

Supplementary Figure S1

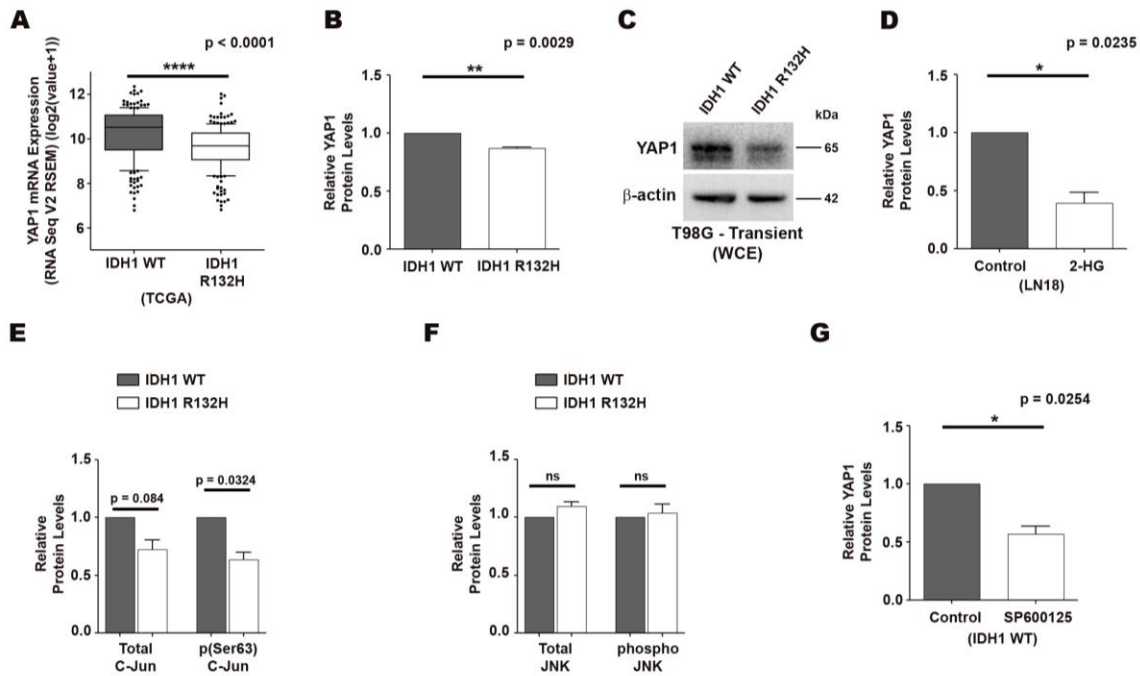


Fig. S1. Reduced YAP1 and C-Jun levels in IDH1 R132H and 2-HG-treated cells

- RNA expression data from TCGA shows lower YAP1 expression in IDH1 R132H gliomas as compared to IDH1 WT gliomas. Data from N=204 IDH1 WT and 206 IDH1 R132H patients from TCGA have been used for analysis. Whiskers represent 10-90 percentile. *****, $p < 0.0001$ (Two-tailed student's t-test)
- Densitometric analysis of immunoblots shows lower YAP1 protein levels in IDH1 R132H as compared to IDH1 WT cells
- Immunoblots show a decrease in YAP1 levels in T98G cells transiently transfected with IDH1 R132H. The blots are representative of two independent experiments with similar results. WCE, whole cell extract
- Densitometric analysis of immunoblots shows a reduction in YAP1 protein levels in LN18 cells upon 2-HG treatment

- E. Densitometric analysis of immunoblots shows a reduction in total and phosphorylated (Ser63) C-Jun protein levels in IDH1 R132H cells
- F. Densitometric analysis of immunoblots shows no difference in total and phosphorylated JNK protein levels between IDH1 WT and IDH1 R132H cells
- G. Densitometric analysis of immunoblots shows a reduction in YAP1 protein levels on treatment of IDH1 WT cells with SP600125

All densitometry graphs represent data expressed as fold change over respective controls, presented as mean \pm SEM. N=3 biological replicates. *, $p<0.05$; **, $p<0.01$. Paired two-tailed student's t-test were used for statistical analysis

