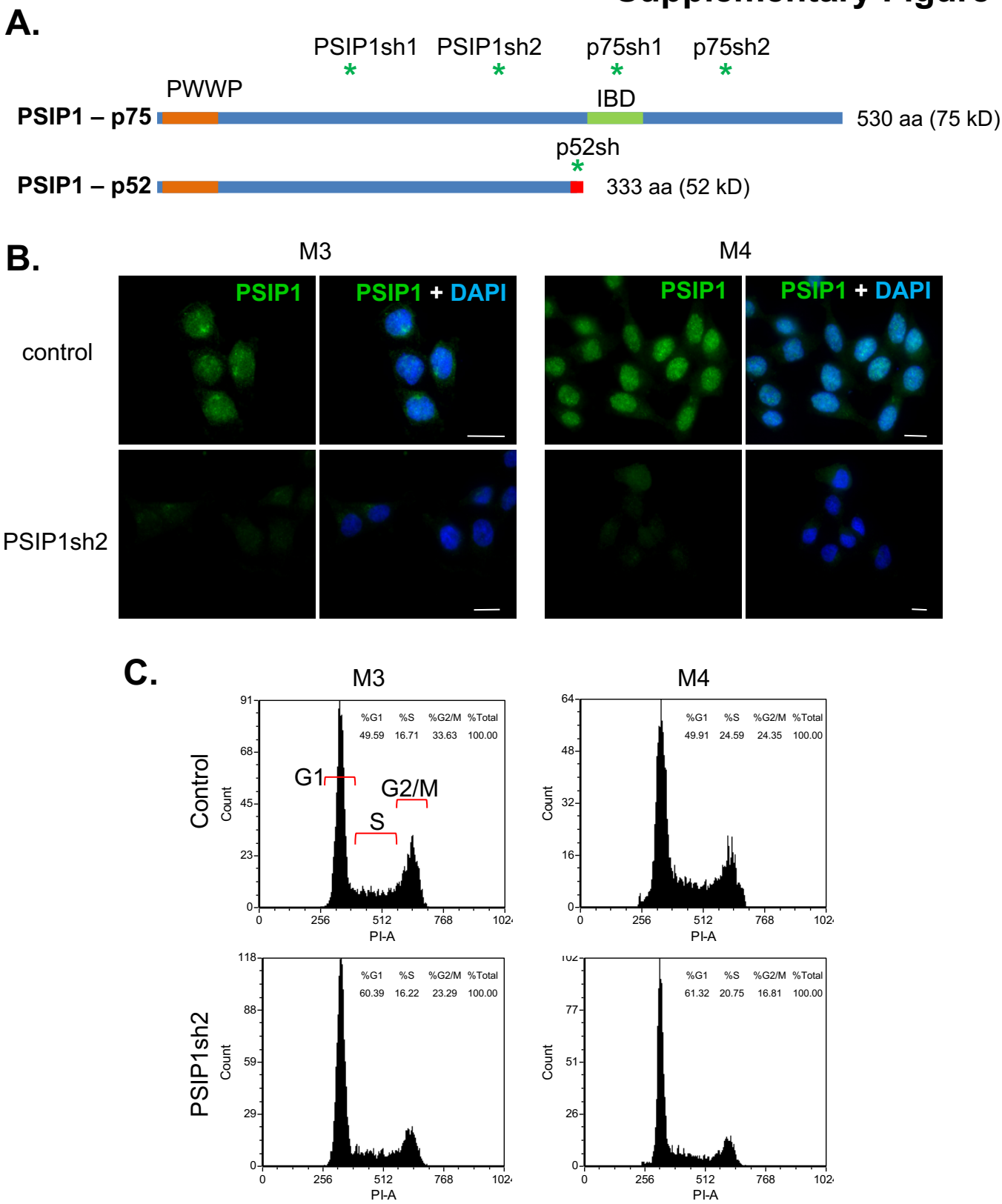
Supplementary Figure 2. (E). Subtype specific expression of PSIP1.

Supplementary Figure 3



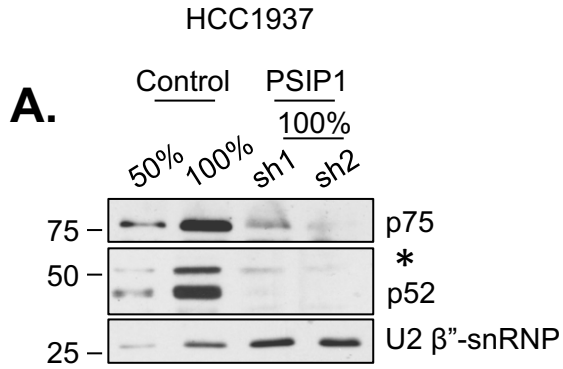
Supplementary Figure 3. Higher exposure of the immunoblot (same figure presented in figure1F) showing low level of PSIP1 in ME16C cells.

