

Supplementary figure legends

Fig. S1. A. Tumor growth in syngeneic C57BL/6 male and female mice bearing murine melanoma derived tumors (YUMM1.7). **B.** Relative YUMM1.7 cell proliferation determined after 6 days of treatment with vehicle (DMSO), 100 nM testosterone (T) or 100 nM dihydrotestosterone (DHT). Graphs represent the average of three independent experiments. Error bars represent standard error of the mean (SEM).

Fig. S2. A. RNA-seq data in 17 cancer types are reported as median FPKM (number Fragments Per Kilobase of exon per Million reads), generated by the The Cancer Genome Atlas (TCGA). RNA cancer tissue category calculated based on mRNA expression levels across all 17 cancer tissues and include: cancer tissue enriched, cancer group enriched, cancer tissue enhanced, expressed in all, mixed and not detected. Normal distribution across the dataset is visualized with box plots, shown as median and 25th and 75th percentiles. Points are displayed as if they are above or below 1.5 times the interquartile range. **B.** ZIP9 levels of expression in a battery of human-derived melanoma cells.

Fig. S3. A. WM46 relative cell proliferation under T and/or TPEN. **B.** WM46 relative cell proliferation in the presence of T, copper sulfate (CuSO₄) and copper chelator (BCS). **C.** Relative Intracellular levels of Zinc in cells treated with T and/or Copper chelator (BCS).

Fig. S4: A. Western blot analysis in YUMM1.7 wtZIP9 and Δ ZIP9. **B.** Relative cell proliferation of YUMM1.7 wtZIP9 and Δ ZIP9 in the presence of testosterone (T). The graphs represent the average of three independent experiments. Error bars represent standard error of the mean (SEM). **C.** Levels of ERK phosphorylation in wtZIP and Δ ZIP9 WM46 cells. **D.** YAP1 protein analysis by Western Blot in WM46 cells after cell fractionation. β -Actin is

used as cytoplasmic fraction positive control. PARP is used as nuclear fraction positive control. **E.** Relative mRNA expression of YAP1 and YAP1 target genes in Δ ZIP19 WM46 cells treated with testosterone and dobutamine. **F.** Basal mRNA relative expression of YAP1 and YAP1 targets in wtZIP9 and Δ ZIP9 isogenic WM46 derived clones.

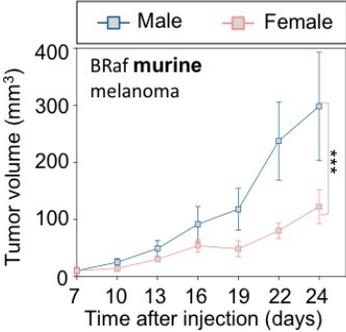
Fig. S5: **A.** Relative cell proliferation in human and murine derived melanoma cell lines treated with the AR inhibitor bicalutamide (BIC) in combination with testosterone (T). **B.** WM46 cells relative cell proliferation treated with AR inhibitors in the absence of testosterone. **C.** Intracellular zinc in the presence of testosterone and/or BIC. **D.** Relative mRNA expression of YAP1 and YAP1 target genes in Δ ZIP9 WM46 cells treated with testosterone and apalutamide. **E.** Tumor growth in mice bearing WM46 derived tumors. Daily treatment with bicalutamide (30mg/kg/day) or vehicle only are shown for both male and female mice after subcutaneous injection of 10⁶ WM46 cells. **F.** Tumor growth in SCID male mice bearing Δ ZIP9 WM46 derived tumors.

Fig. S6: Relative cell proliferation in a battery of cell lines derived from diverse tumor types in response to testosterone and bicalutamide treatment.

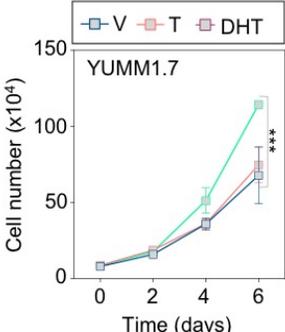
Table. S2: Primers used for Real-Time Quantitative PCRs.

