**Supplemental Figure and Table Legends:**

**Figure S1. DepMap dependency scores for melanoma cell lines.** Plots downloaded directly from DepMap showing Dependency Scores (CRISPR Public23Q2+Score, Chronos) and log2(TPM+1) expression for *YAP1*, *WWTR1*, or *TEAD1*. Cell lines with a Chronos Dependency Score of < -0.65 are colored in red. The dependency scores and expression data for each cell line are listed in **Table S4, Tab 1**.

**Figure S2. *YAP* and *WWTR1* mRNA expression do not strongly correlate with the mRNA expression of their target genes.** RNA-seq data from the TCGA-SKCM project was downloaded and analyzed. **(A)** X-Y plots show the TPM value for the indicated gene for each individual tumor (dots). Correlation analysis was run for each comparison and the Pearson Correlation Coefficient (r) is indicated on the plots. **(B)** TCGA-SKCM tumors with high (> 1 standard deviation from the mean) or low (< -1 standard deviation from the mean) expression of *YAP*1, *WWTR1*, or *CTGF* **(B)** were analyzed for expression of each indicated gene for each individual tumor (dots). Mean + S.E.M. is shown. Statistical significance was determined using two-tail unpaired t-test; \*\* p ≤ 0.01, \*\*\*\* p ≤ 0.0001, n.s. p>0.05. **(C)** GSEA was run on the TCGA-SKCM RNA-seq data to test for enrichment of our YAP/TAZ Up geneset in *CTGF* or *CYR61* high vs. low tumors. The data used to generate this figure is found in **Table S5**.

**Figure S3. Downregulated YAP/TAZ signature genes are not negatively correlated with YAP/TAZ activity in human melanomas.** RNA-seq data from the TCGA-SKCM project was downloaded and tumors with high (> 1 standard deviation from the mean) or low (< -1 standard deviation from the mean) expression of *CTGF* **(A)** or *CYR61* mRNA **(B)** were analyzed. **(A&B)** GSEA analysis was performed to test for enrichment of our YAP/TAZ Down geneset in *CTGF* or *CYR61* high vs. low tumors (NES and FDR are indicated). The plots show the relative expression (Z-Score of the log transformed TPM (log2(1+TPM))) of each of the 52 YAP/TAZ Down genes in *CTGF* **(A)** or *CYR61* **(B)** high vs. low tumors. The tumors are sorted by *CTGF* or *CYR61* mRNA expression and genes are ranked from highest (top) to lowest (bottom) based on the Spearman Rank Correlation of the gene with either *CTGF* **(A)** or *CYR61* **(B)**. **(C)** The heatmap shows the Spearman Rank Correlation values for each gene compared to *CTGF* and *CYR61*. The data used to generate this figure is found in **Table S5**.

**Table S1. Reagents and datasets used in this study. (Tab 1)** The top table shows existing, purchased, or gifted vectors used in this study and their source. The bottom table shows all new vectors that were cloned for this study and lists the source vector for the insert and the backbone. For new mutant constructs, the insert that was mutated is listed. The publications that describe each vector are indicated [32,41,44,73]. **(Tab 2)** Provides a list of qPCR primers used in this study. **(Tab 3)** shows the list of publicly available gene expression datasets used in this study. The GEO accession number for each dataset, cell line name, species, type of cell line, comparison made, and the citation with Pubmed ID are listed for each dataset [1,3,42,68,74-91]. **(Tab 4)** Provides a list of YAP and YAP/TAZ genesets used in this study and their source [45-47]. **(Tab 5)** The list of ENCODE datasets used in this study with ENCODE experiment names and numbers, Conservative IDR Threshold Peaks, " .Bed” Data file accession numbers, and the TEAD that was immunoprecipitated indicated.

**Table S2. Processed A375 RNA-seq data.** Tables include RNA-seq data from A375 cells expressing control empty vector or the indicated YAP constructs. **(Tab 1)** Shows the entire dataset with the log2 fragments per kilobase million (l2FPKM) for each replicate and then the log2FC, adjusted pValue and qValue for each gene for the indicated comparisons. **(Tab 2)** includes the same data as **(Tab 1)**, but only shows differentially expressed genes (DEG) (fold change > 2, adjusted pValue < 0.05) for each comparison. **(Tabs 3 and 4)** provide lists of up and downregulated genes in each comparison. “1” indicates the gene was differentially expressed (fold change > 2, adjusted pValue < 0.05) in that comparison and an empty cell indicates that it was not.

