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Supplemental Information

YAP/TAZ Activation Drives Uveal Melanoma

Initiation and Progression

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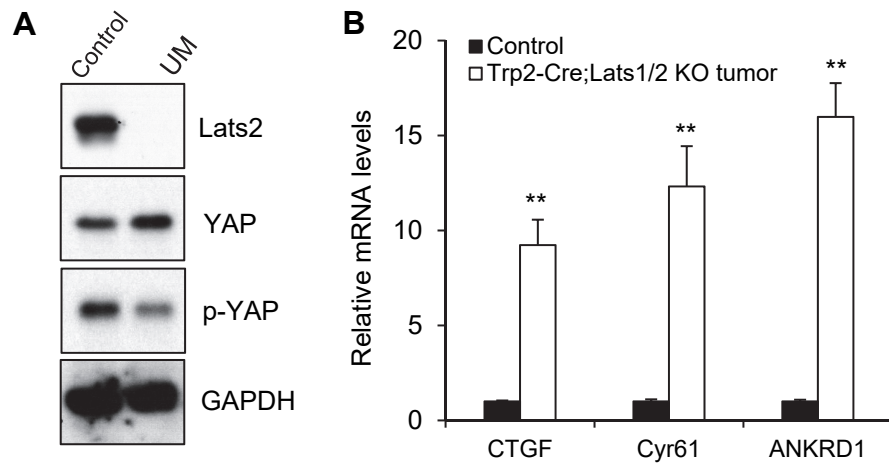


Figure S1 (Related to Figure 2). Lats2 and YAP expression and YAP-mediated transcriptional activity in UM from AAV5-Trp2-GFPCre; Lats1/2 KO mice.

(A) Immunoblot analysis of protein expression of Lats2, YAP, p-YAP and GAPDH in control tissues and AAV5-TRP2-GFPCre; Lats1/2 KO UMs using the antibodies against Lats2, p-YAP, YAP and GAPDH. (B) qPCR analysis of mRNA levels of *CTGF*, *Cyr61*, and *ANKRD1* in control and UM tissues. Data are mean \pm S.D., ** = p value \leq 0.01.

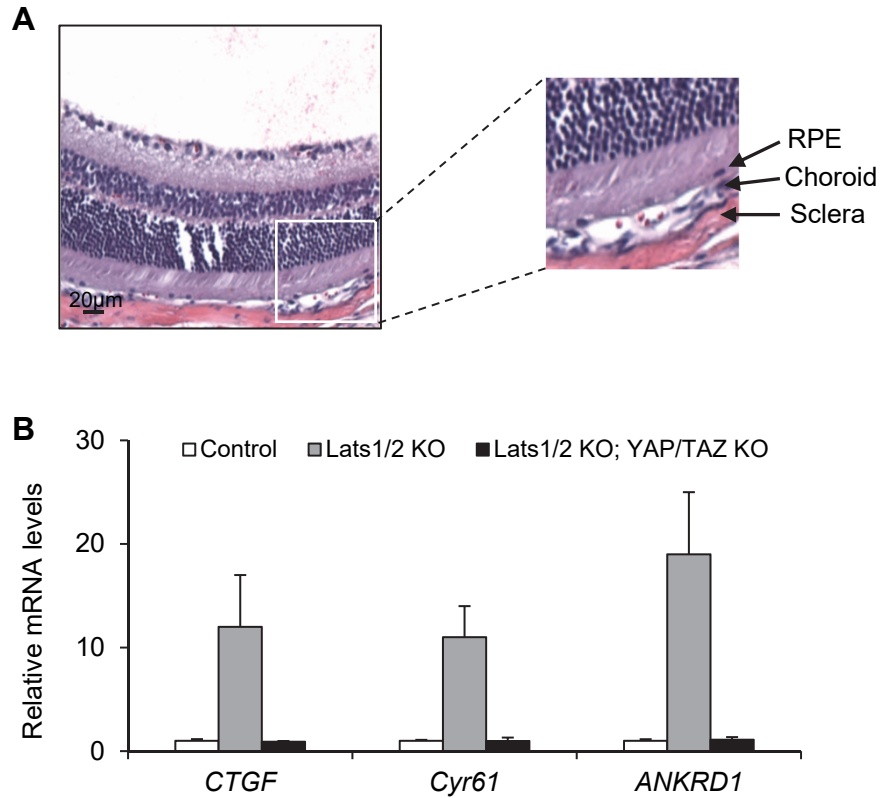


Figure S2 (Related to Figure 3). YAP and TAZ are required for UM genesis induced by Lats1/2 deletion.