Supplementary Figure S2

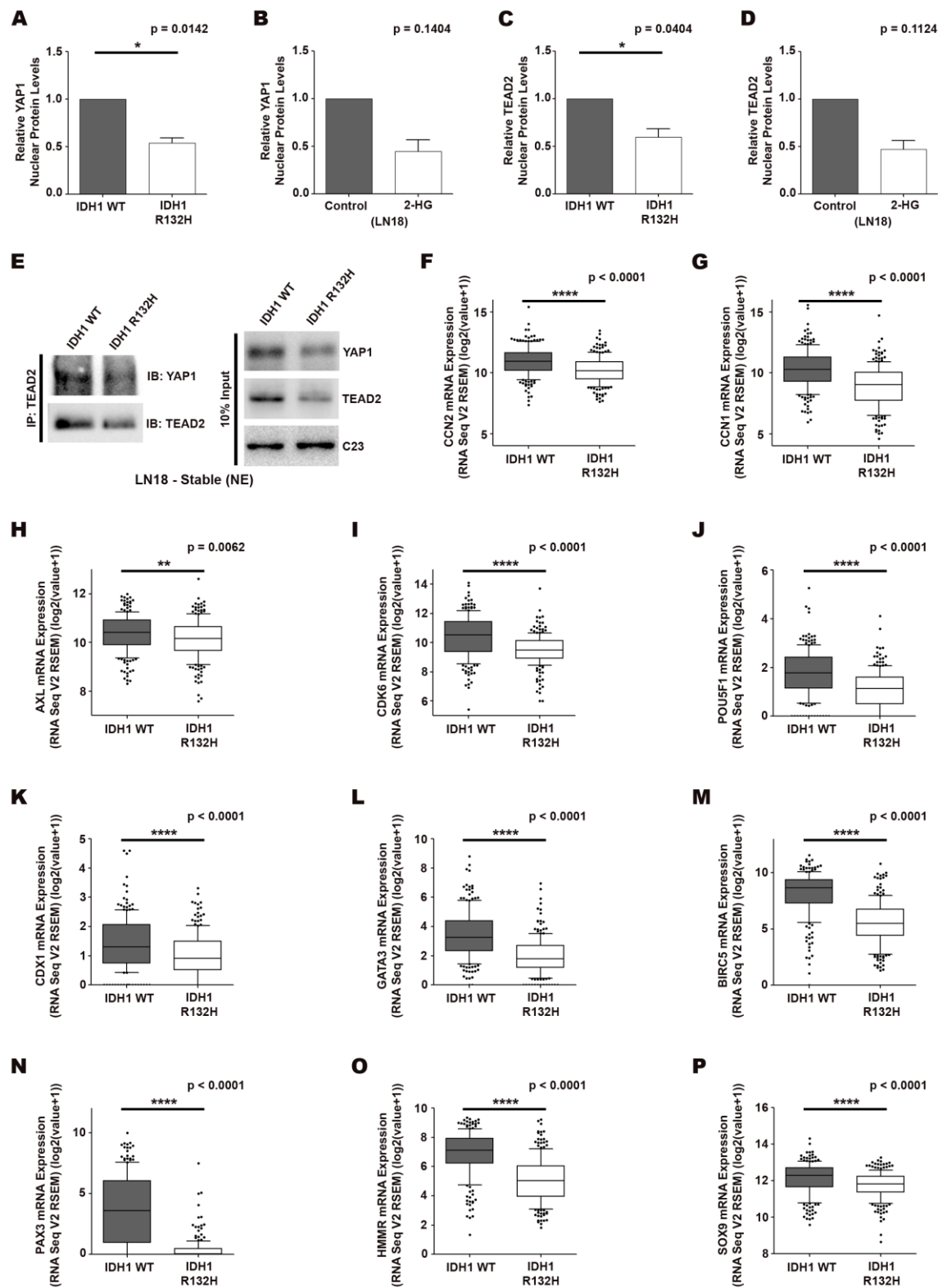


Fig. S2. Reduced Nuclear YAP1 and TEAD2 levels and diminished YAP1/TEAD activity in IDH1 R132H