Supplementary Figure 1

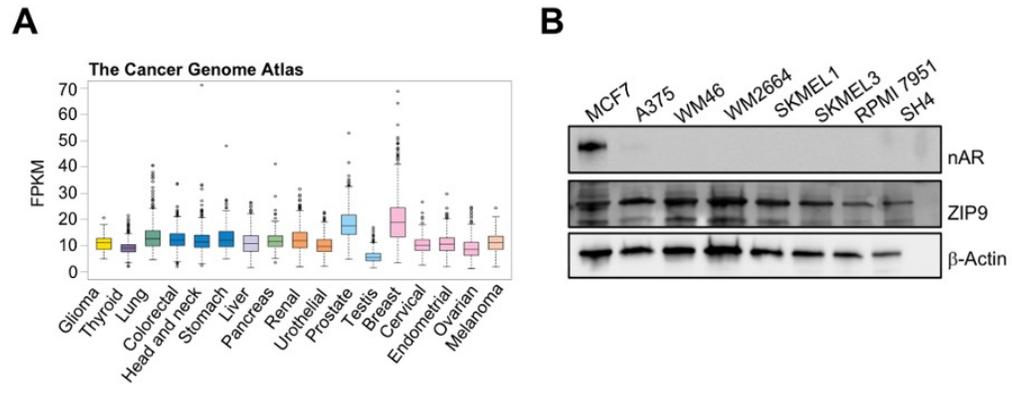
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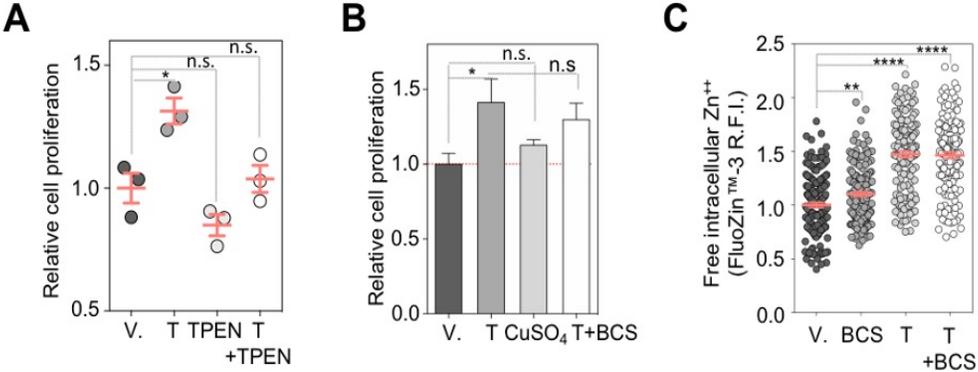
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Supplementary Figure 2