(A) Representative histological images of the uveal tract in *AAV5-CMV-Cre;Lats1^{f/f};Lats2^{f/f};YAP^{f/f};TAZ^{f/f}* (6 months after Cre injection) mice. (B) qPCR analysis of mRNA levels of *CTGF*, *Cyr61*, and *ANKRD1* in uveal tract tissues from control and *AAV5-CMV-Cre;Lats1^{f/f};Lats2^{f/f};YAP^{f/f};TAZ^{f/f}* (Lats1/2 KO, YAP/TAZ KO) mice as well as UM from *AAV5-CMV-Cre;Lats1^{f/f};Lats2^{f/f}* (Lats1/2 KO) mice.

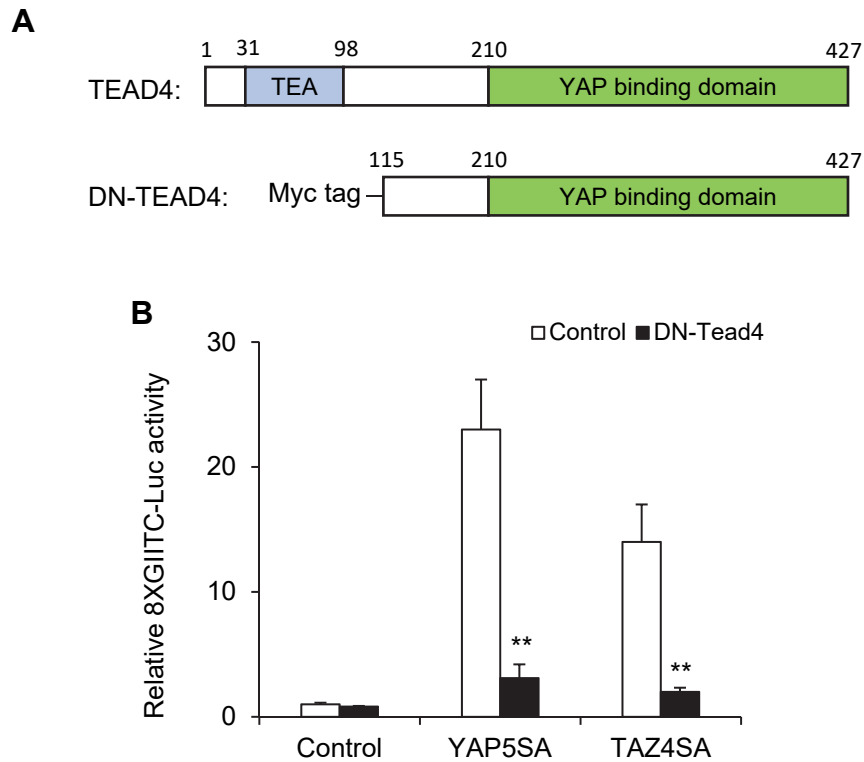


Figure S3 (Related to Figure 4, 6, 7). DN-TEAD4 inhibits YAP and TAZ induced downstream gene transcription.

(A) Schematic diagrams of TEAD4 and DN-TEAD4. DN-TEAD4 retains the entire YAP binding domain and carries a N-terminal myc tag. (B) The activity of TEAD-dependent 8XGIITC-Luc reporter in HEK293T cells expressing the activated forms of YAP (YAP5SA) or TAZ (TAZ4SA) with or without co-expression of DN-TEAD4. Data are mean \pm S.D., ** = p value \leq 0.01.