- A. Densitometric analysis shows diminished nuclear YAP1 levels in IDH1 R132H as compared to IDH1 WT cells
- B. Densitometric analysis shows a reduction in nuclear YAP1 levels in 2-HG-treated LN18 cells
- C. Densitometry shows diminished nuclear TEAD2 levels in IDH1 R132H as compared to IDH1 WT cells
- D. Densitometric analysis shows a reduction in nuclear TEAD2 levels upon 2-HG treatment in LN18 cells
- E. Coimmunoprecipitation (CoIP) demonstrates reduced YAP1/TEAD2 complex formation in IDH1 R132H cells. The blots are representative of two independent experiments with similar results.
NE, nuclear extract
- F-P. TCGA data analysis shows lower expression of known TEAD-responsive genes in IDH1 R132H gliomas as compared to IDH1 WT gliomas. Data from N=204 IDH1 WT and 206 IDH1 R132H patients have been used for the analysis. Whiskers represent 10-90 percentile. **, $p < 0.01$; ****, $p < 0.0001$ (Two-tailed student's t-test)

All densitometry graphs represent data expressed as fold change over respective controls, presented as mean \pm SEM. N=3 biological replicates (N=2 biological replicates for nuclear protein levels in 2-HG-treated cells). *, $p < 0.05$. Paired two-tailed student's t-test was used for statistical analysis

Supplementary Figure S3

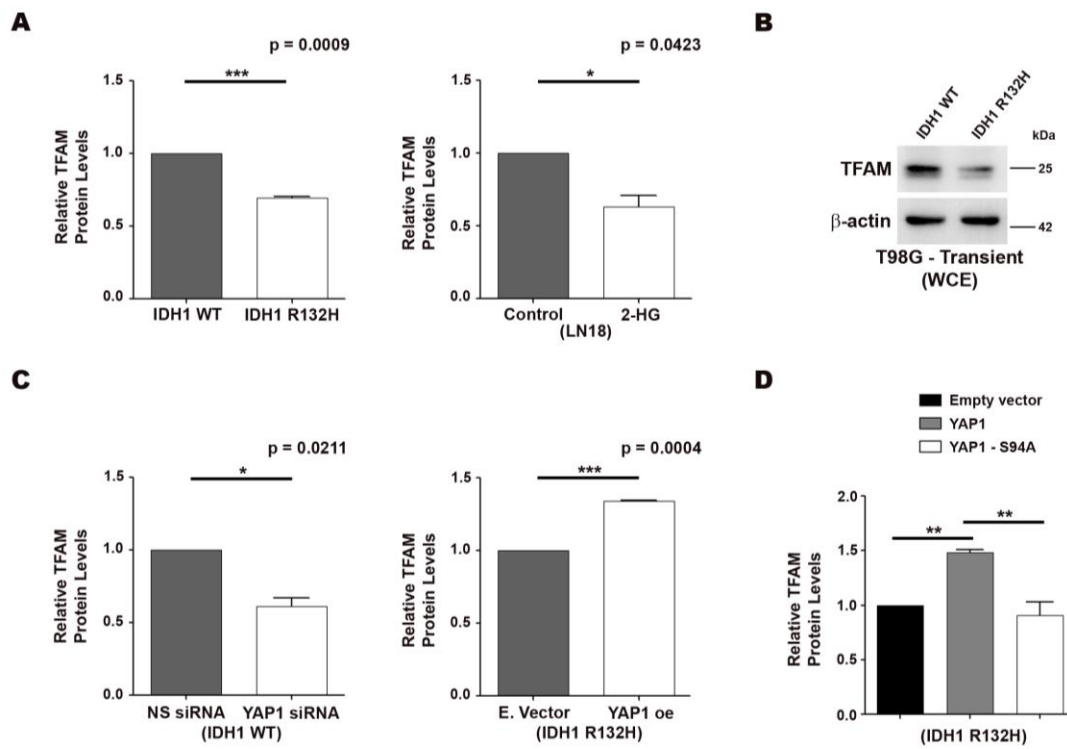


Fig. S3. YAP1-dependent TFAM levels

- Densitometric analysis of immunoblots shows lower TFAM protein levels in IDH1 R132H cells and 2-HG-treated LN18 cells as compared to IDH1 WT and control cells respectively
- Immunoblots show a decrease in TFAM levels in T98G cells transiently transfected with IDH1 R132H. The blots are representative of two independent experiments with similar results. WCE, whole cell extract
- Densitometric analysis shows a reduction in TFAM levels upon siRNA-mediated knockdown of YAP1 in IDH1 WT cells, and an increase in TFAM levels on overexpressing YAP1 in IDH1 R132H cells
- Densitometric analysis shows an increase in TFAM levels on overexpressing wild type YAP1 in IDH1 R132H cells, but not on overexpressing YAP1-S94A mutant.