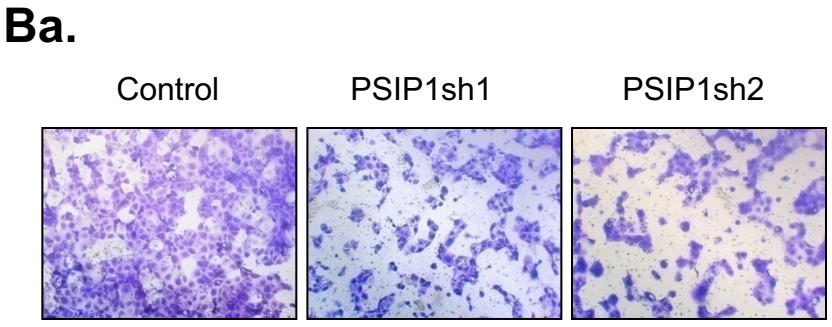
Supplementary Figure 4

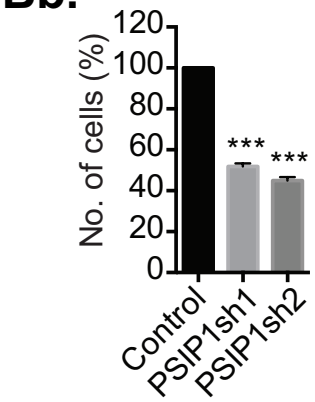


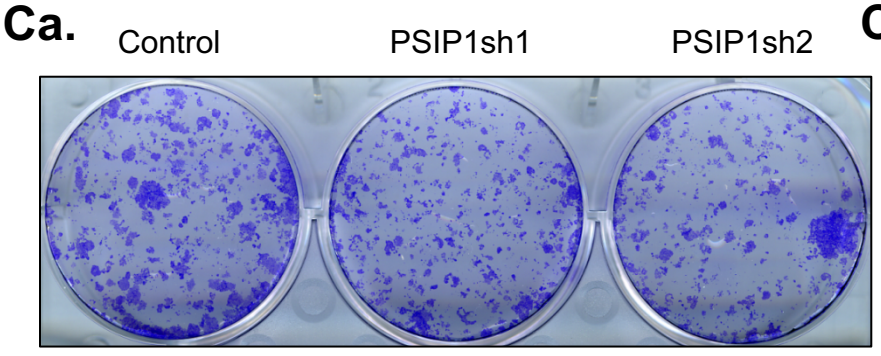
Supplementary Figure 4. (A) Schematic of PSIP/p75 and PSIP/p52 proteins showing different domains. Star depicts position from where shRNAs were designed. **(B)** Immunofluorescence staining showing reduced levels of PSIP1 in PSIP1-specific shRNA-transduced M3 and M4 cells. DNA is counterstained with DAPI. Scale bar represents 10 μm. **(C)** Flow cytometry analyses showing cell cycle profile of control and PSIP1-depleted M3 and M4 cells.

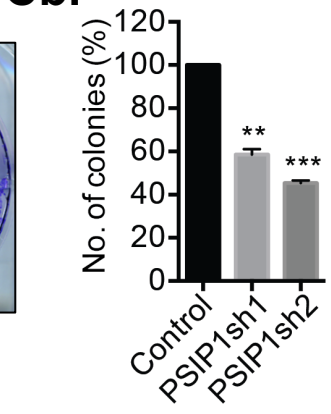
Supplementary Figure 5





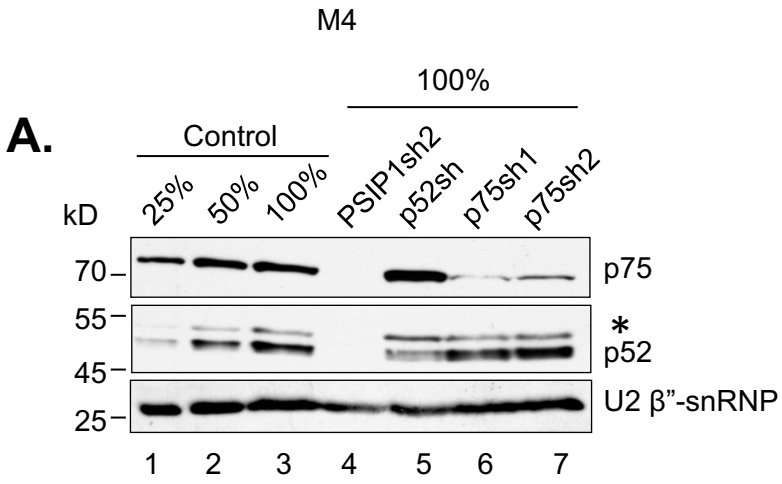


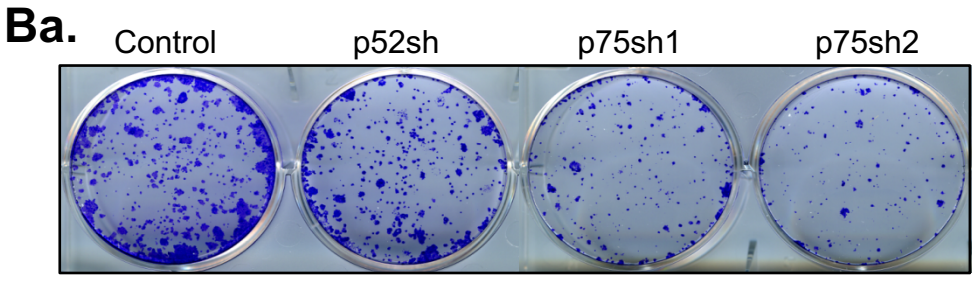


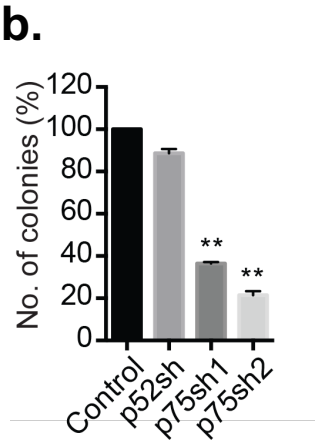


Supplementary Figure 5. (A) Immunoblot shows the shRNA-mediated depletion of PSIP1 in HCC1937 cells. * denotes the p52 variant. **(B)** Migration assay in control and PSIP1-depleted HCC1937 cells and corresponding quantification from triplicate experiments. **(C)** Anchorage-dependent colony formation assay in control and PSIP1-epleted HCC1937 cells and corresponding quantification from triplicate experiments. p-value ** < 0.01 and *** < 0.001.