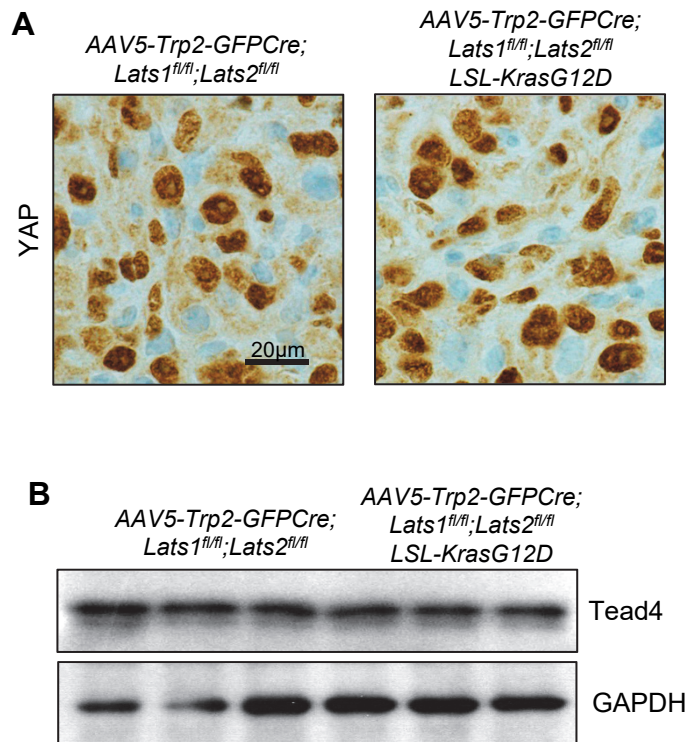


Figure S4 (Related to Figure 5). YAP and Tead4 expression in UM with *Lats1/2* deletion and *Kras* activation.

(A) Immunohistochemistry of YAP showing YAP nuclear localization in UMs from *AAV5-Trp2-GFPCre;Lats1^{fl/fl};Lats2^{fl/fl}* and *AAV5-Trp2-GFPCre;Lats1^{fl/fl};Lats2^{fl/fl};LSL-Kras^{G12D}* mice.

(B) Immunoblot analysis of Tead4 expression in UMs from *AAV5-Trp2-GFPCre;Lats1^{fl/fl};Lats2^{fl/fl}* and *AAV5-Trp2-GFPCre;Lats1^{fl/fl};Lats2^{fl/fl};LSL-Kras^{G12D}* mice.

Table S2 (Related to STAR Methods). RT-qPCR and ChIP-qPCR Primers

qPCR Primers	Sequence
mouse CTGF forward	TGTGCACTGCCAAAGATGGTGCAC
mouse CTGF reverse	TGGGCAGGCGCACGTCCATG
mouse Cyr61 forward	GAGGCTTCCTGTCTTTGGCAC
mouse Cyr61 reverse	ACTCTGGGTTGTCATTGGTAAC
mouse ANKRD1 forward	GGAACAACGGAAAAGCGAGAA
mouse ANKRD1 reverse	GAAACCTCGGCACATCCACA
mouse Lats1 forward	CTTCTCTTCACATCCCTCCTCAAGC
mouse Lats1 reverse	AGCCTTTATCTCATCAGCACCGTTC
mouse Lats2 forward	ATCCTCCCAAAGGGTACAGCACAG
mouse Lats2 reverse	TGGTGGCGTCTTGTTCTGGAAG
mouse YAP forward	AAATGCTCCAAAATGTCAGGA
mouse YAP reverse	CATTCGGAGTCCCTCCATC
mouse TAZ forward	TGCTACAGTGTCACCCACAAC
mouse TAZ reverse	TGACCGGAATTTTCACCTGT
mouse TEAD1 forward	CATCGCAGGGTGTGTCAGTGTGA
mouse TEAD1 reverse	AGGCTGGCGGCTACAAGGTA
mouse TEAD4 forward	AGGCCGGCACCATACCTC
mouse TEAD4 reverse	TGGATCTCCCGGGCTTTTC
mouse Pkrcd forward	CAGACCAAGGACCACCTGTT
mouse Pkrcd reverse	GCATAAAACGTAGCCCGGTA
mouse Nras forward	TGACGATGGCACTCAAGGTTGTATGGG
mouse Nras reverse	CCAGGGATGTCAGAACCAGGGCA
mouse Rras2 forward	GTGGATGGCTTCTGACTTTG
mouse Rras2 reverse	AAACTTCAATGGGGCTGTTG
mouse RasGRP1 forward	GGCTTTCCA CACAACCTTC
mouse RasGRP1 reverse	TCATCCCGCAGTCTTTAC
mouse Myc forward	TGAGCCCCTAGTGCTGCAT
mouse Myc reverse	AGCCCGACTCCGACCTCTT
mouse Cyclin D1 forward	CTCTGGCTCTGTGCCTTTCT
mouse Cyclin D1 reverse	CCGGAGACTCAGAGCAAATC
mouse cJun forward	AAGCGCAAACTCCGAGCT
mouse cJun reverse	CATGAGTTGGCACCCACTGT
mouse JunB forward	GGAGGACAAGGTGAAGACTCA
mouse JunB reverse	GGCAAGGGAGGCTCTCAGA