All densitometry graphs represent data expressed as fold change over respective controls, presented as mean \pm SEM. N=3 biological replicates. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$. Comparisons between two groups were done using paired two-tailed student's t-test, and comparisons among multiple groups were done using one-way ANOVA with Tukey's multiple comparison test. NS siRNA, Non-specific siRNA; E. vector, Empty vector; YAP1 oe, YAP1 overexpression

Supplementary Figure S4

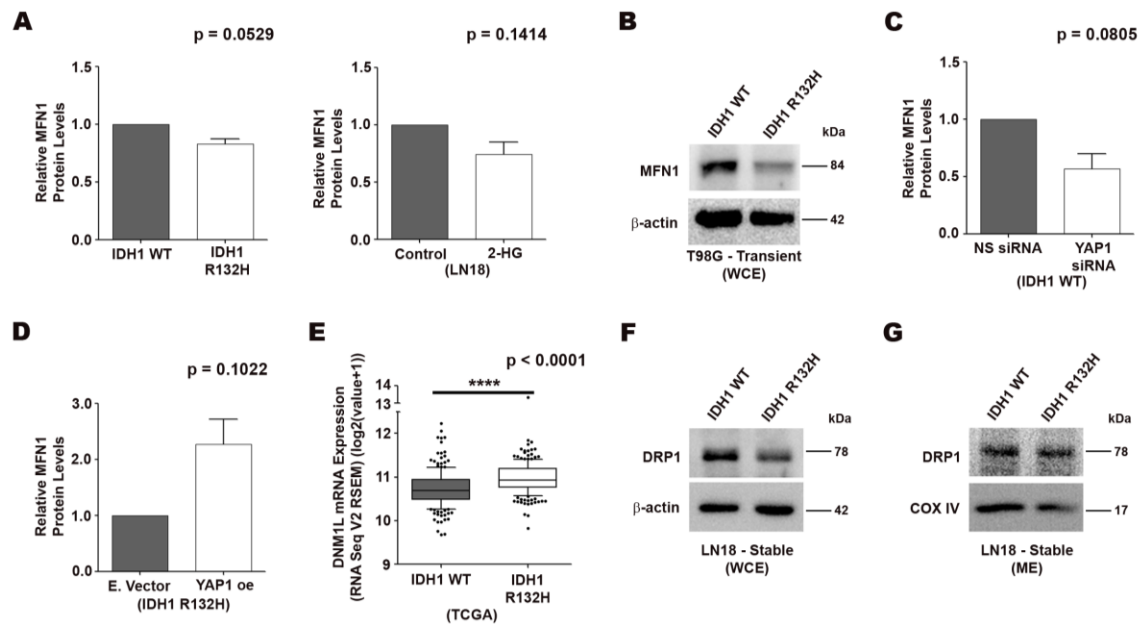


Fig. S4. Altered MFN1 and DRP1 levels in IDH1 R132H cells

- A. Densitometric analysis shows lower MFN1 protein levels in IDH1 R132H cells and 2-HG-treated LN18 cells
- B. Immunoblot shows a decrease in MFN1 levels in T98G cells transiently transfected with IDH1 R132H. The blots are representative of two independent experiments with similar results. WCE, whole cell extract
- C. Densitometry shows a reduction in MFN1 protein levels upon siRNA-mediated knockdown of YAP1 in IDH1 WT cells
- D. Densitometry shows an increase in MFN1 levels on overexpressing YAP1 in IDH1 R132H cells
- E. TCGA data analysis shows higher DNM1L (DRP1) expression in IDH1 R132H gliomas as compared to IDH1 WT gliomas. Data from N=204 IDH1 WT and 206 IDH1 R132H patients from TCGA have been used for analysis. Whiskers represent 10-90 percentile. *****, $p < 0.0001$ (Two-tailed student's t-test)

- F. Immunoblots show reduced levels of DRP1 in IDH1 R132H cells. The blots are representative of three independent experiments with similar results.
- G. Immunoblots with mitochondrial protein fractions show higher recruitment of DRP1 in the mitochondria of IDH1 R132H cells as compared to IDH1 WT. The blots are representative of two independent experiments with similar results.