Supplementary Figure 6

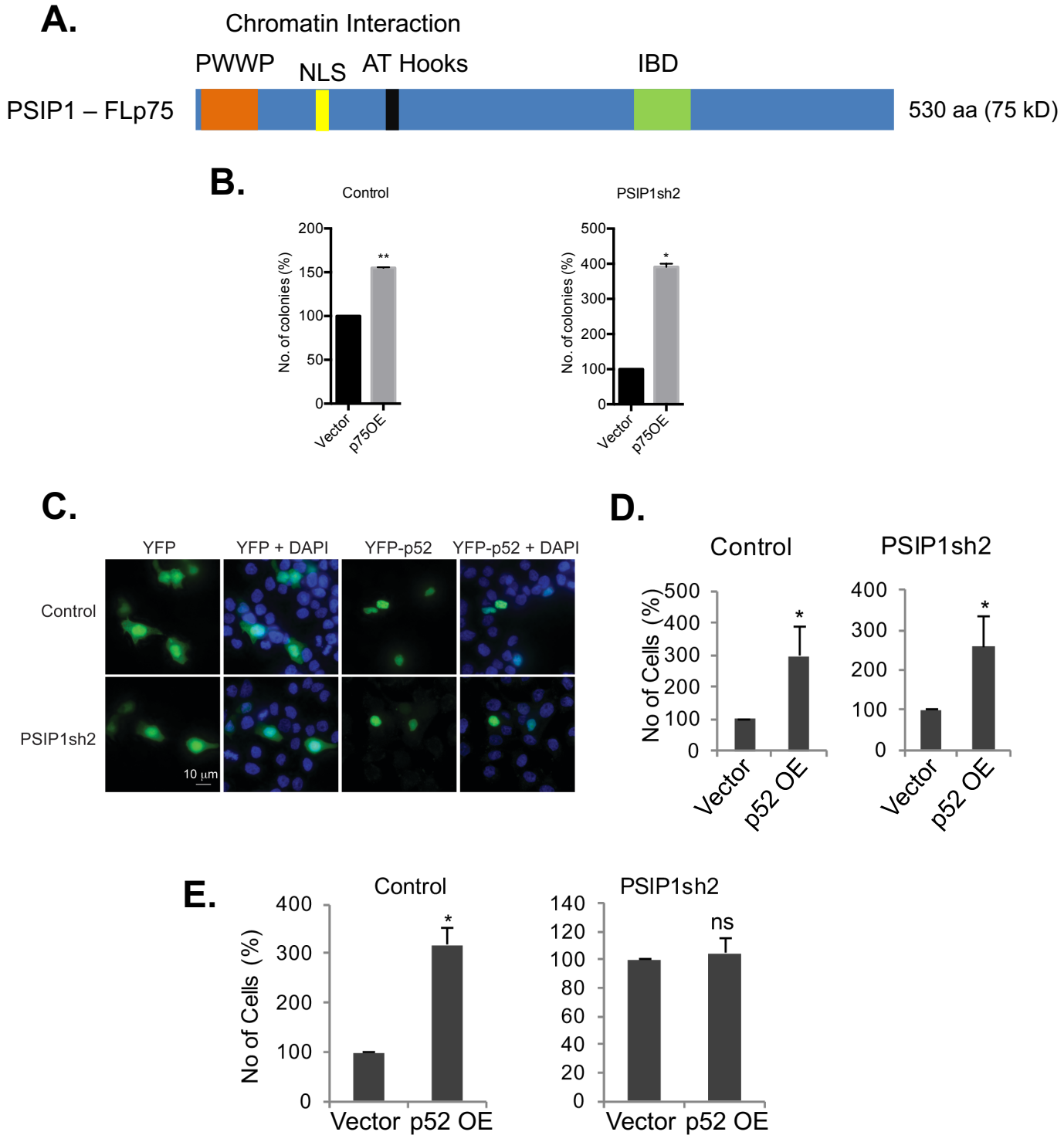






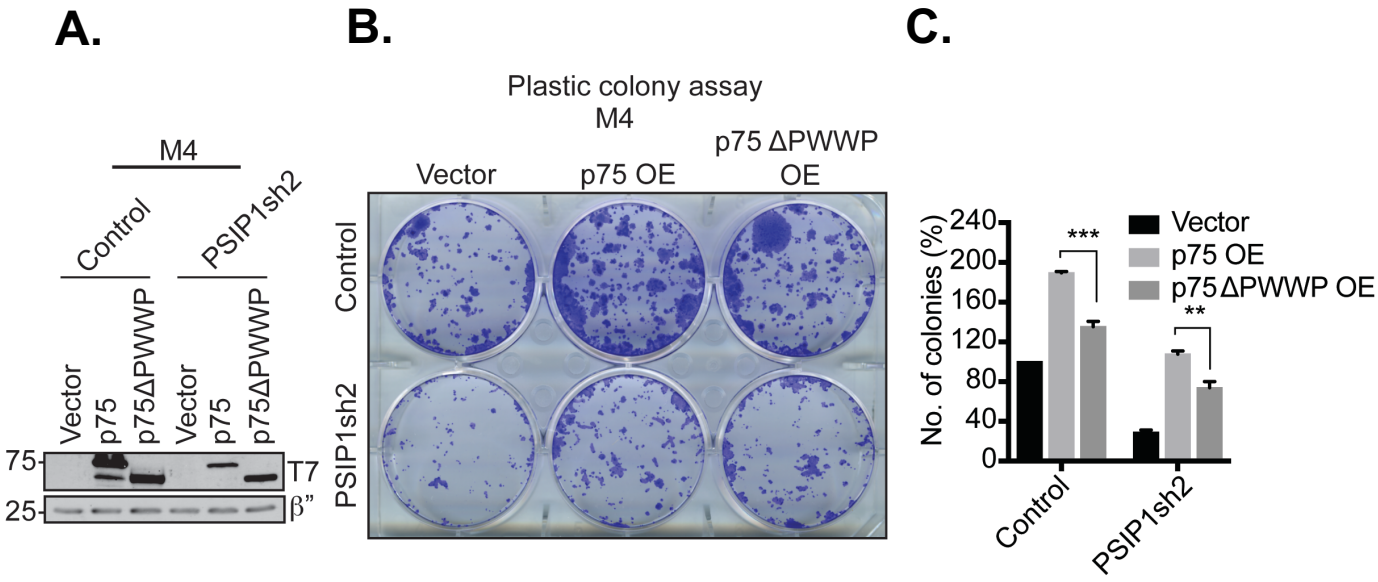
Supplementary Figure 6. (A) Immunoblot of p75 and p52 in control and PSIP1 isoform-specific shRNA-treated M4. Note that cells depleted of p52 (lower band in the p52 blot) show marginal increase in the levels of p75 (compare lanes 3 with 5). * designates the p52 variant. **(Ba & b)** Anchorage-dependent colony formation assay in control, p52 or p75 alone depleted M4 cells, and its corresponding quantification from three replicates. p-value ** < 0.01.