mouse JunD forward	GACACGCAAGAACGCATCAA
mouse JunD reverse	TTGACGTGGCTGAGGACTTTC
mouse Fos forward	TGGCCCTGTGAGCAGTCA
mouse Fos reverse	AGCCTGGTGTGTTTCACGAAC
mouse FosL1 forward	GAGACGCGAGCGGAACAAG
mouse FosL1 reverse	CTTCCAGCACCAGCTCAAGG
mouse FosL2 forward	TTATCCCGGGAAC TTGACACCTC
mouse FosL2 reverse	CGGCGTTCCTCGGGGCTGATT
mouse GAPDH forward	GTGAAGGTCGGTGTGAACG
mouse GAPDH reverse	ATTTGATGTTAGTGGGGTCTCG
human CTGF forward	TGCCCTCGCGGCTTACCGACTG
human CTGF reverse	TGCAGGAGGCGTTGTCATTGGTAAC
human CYR61 forward	GAGTGGGTCTGTGACGAGGAT
human CYR61 reverse	GGTTGTATAGGATGCGAGGCT
human ANKRD1 forward	CGAGATAAGTTGCTCAGCACAG
human ANKRD1 reverse	GTTTCAGTCTCACCGCATCATG
human PKRCD forward	AAAGGCAGCTTCGGGAAGGT
human PKRCD reverse	TGGATGTGGTACATCAGGTC
human NRAS forward	AGCAGGTGGTGTGGGAAAA
human NRAS reverse	TGTCCAACAAACAGGTTTCACC
human RRAS2 forward	AGCACGGCAGCTTAAGGTAA
human RRAS2 reverse	CTTTCCGTGTTGGTTCTGGT
human RASGRP1 forward	GGCTCAAGGAGACAAGTTCG
human RASGRP1 reverse	GAAGTCGGTGC ACTCTCCATA
human RASGRP3 forward	CTCTGCATGTATCGAAATGCCA
human RASGRP3 reverse	CTACTTCCCGAAATTCCTCAGTC
human cJun forward	ATCAAGGCGGAGAGGAAGCG
human cJun reverse	TGAGCATGTTGGCCGTGGAC
human JunB forward	ATCCCTATCGGGGTCTCAAG
human JunB reverse	CCTGTGTCTGATCCCTGACC
human JunD forward	TCGCGCCTGGAAGAGAAAGTGAAG
human JunD reverse	CCGCTGTTGACGTGGCTGAGG
human Fos forward	CTGGCGTTGTGAAGACCAT
human Fos reverse	TCCCTTCGGATTCTCCTTTT
human FosL1 forward	CAAGGAGGGGACACAGGCAGTA
human FosL1 reverse	TGAAAGGAGTTAGGGAGGGTGTGG

human FosL2 forward	ACGGCCCAGTGTGCAAGATTAGC
human FosL2 reverse	AGCCCCGCCGACGAGGAC
human Myc forward	CGTCTCCACACATCAGAGCACAA
human Myc reverse	TCTTGGCAGCAGGATAGTCCTT
human Cyclin D1 forward	TGCATGTTTCGTGGCCTCTAA
human Cyclin D1 reverse	TCGGTGTAGATGCACAGCTT
human BirC5 forward	ACCACCGCATCTCTAC
human BirC5 reverse	TCCTCTATGGGGTCGT
human GAPDH forward	ATGGGGAAGGTGAAGGTCG
human GAPDH reverse	GGGGTCATTGATGGCAACAATA
ChIP-qPCR Primers	Sequence
mouse Cyr61 forward	CTCTGATGGATCTGAGAAGAGG
mouse Cyr61 reverse	GCCCTTTATAATGCCTGCCTA
mouse Ctgf forward	CAATCCGGTGTGAGTTGATG
mouse Ctgf reverse	GGCGCTGGCTTTTATACG
mouse Ankr1 forward	TCAGACGCACATTTTTCTCG
mouse Ankr1 reverse	GGCAGCCGTGAGTCTATGTT
mouse Nras forward	TGCAGCTTCTAGGACCCAGT
mouse Nras reverse	TACCTCAAACCTCCGCAGACC
mouse Rras2 forward	AGGCTGGCCTTGAACCTTT
mouse Rras2 reverse	CGGGAGGAGAAGGAAGAAAC
mouse Pkrcd forward	CCTCTTGTATCCTCCCAGGAA
mouse Pkrcd reverse	GCGTCTCAGCCTCTTTGAGT
mouse RasGRP1 forward	GAAATGCACGCGTTATAGCA
mouse RasGRP1 reverse	GAATCCTGCCCCATTACTT
mouse GADPH forward	GCCTCTGCGCCCTTGAGCTA
mouse GADPH reverse	GATGCGGCCGTCTCTGGAAC