All densitometry graphs represent data expressed as fold change over respective controls, presented as mean \pm SEM. N=3 biological replicates. Paired two-tailed student's t-test was used for statistical analysis. WCE, whole cell extract; ME, mitochondrial extract; NS siRNA, Non-specific siRNA; E. vector, Empty vector; YAP1 oe, YAP1 overexpression

Supplementary Figure S5

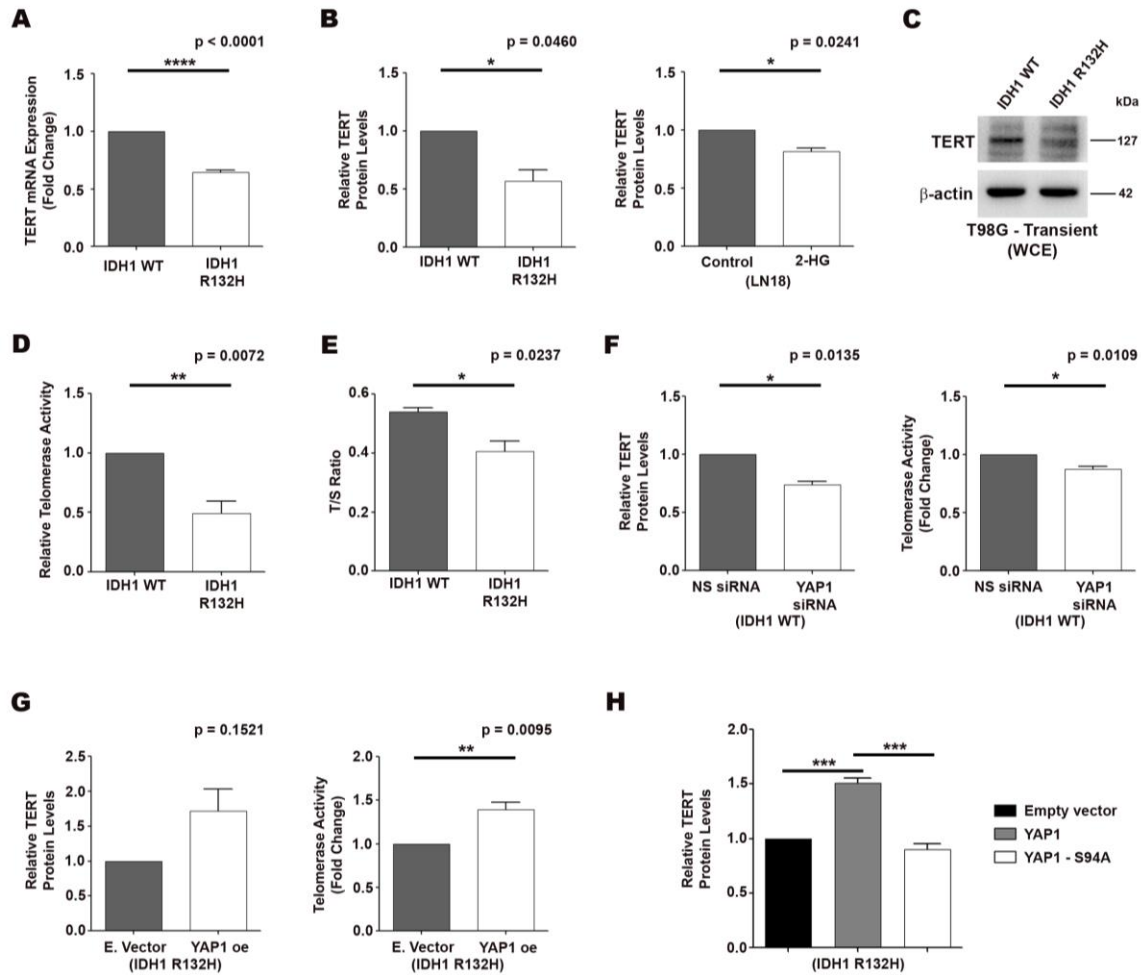


Fig. S5. YAP1-dependent TERT expression and telomerase activity

- qRT-PCR shows reduced TERT mRNA levels in IDH1 R132H cells. Data are expressed as fold change over IDH1 WT and presented as mean \pm SEM. N=5 biological replicates. ****, $p < 0.0001$ (Two-tailed student's t-test)
- Densitometric analysis of immunoblots shows lower TERT protein levels in IDH1 R132H cells and 2-HG-treated LN18 cells as compared to IDH1 WT and control cells respectively
- Immunoblots show a decrease in TERT levels in T98G cells transiently transfected with IDH1 R132H. The blots are representative of two independent experiments with similar results. WCE, whole cell extract
- Telomeric repeat amplification protocol (TRAP) assay shows decreased telomerase activity in IDH1 R132H cells as compared to IDH1 WT. Data are expressed as fold change over IDH1 WT and presented as mean \pm SEM. N=3 biological replicates. **, $p < 0.01$ (Two-tailed student's t-test)

- E. Telomere length measurement by qPCR shows a reduction in IDH1 R132H cells. Data are presented as mean \pm SEM. N=3 biological replicates. T/S ratio, ratio of telomere to single copy gene 36B4; *, $p < 0.05$ (Two-tailed student's t-test)
- F. Densitometry shows a reduction in TERT protein levels upon siRNA-mediated knockdown of YAP1 in IDH1 WT cells. TRAP assay reveals a decrease in telomerase activity on siRNA-mediated knockdown of YAP1 in IDH1 WT cells
- G. Densitometry shows an increase in TERT protein levels upon overexpression of YAP1 in IDH1 R132H cells. TRAP assay reveals an increase in telomerase activity on overexpressing YAP1 in IDH1 R132H cells
- H. Densitometric analysis shows an increase in TERT levels on overexpressing wild type YAP1 in IDH1 R132H cells, but not on overexpressing YAP1-S94A mutant

All densitometry graphs represent data expressed as fold change over respective controls, presented as mean \pm SEM. N=3 biological replicates. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$. Comparisons between two groups were done using paired two-tailed student's t-test, and comparisons among multiple groups were done using one-way ANOVA with Tukey's multiple comparison test. NS siRNA, Non-specific siRNA; E. vector, Empty vector; YAP1 oe, YAP1 overexpression