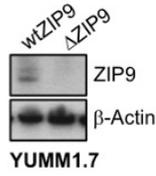


Supplementary Figure 3

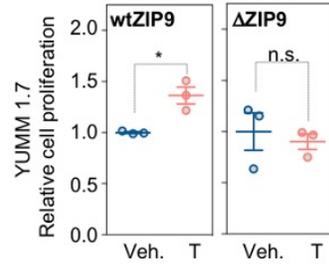


Supplementary Figure 4

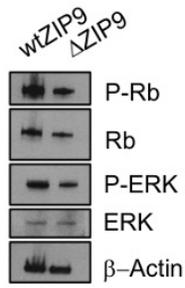
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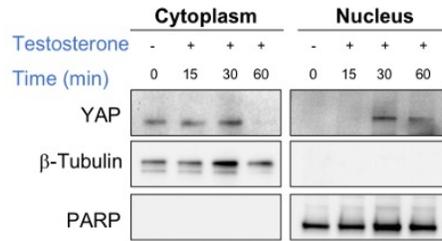
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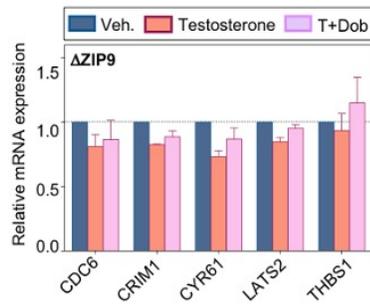
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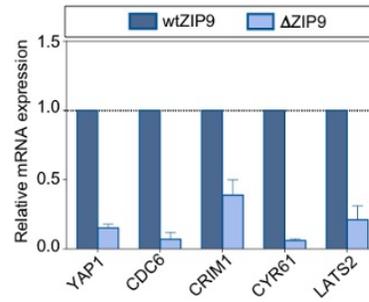
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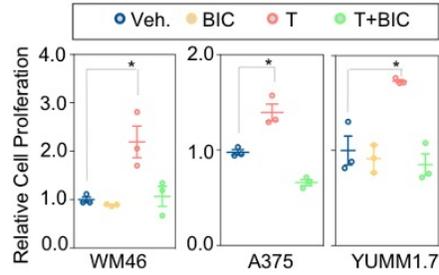


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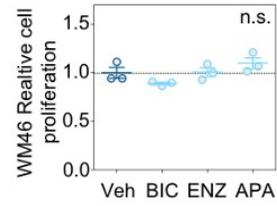


Supplementary Figure 5

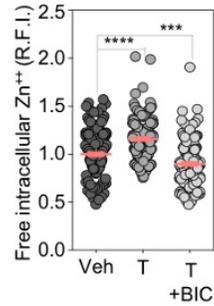
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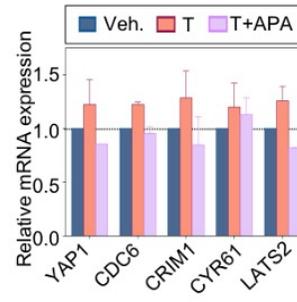
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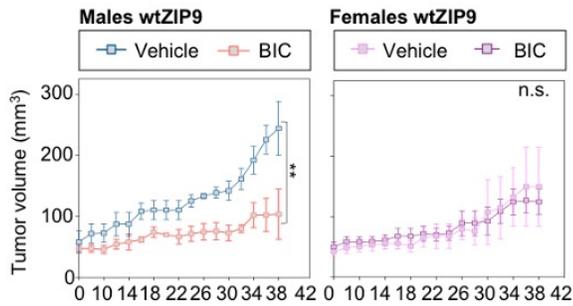
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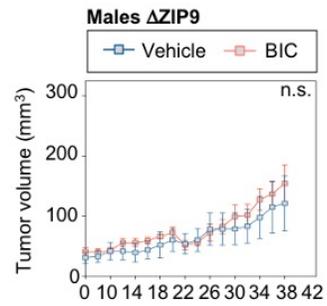
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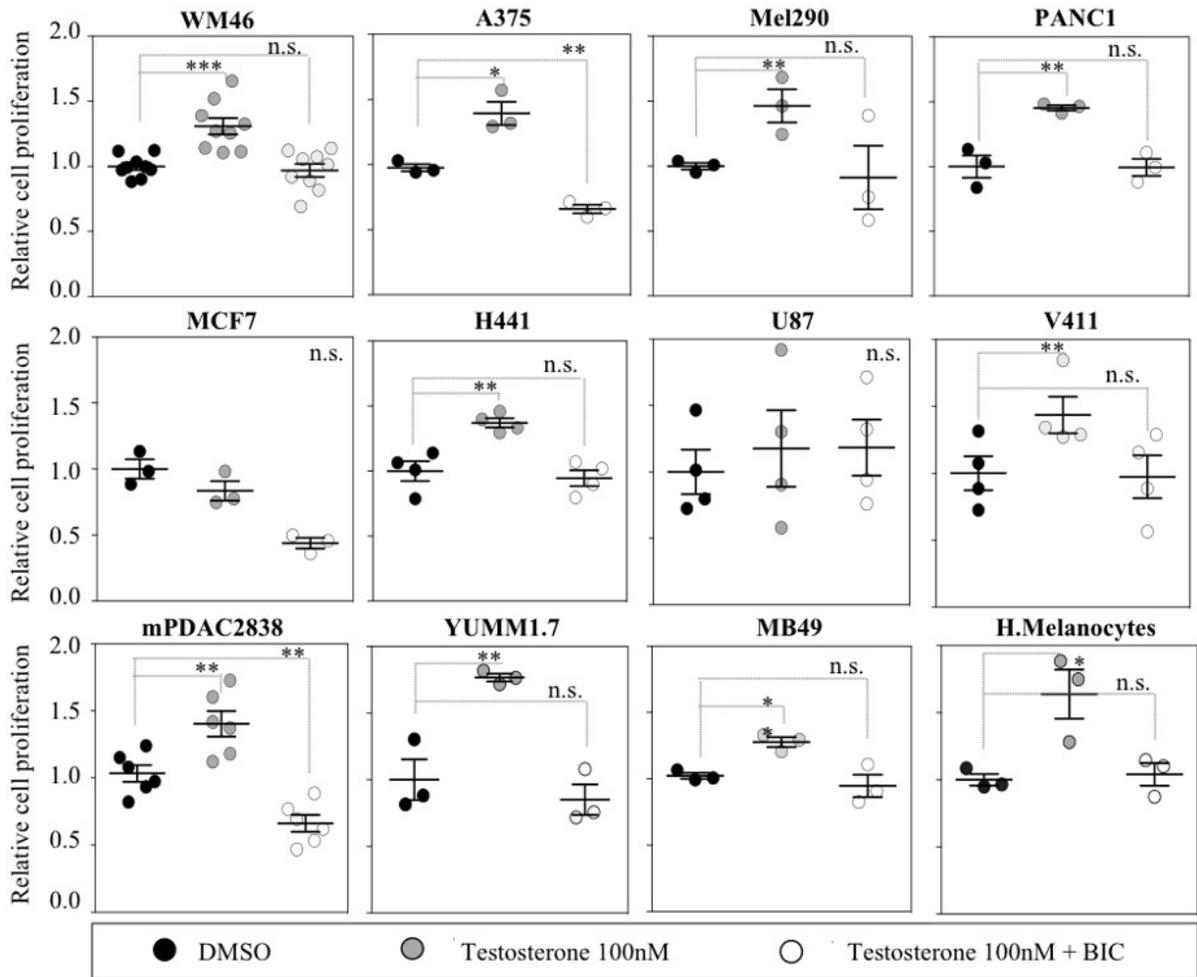
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F