Supplementary Figure 7



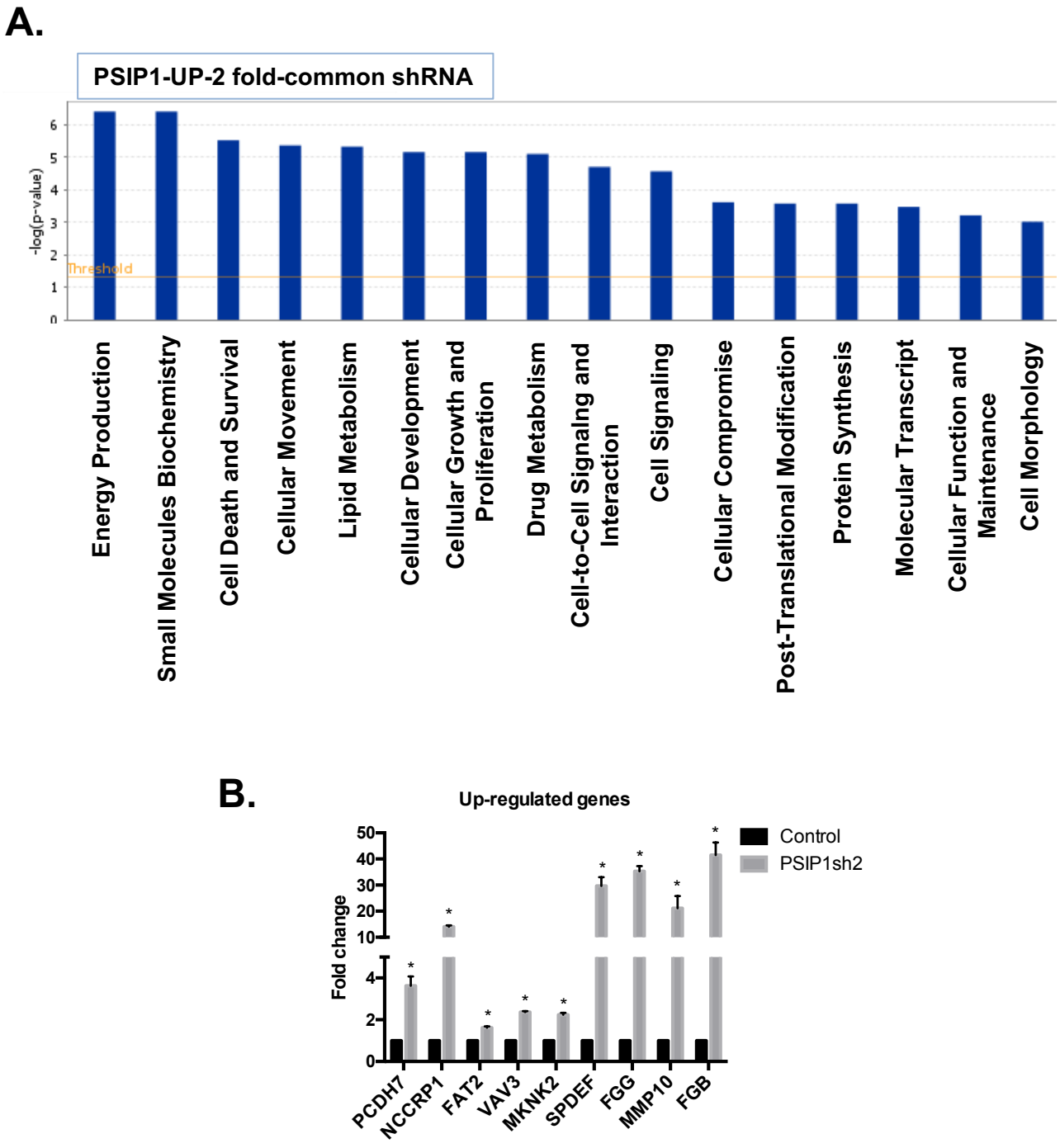
Supplementary Figure 7. (A) Schematic showing FL p75 construct that was used for overexpression experiments. **(B)** Anchorage-independent colony formation assay in vector or p75 overexpessed M4 cells that are transduced with control or PSIP1 specific shRNAs. **(C)** Over-expression of YFP-p52 in M4 control and PSIP1 KD cells. YFP vector shows both cytoplasmic and nuclear staining while YFP-p52 localized to nucleus only. **(D)** Graph from three biological repeats showing increased plastic colony formation after p52 OE. **(E)** No significant increase in the migration by p52 OE in PSIP1 KD cells. p-value * < 0.05, ** < 0.01 and ns: not significant.