Supplementary Figure S6

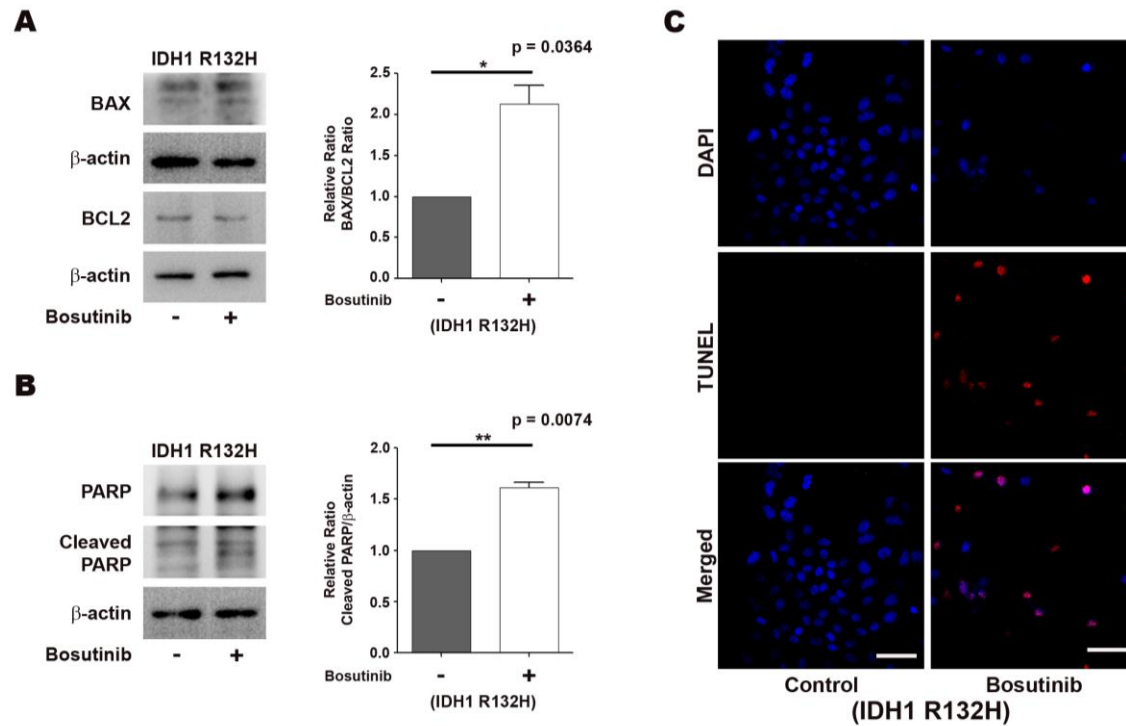


Fig. S6. Apoptosis in IDH1 R132H cells upon Bosutinib treatment

- Immunoblots and densitometric analysis show an increase in BAX/BCL2 ratio in Bosutinib-treated IDH1 R132H cells
- Immunoblots and densitometric analysis show an increase in cleaved PARP levels in Bosutinib-treated IDH1 R132H cells
- Maximum intensity projections of confocal microscopic images of IDH1 R132H cells showing TUNEL staining under control and Bosutinib-treated conditions

Graphs represent data expressed as fold change over control, presented as mean \pm SEM. N=3 biological replicates. *, $p < 0.05$; **, $p < 0.01$ (Paired two-tailed student's t-test)