Supplementary Figure 6



Cell types

WM46: Human skin melanoma
A375: Human skin melanoma
Mel290: Human uveal melanoma
YUMMS1.7: Murine skin melanoma
PANCI1: Human pancreatic adenocarcinoma
mPDAC: Murine pancreatic adenocarcinoma

MCF7: Human breast cancer
MB49: Mouse bladder cancer
H441: Human lung adenocarcinoma
U87: Human glioblastoma
V411: Human adult acute myeloid leukemia

Supplementary Table 2

	Gene	Sequence 5'-3'
1	β -Actin_Fw β -Actin_Rv	AGACGCAGGATGGCATGGG GAGACCTTCAACACCCCAGCC
2	YAP1_Fw YAP1_Rv	CGCTCTTCAACGCCGTCA AGTACTGGCCTGTCTGGGAGT
3	LATS2_Fw LATS2_Rv	ACATTCAGTGGTGGGGACTC GTGGGAGTAGGTGCCAAAAA
4	CRM1_Fw CRM1_Rv	GCACCTCTTGGACTGAATCG AAGCGACAGCACACACACAC
5	CDC6_Fw CDC6_Rv	AGCCTCGCATCCTATAACAACC TTCTTTCACAAGGCGGCACTC
6	CYR61_Fw CYR61_Rv	AGCCTCGCATCCTATAACAACC TTCTTTCACAAGGCGGCACTC
7	THBS1_Fw THBS1_Rv	TTGTCTTTGGAACACAC CA CTGGACAGCTCATCACAG

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