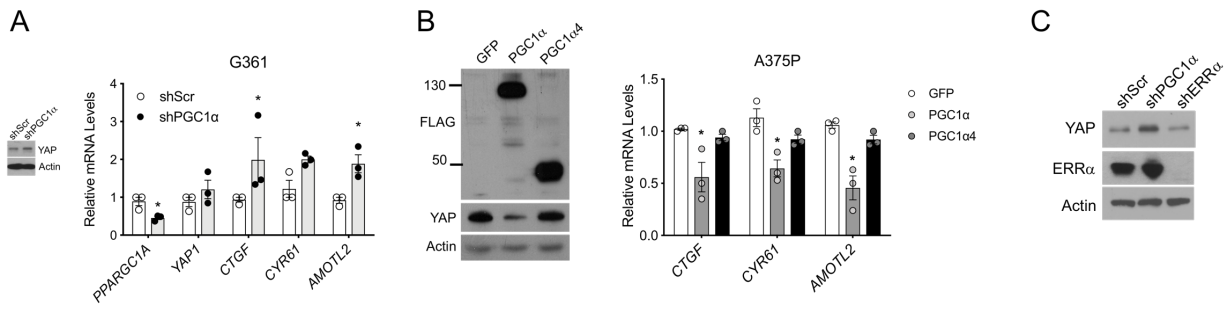


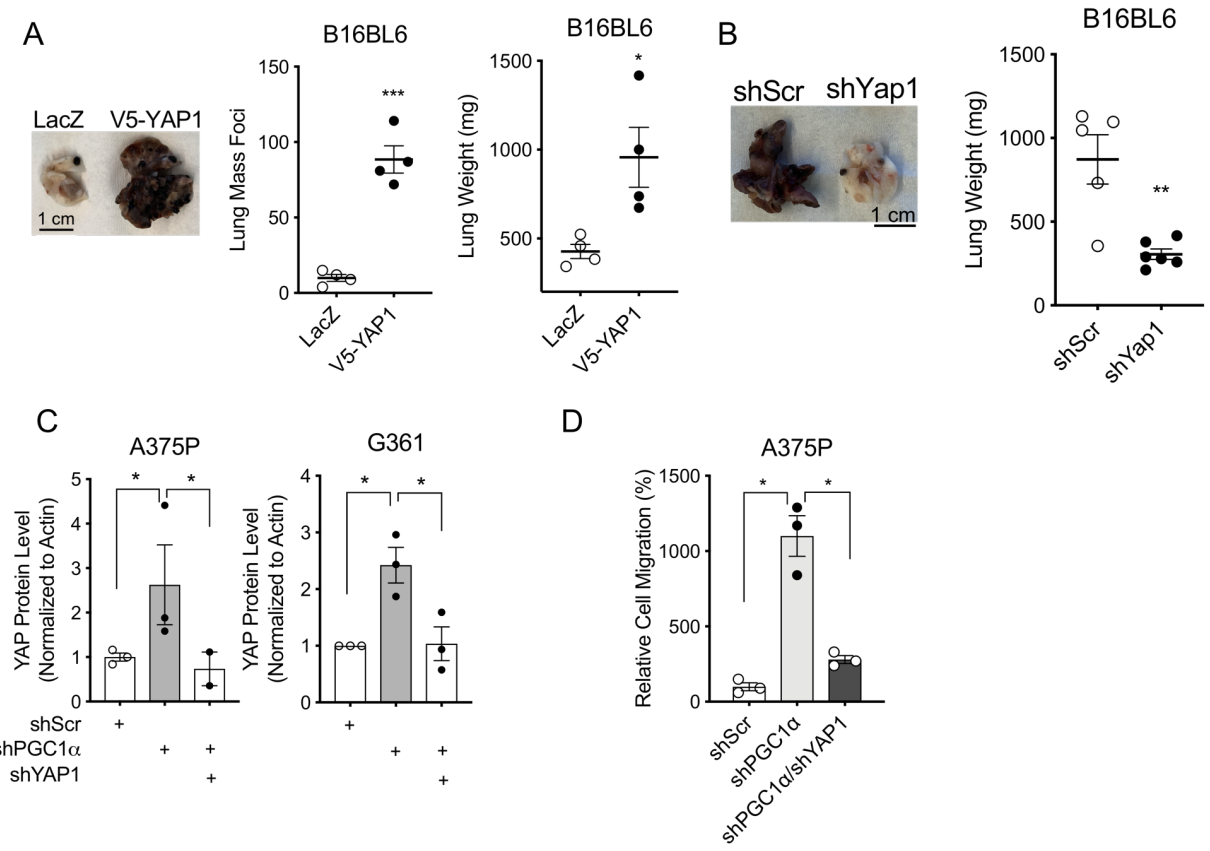
Supplementary Figure 1. PGC1α directly regulates YAP expression.