Supplementary Figure 8



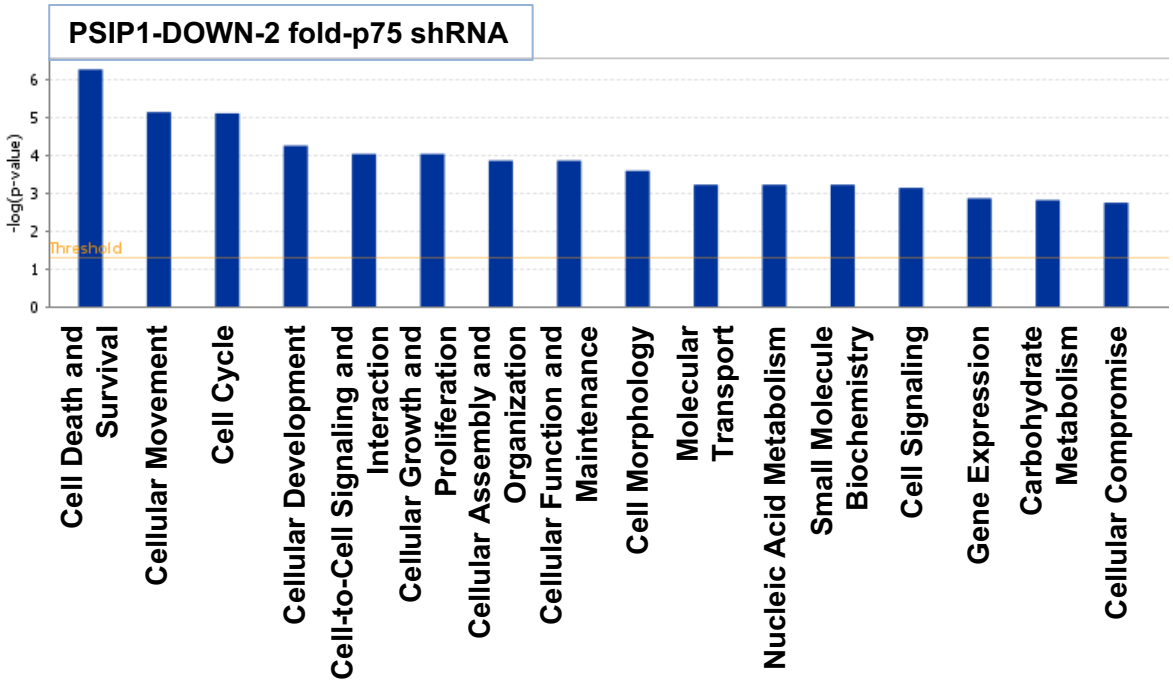
Supplementary Figure 8. (A) Western blot showing over-expression of T7 tagged p75 and PWWP deleted p75 mutant. **(B and C)** Anchorage-dependent colony formation assay in p75 and △p75 over-expressed cells, and its corresponding quantification from three replicates. p-value ** < 0.01 and *** <0.0001.

Supplementary Figure 9

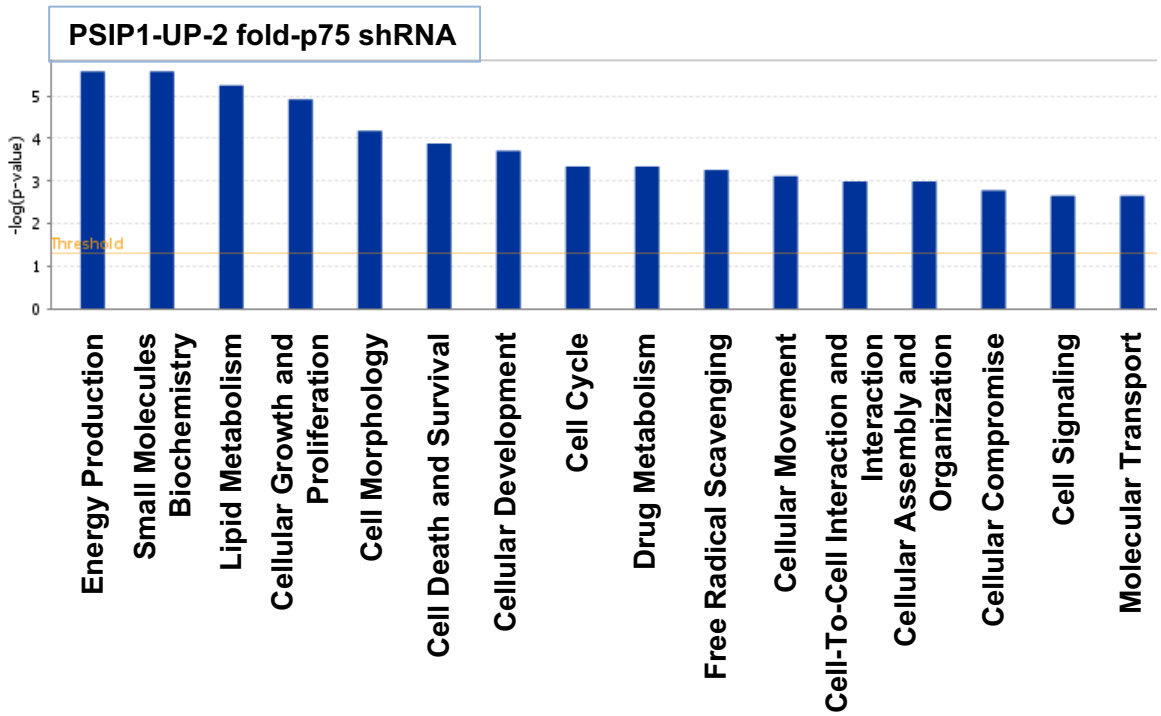


Supplementary Figure 9. (A) GO pathway from microarray data representing genes that are upregulated in PSIP1 (all of the idoforms)-depleted M4 cells **(B)** RTq-PCR validation of upregulated genes. p-value * < 0.05.

C.