Supplementary Figure S7

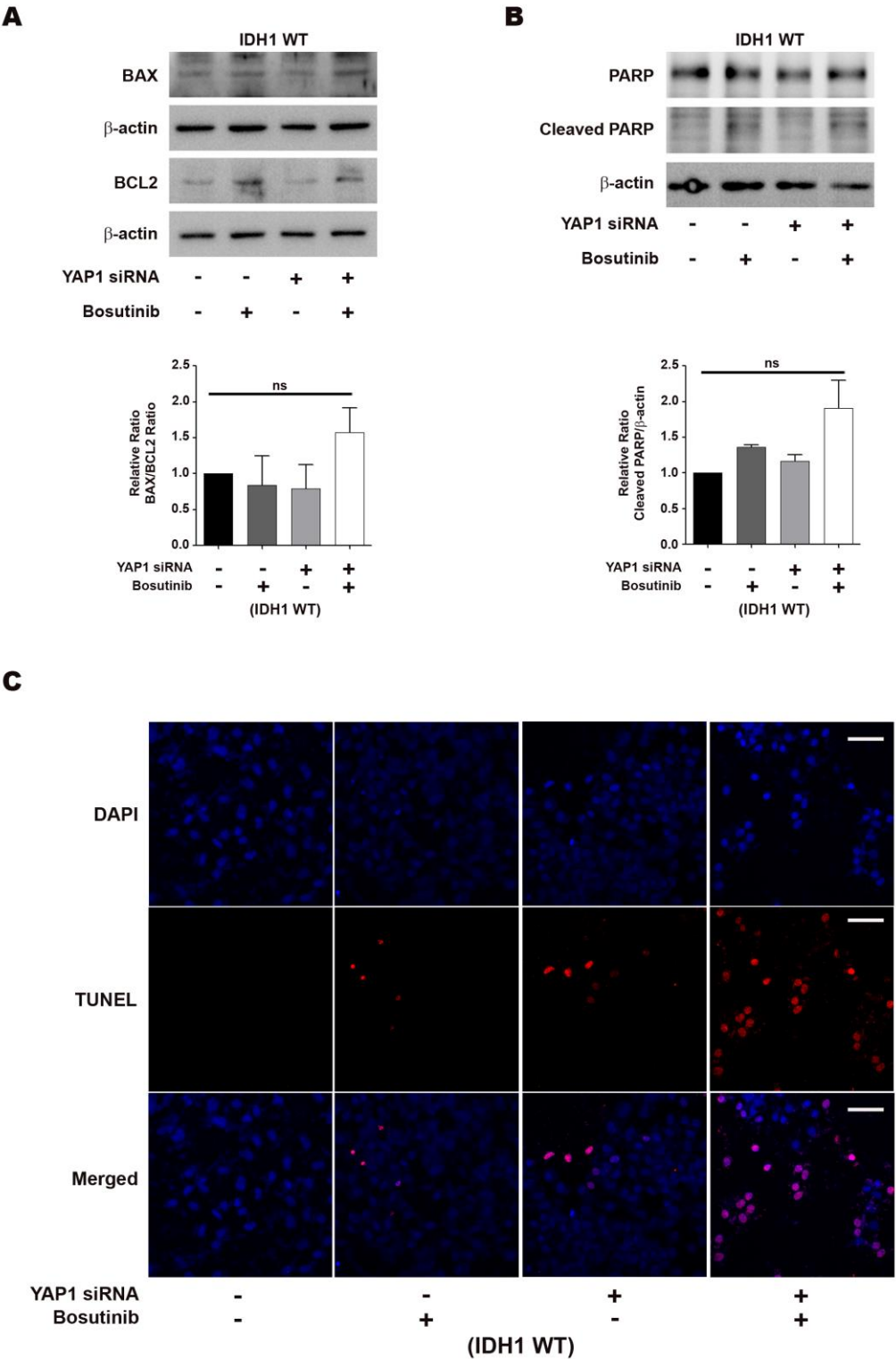


Fig. S7. Apoptosis in IDH1 WT cells upon YAP1 depletion and Bosutinib treatment

- A. Immunoblots and densitometric analysis show an increase in BAX/BCL2 ratio upon Bosutinib treatment along with siRNA-mediated knockdown of YAP1 in IDH1 WT cells
- B. Immunoblots and densitometric analysis show an increase in cleaved PARP levels in IDH1 WT cells on treatment with Bosutinib along with siRNA-mediated knockdown of YAP1.
- C. Maximum intensity projections of confocal microscopic images of IDH1 WT cells showing TUNEL staining under the specified conditions

Graphs represent data expressed as fold change over control, presented as mean \pm SEM. N=3 biological replicates (N=2 for cleaved PARP). ns, not significant (One-way ANOVA with Tukey's multiple comparison test)

Table S1. Sequences of primers used in the study

Gene	Primer Sequences
1. pGL3 TFAM WT (Cloning)	Forward: CGACGCGTTGCTCAAATTAAGCAAGCTG Reverse: GGAAGATCTCGCTCCGGTGGATGAGGCAG