A. Depletion of PGC1α by shRNA enhances YAP protein expression and activation without altering its mRNA level in G361 melanoma cell line (n=3).

B. The regulation of YAP is specific to full-length PGC1α but not the N-terminal isoform PGC1α4 (n=3).

C. The regulation of YAP by PGC1α does not require PGC1α's interaction with ERRα, the nuclear regulator mediating PGC1α's bioenergetic effects (n=3).

Quantitative results were analyzed by Student's *t*-test (A) or one-way ANOVA (B) with $P \leq 0.05$ considered significant and are shown as mean ± SEM. *$P < 0.05$.



Supplementary Figure 2. YAP is required for melanoma migration and metastasis.

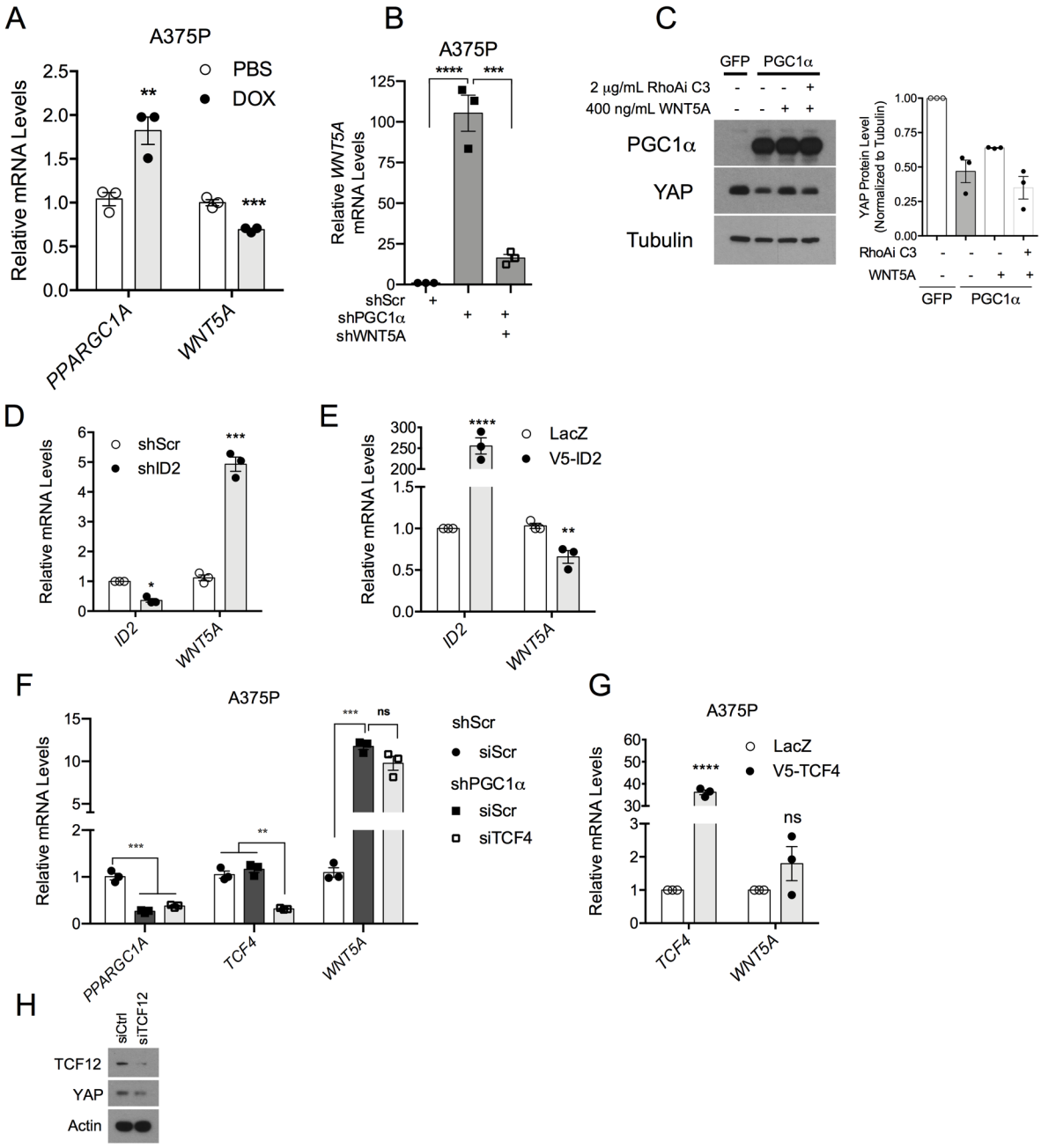
A. Overexpression of YAP1 in murine B16BL6 melanoma cells increases lung metastasis following tail-vein inoculation (n=4 mice per group). $1X10^5$ cells were i.v. injected into C57BL6 mice. Lung tissues were harvested 3-week post injection for metastasis quantification.