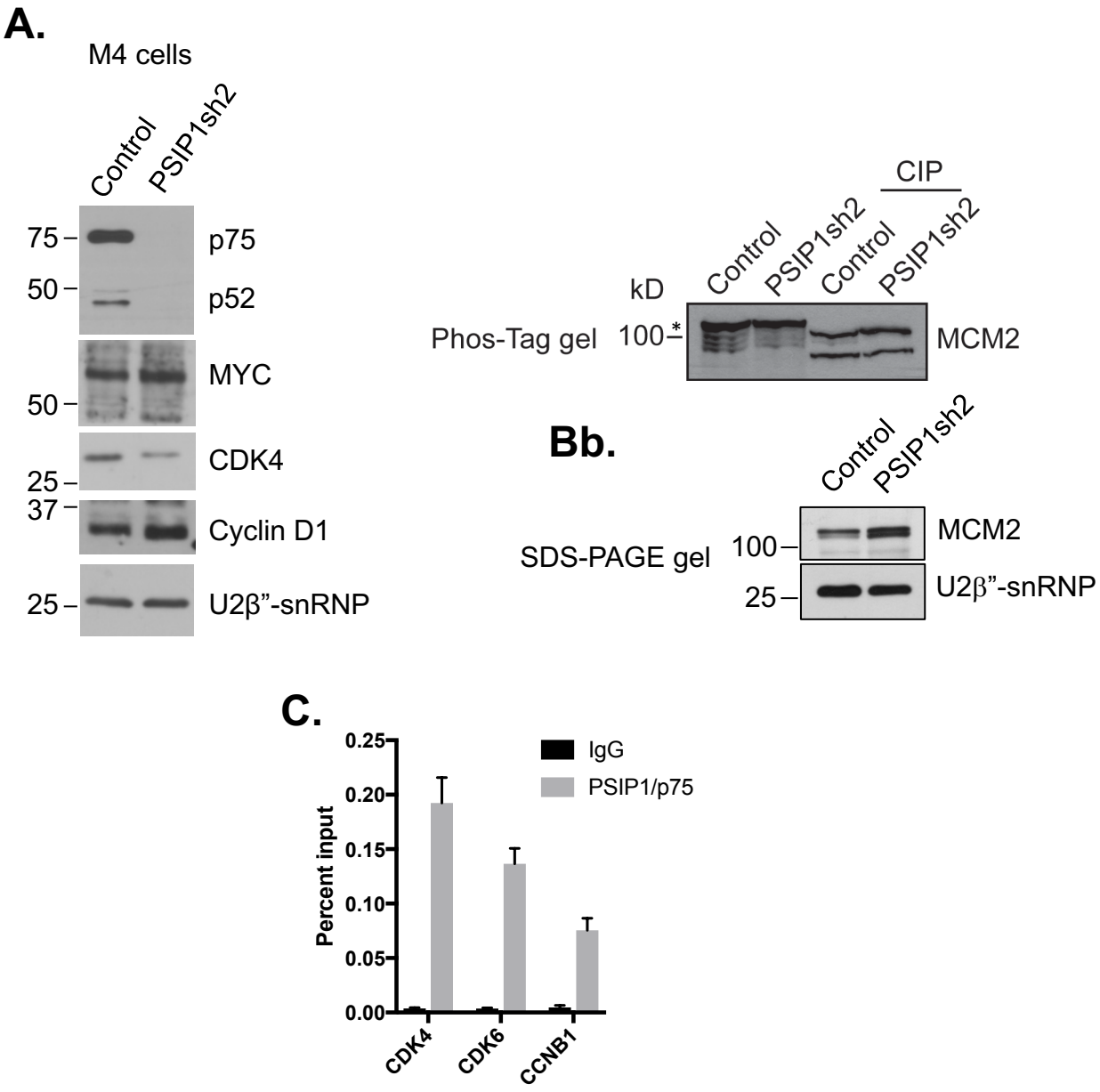


D.



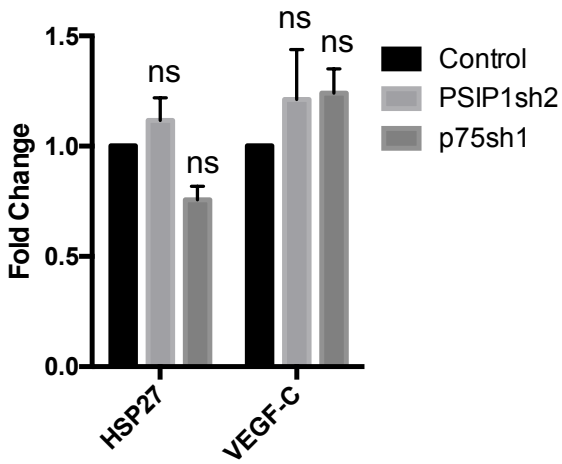
Supplementary Figure 9. (C and D) GO pathways from microarray data representing downregulated or upregulated genes in M4 cells that are depleted of only PSIP1/p75 isoform.

Supplementary Figure 10



Supplementary Figure 10. (A) Immuoblot data showing levels of proteins in control and PSIP1-depleted M4 cell extracts. U2β"-snRNP is used as loading control. **(Ba)** Phos-tag western blot showing comparable levels of phosphorylated MCM2 (*) in control and PSIP1 depleted cells. CIP (Calf intestinal phosphatase) treated samples showed increased mobility of the dephosphorylated MCM2. **(Bb)** Western blot showing MCM2 expression in control and PSIP1-depleted M4 cells. **(C)** PSIP1/p75 ChIP-qPCR showing increased association of p75 to the promoters of cell cycle genes (CDK4 & CDK6). Note that both CDK4 and CDK6 showed reduced expression in PSIP1/p75-depleted cells. Also. RNA pol II showed reduced association to these promoters in the absence of PSIP1.

A.