**Table S3. Lists of YAP/TAZ-regulated genes in metastatic melanoma cell lines. (Tab 1)** shows differentially expressed genes (DEG) (fold change > 2, adjusted pValue < 0.05) in A375-YAP2SA vs. Control cells. **(Tabs 2&3)** The GSE68599 array dataset [42] was analyzed in ExAtlas to identify genes up or downregulated in siControl vs. siYAP/siTAZ SK-MEL-28 or WM3248 cells (fold change > 2, FDR<0.05). **(Tab 4)** Shows the list of up or downregulated genes in MeWo cells expressing YAP5SA vs. Control (Zhang et al. 2020). **(Tab 5)** Shows the list of all up or down regulated genes from **(Tabs 1-4).** **(Tab 6)** A YAP/TAZ gene signature consisting of genes up or downregulated in A375-YAP2SA cells and at least 2 of the 3 other melanoma cell lines. Included are the log2FC values from **(Tabs 1-4)**.

**Table S4. DepMap data.** RNA-seq for protein coding genesand Dependency Scores (CRISPR Public23Q2+Score, Chronos) for *YAP1*, *WWTR1* (TAZ), and *TEADs1-4* that were downloaded from the DepMap portal are provided here. **(Tab 1)** Dependency Scores (CRISPR Public23Q2+Score, Chronos) for *YAP1*, *WWTR1*, and *TEADs1-4* for each melanoma cell line in the DepMap dataset. **(Tab 2)** RNA-seq data for each melanoma cell line downloaded from DepMap (values are log2(TPM+1)). **(Tab 3)** Melanoma cell line Dependency Scores and RNA-seq data (TPM) from **(Tabs 1 & 2)** for all 132 genes in our YAP/TAZ signature. Green genes are in the YAP/TAZ Up geneset and red genes are in the YAP/TAZ Down geneset. Cell lines are organized based on Dependency Scores for *TEAD1*, *WWTR1* and then *YAP1* with yellow cells highlighting dependent lines. Dependency scores were used to generate the heatmap in **Figure 5B, top**. **(Tab 4)** RNA-seq data for each YAP/TAZ Up gene in the melanoma cell lines was Z-Scored and then the Spearman’s Rank Correlation of each gene with *CTGF* was calculated. Spearman’s Rank Correlation values (column B) were used to sort genes (highest to lowest). The Z-Scored expression data was used for the heatmap in **Figure 5B bottom**.

**Table S5. TCGA Data.** RNA-seq data from human melanoma samples in the TCGA-SKCM project was downloaded and processed. Tumors with high (>1 standard deviation from the mean) and low (< -1 standard deviation from the mean) expression of *YAP1*, *WWTR1*, *CTGF*, and *CYR61* were identified. **(Tabs 1-4)** showexpression (TPM) of each gene in our YAP/TAZ signature in tumors with high and low expression of *YAP1* **(Tab 1)**, *WWTR1* **(Tab 2)**, *CTGF* **(Tab 3)**, and *CYR61* **(Tab 4)**. **(Tab 5)** Shows the Spearman Rank Correlation values for each gene compared to *YAP1*, *WWTR1*, *CTGF*, and *CYR61*. Genes with correlation values > 0.4 are indicated in blue and between 0.39 and 0.3 in yellow. **(Tab 6)** The Spearman Rank Correlation value for each pairwise comparison of genes in the *CTGF* high and low tumors from **(Tab 3)**. This data was used to generate the heatmap in **Figure 6C**. **(Tab 7)** The Spearman Rank Correlation value for each pairwise comparison of genes in the *CYR61* high and low tumors from **(Tab 4)**. This data was used to generate the heatmap in **Figure 6F**.

**Table S6. YAP/TAZ signature genes are YAP/TAZ responsive in other cell lines. (Tab 1)** GSEA was used to generate a rank-ordered list for the indicated comparison in each cell line. For each comparison the % Rank (the gene’s rank/total genes in rank-ordered list\*100) of each of the 132 YAP/TAZ signature genes is shown. Green genes are in the YAP/TAZ Up geneset and red genes are in the YAP/TAZ Down geneset. **(Tab 2)** indicates which 132 YAP/TAZ signature genes are YAP/TAZ responsive in each indicated cell line and comparison. If a gene’s % Rank was between 0-15% or 85-100% in **(Tab 1)**, it was considered up or down regulated, respectively. This is indicated by a “1” in the corresponding cell. YAP/TAZ Up genes are sorted by the total number of cells lines where the gene was upregulated (Total Up) and the YAP/TAZ Down genes are sorted by the total number of cells lines where the gene was downregulated (Total Down). **(Tab 3)** GSEA was performed on the indicated datasets and comparisons using our the indicated genesets. The table lists the Normalized Enrichment Score (NES), False Discovery Rate (FDR) and % of each geneset that was in the Leading Edge (% Leading Edge) for Phenotype #1. A positive NES indicates the geneset was enriched in Phenotype #1 and a negative NES indicates the geneset was enriched in Phenotype #2. If a geneset was not enriched, there is no leading edge for that geneset, which is indicated by an “x”.