B. Depletion of Yap1 by shRNA suppresses lung metastasis in B16BL6 melanoma cell line (n=5 or 6 mice per group). $2X10^5$ cells were i.v. injected into C57BL6 mice. Lung tissues were harvested 3.5-week post injection for metastasis quantification.

C. Quantification of YAP protein level upon PGC1α knock-down related to Figure 4C.

D. Knock-down of YAP blocks increased migration induced by loss-of-PGC1α in A375P melanoma cells (n=3).

Quantitative results were analyzed by Student's *t*-test (A) or one-way ANOVA (B) with $P \leq 0.05$ considered significant and are shown as mean ± SEM. *$P < 0.05$, **$P < 0.01$, and ***$P < 0.005$.



Supplementary Figure 3. PGC1α regulates WNT5A expression.

A. Overexpression of PGC1α by a doxycycline-inducible vector suppresses WNT5A expression in A375P cells (n=3).

B. The knock-down efficiency of the shRNA against WNT5A in cells used in Figure 5D (n=3).

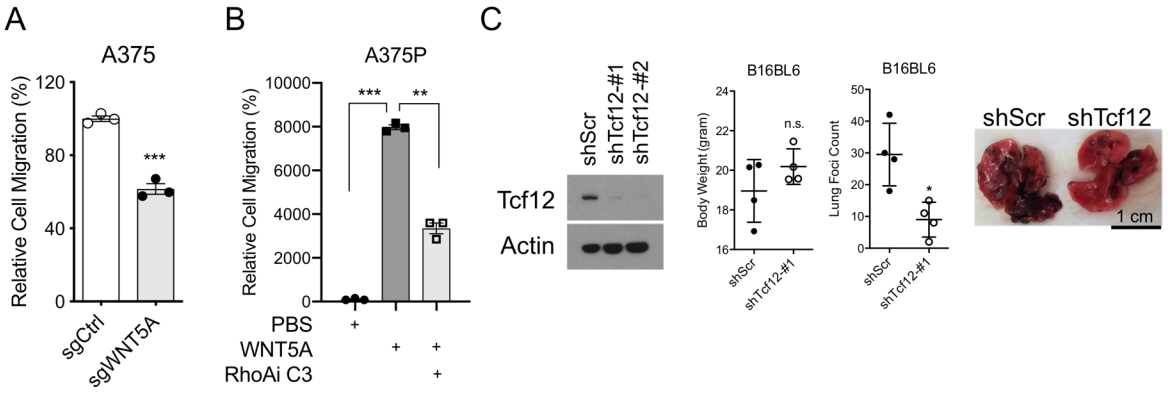
C. Treatment of exogenous WNT5A can rescue the reduction of YAP protein by PGC1α overexpression, which can be blocked by inhibition of RhoA activity (n=3).

D-E. WNT5A expression in A375P melanoma is sensitive to manipulations of ID2 levels (n=3).

F-G. Manipulations of TCF4 expression level do not affect WNT5A expression in A375P cells (n=3).

H. Knock-down of TCF12 reduces YAP protein abundance in A375 melanoma cells.

Quantitative results were analyzed by Student's *t*-test or one-way ANOVA (B, F) with $P \leq 0.05$ considered significant and are shown as mean ± SEM. *P < 0.05, **P < 0.01, ***P < 0.005 and ****P < 0.001.



Supplementary Figure 4. WNT5A and TCF12 regulate melanoma migration and metastasis.