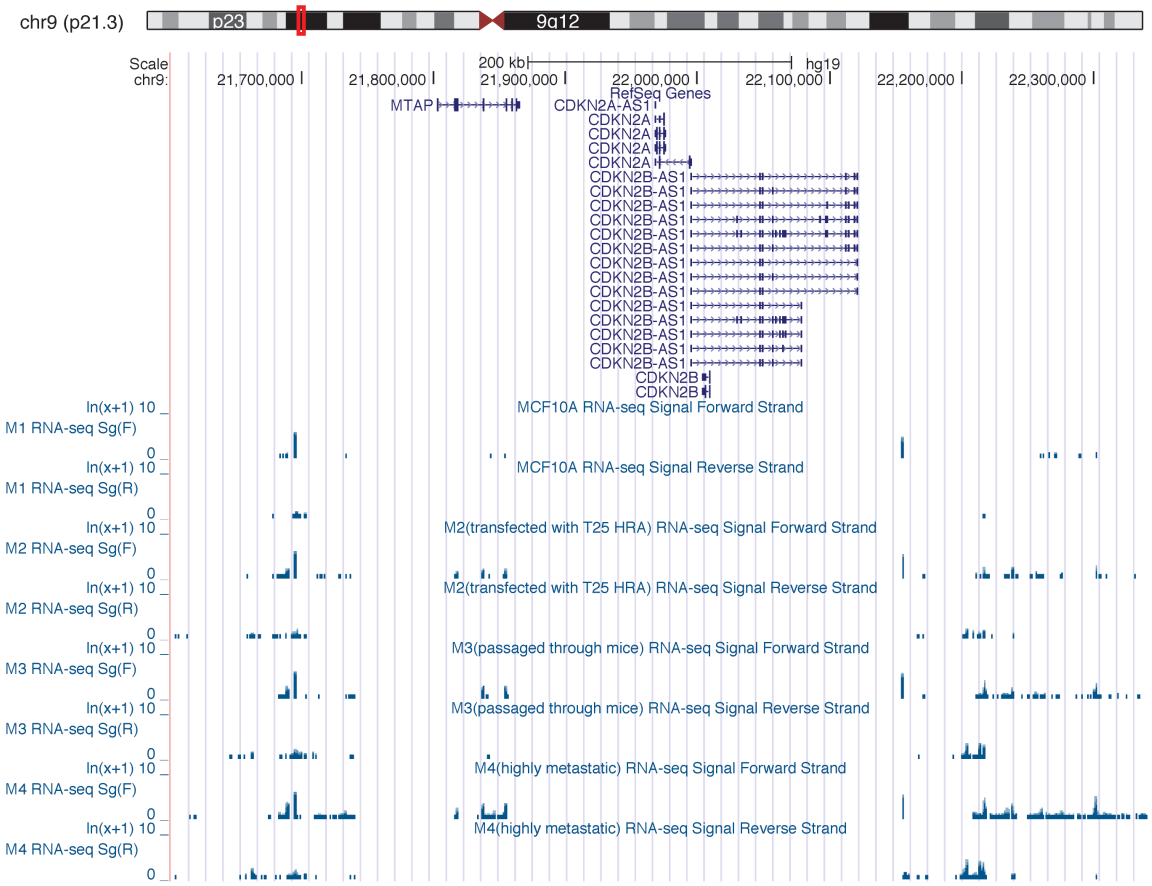
B.

TFs for down-regulated genes	TFs for up-regulated genes	
GTF2A1 (118)	SP1 (177)	RFXANK (47)
LHX5 (52)	EP300 (162)	GRHL1 (36)
MXI1 (41)	EIF5A2 (89)	NFYA (35)
IKZF1 (32)	PIK3C3 (78)	FOXO1 (23)
MYC (25)	ESR1 (60)	POU2F2 (21)
RHOXF1 (23)	NFIL3 (58)	
FOXO1 (15)	SOX13 (58)	
SREBF1 (10)	POU2F1 (49)	

Supplementary Figure 11. (A) RT-qPCR to show the levels of *HSP27* and *VEGF-C* mRNA in control, PSIP1 (all isoforms), PSIP1/p75-depleted M4 cells. ns : not significant. **(B)** Table representing the list of transcription factors those recognize the promoters of genes that are differentially expressed in PSIP1-depleted M4 cells. Number within the parenthesis denotes the number of differentially expressed genes that those contain the candidate TF binding sites.

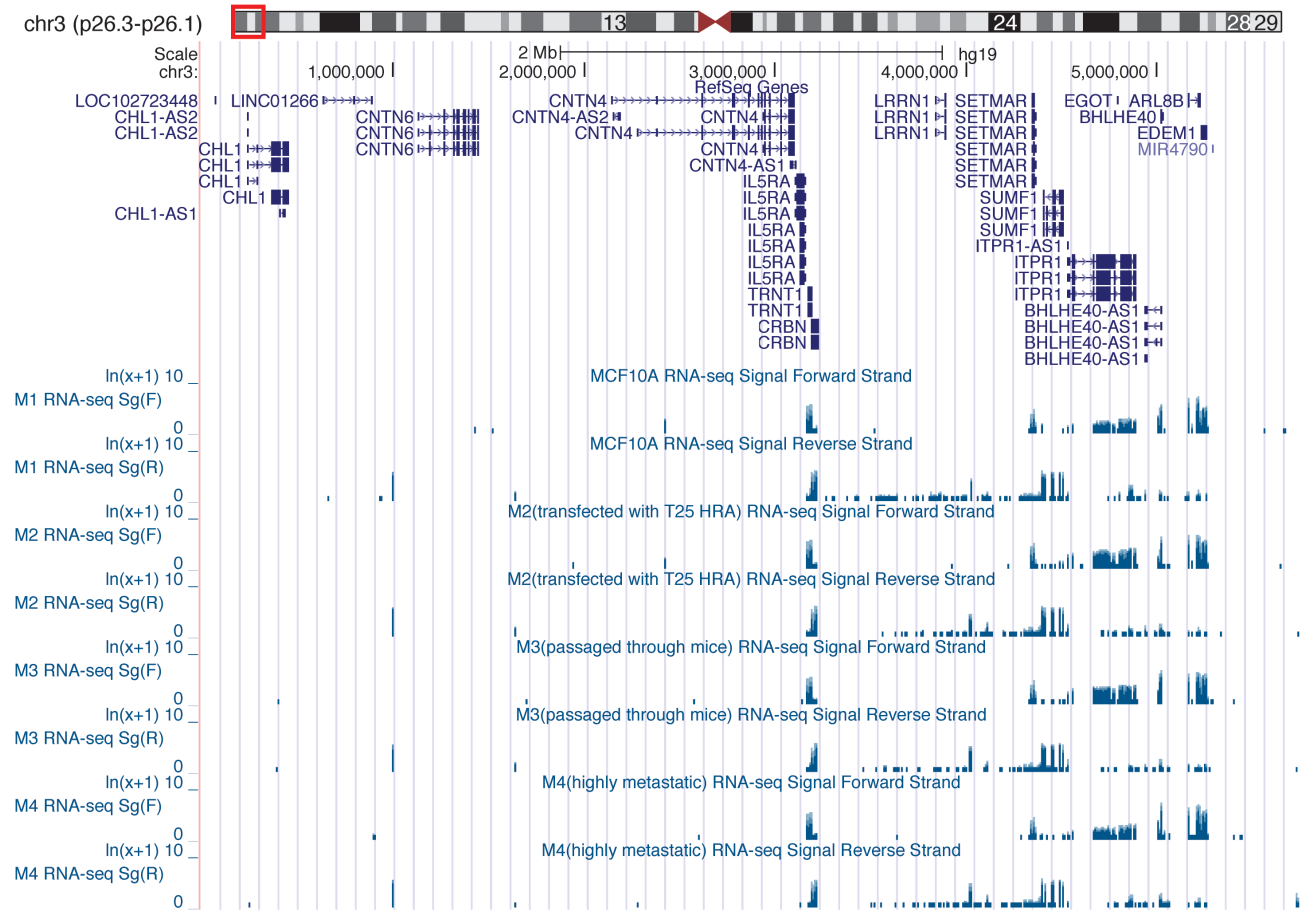
A.