2. pGL3 TFAM Δ (SDM)	Forward: TCCGCCCCGACTGGAGCACATCTACCGACCGGATGT Reverse: CGGTAGATGTGCTCCAGTCGGGGCGGAATTGGCGCA
3. pBABE YAP1 S94A (SDM)	Forward: TGCCCGACGCGTTCTCAAGCCGCCGGA Reverse: TTGAAGAACGCGTCGGGCAGCTTCCGGA
4. <i>YAP1</i>	Forward: GGCGCTCTCAACGCCGTCATGAAC Reverse: CCTGTCGGGAGTGGGATTT
5. <i>TERT</i>	Forward: GGATGAAGCGGAGTCTGGA Reverse: CGGAAGAGTGTCTGGAGCAA
6. <i>TFAM</i> (ChIP)	Forward: ATTGCGGTTTCCCTTCATCT Reverse: GCCACTAGCGAGGCACTATG
7. <i>GAPDH</i> (ChIP)	Forward: TACTAGCGGTTTTACGGGCG Reverse: TCGAACAGGAGGAGCAGAGAGCGA
8. Telomere	Forward: GGTTTTTGAGGGTGAGGGTGAGGGTGAGGGTGAGGGT Reverse: TCCCGACTATCCCTATCCCTATCCCTATCCCTATCCCTA
9. <i>36B4/RPLP0</i>	Forward: CAGCAAGTGGGAAGGTGTAATCC Reverse: CCCATTCTATCATCAACGGGTACAA
10. <i>ND1</i>	Forward: ACGCCATAAACTCTTCACCAAAG Reverse: TAGTAGAAGAGCGATGGTGAGAGCTA
11. <i>B2M</i>	Forward: TGCTGTCTCCATGTTTGATGTATCT Reverse: TCTCTGCTCCCCACCTCTAAGT

SDM, site directed mutagenesis.