A. In the highly invasive A375 melanoma cells, depletion of WNT5A by CRISPR compromises its migratory ability (n=3).

B. Inhibiting the RhoA signaling, which mediates WNT5A's regulation of YAP, suppresses A375P cell migration (n=3).

C. Knock-down of Tcf12 in murine B16BL6 melanoma cells reduces their metastatic propensity (n=4 mice per group). $1X10^5$ cells were subcutaneously injected into female C57BL6 mice. Tumors were monitored until they reached the size of 2 cm in diameter. Both tumor masses and lungs were collected for quantification.

Quantitative results were analyzed by Student's *t*-test or one-way ANOVA (B) with $P \leq 0.05$ considered significant and are shown as mean ± SEM. *P < 0.05, **P < 0.01, and ***P < 0.005.

Supplementary Table 1: Sequences of primers used in the manuscript.

qPCR primers			
Names	**Forward**	**Reverse**	**Note**
PGC1α	GTAAATCTGCGGGATGATGG	AATTGCTTGCGTCCACAAA	Human
EZH2	AGTGTGACCCTGACCTCTGT	AGATGGTGCCAGCAATAGAT	
YAP1	TAGCCCTGCGTAGCCAGTTA	TCATGCTTAGTCCACTGTCTGT	
CTGF	CAGCATGGACGTTCGTCTG	AACCACGGTTTGGTCCTTGG	
CYR61	CTCGCCTTAGTCGTCACCC	CGCCGAAGTTGCATTCCAG	
AMOTL2	CAGCATGGACGTTCGTCTG	CATGAGCTAGTACAACATGAGGG	
FGF2	AGAAGAGCGACCCTCACATCA	CGGTTAGCACACACTCCTTTG	
DDAH1	CAAAAGGACAAATCAACGAGGTG	TGTGCAGATTCACTAGACCCAA	
FSCN1	CACAGGCAAATACTGGACGGT	CCACCTTGTTATAGTCGCAGAAC	
WNT5A	ATTCTTGGTGGTCGCTAGGTA	CGCCTTCTCCGATGTACTGC	
TCF12	GGAAGGACTTGGTTGACCACT	GACCAACTACACTGGGAAGCA	
ID2	CAACACGGATATCAGCATCC	CGCTTATTCAGCCACACAGT	
TCF4	TCTCCATAGTTCCTGGACGG	CCAACTTCTTTGGCAAGTGG	
Yap1	ACCCTCGTTTTGCCATGAAC	TGTGCTGGGATTGATATTCCGTA	Mouse
Ctgf	GGGCCTCTTCTGCGATTTC	ATCCAGGCAAGTGCATTGGTA	
Cry61	CTGCGCTAAACAACTCAACGA	GCAGATCCCTTTCAGAGCGG	
Tcf12	CGCGATAGGGACCGACAAG	ACCCGCTGAACTGACTACTTC	
Primers for ChIP			
ChIP1	ACTCAAGGTACTGGACACAGTGG	TGGGGGATTGTTTTCAGGTA	Human
ChIP2	ATACAGTCGCTGCTGCTCTG	TGTGTTGGTATTTTTCCCTCAGT	
ChIP3	AGCTAAAACGTGTATTCCCTAAG	TCTGGGTGGAGGAGTTTGTT	
ChIP4	CTTAGACTTTTGGAGGCTTCAAGC	AGCTTTGCCACTTGCTTGTT	
ChIP5	CACCTCGATGTCACTCCATACAGAC	TGTCATGTGACTGGGGACTG	
ChIP6	CAGCATCGTTGTTTTGTGTTCTG	GTTTAGTGGCCTGGTTGGAA	
ChIP7	TTCCTGTACCACGGAGAGCTG	GTAGCCAGCAGAGACTGTGGAA	
ChIP8	GGACCTCGGCGTGTTTGCATTC	CCAGAGGAAACACTCGCAGTCT	
ChIP9	GCAAACCCAGCAAAGAGTTAAG	GCGAGTGTTTCCTCTGGGTA	
ChIP10	GCTGGACAAGTAGCCAAGACC	TTGAGTAGCCGGAGTGTCCT	
ChIP11	CCTCTGTAACAGGTGTGCTTTA	GAGAAAAGTCTGTTGGGGTGA	
ChIP12	GTTGAGAAAAGTGCATGTGTTC	GGACAGTTACAGGGCTTGGA	