CDN2A, CDKN2B deletion



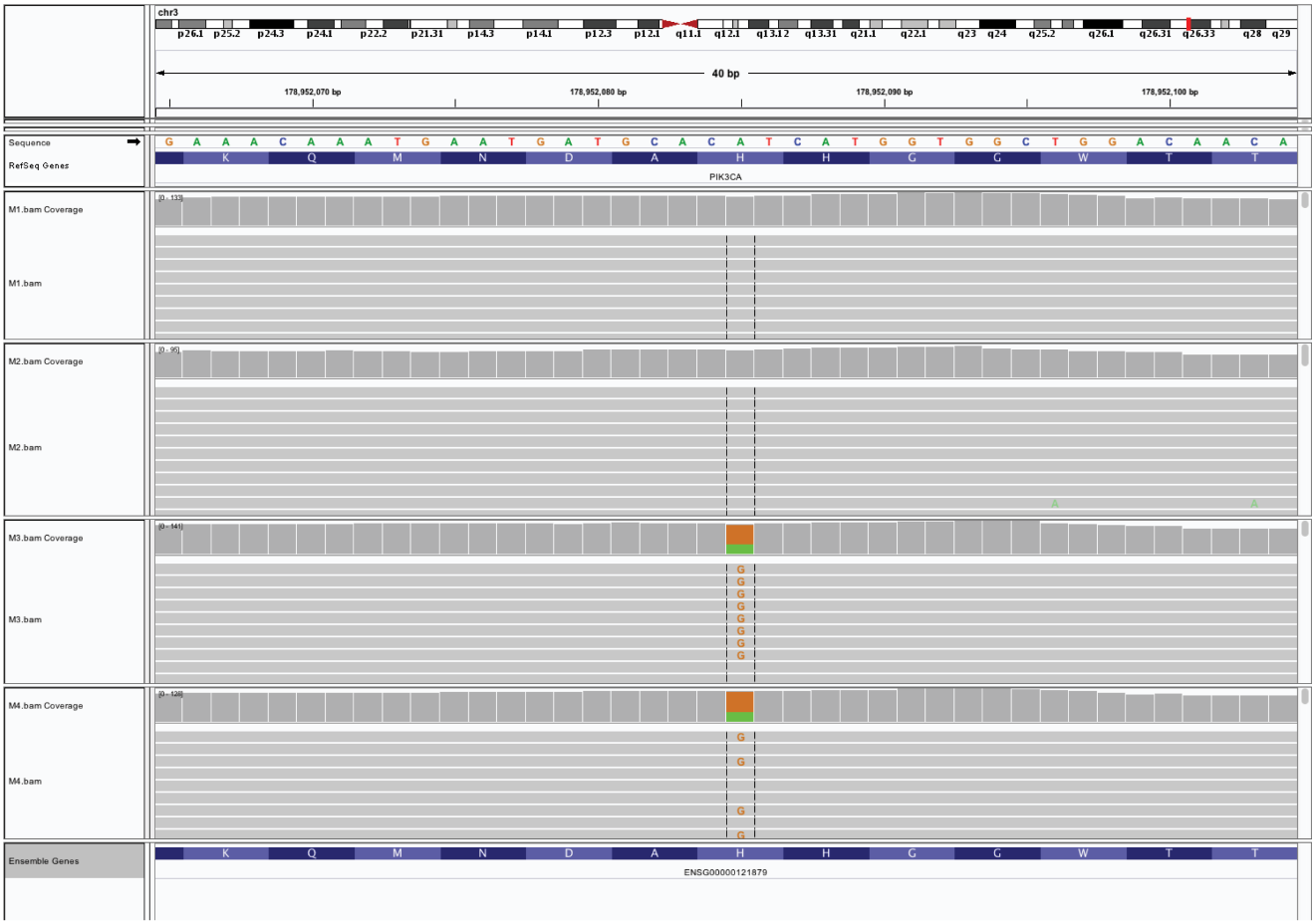
B.

CHL1, CNTN6 Focal deletion



C.

PIk3A – H1047R Mutation



Supplementary Figure 12. Validation of M1-M4 cell lines. (A) RNA-seq snap shot showing no expression of deleted CDKN1A and DDKN2B in M1-M4 cells. (B) Region close to p26.3 (CHL1 and CNTN6) is deleted as confirmed with no RNA expression signal. (C) Mutation in the PIK3A gene at the locus 1047.