

Supplemental Figure legends

Supplemental Figure 1. (A) Relative VEGF mRNA levels measured by q-RT-PCR (n=3). VEGF expression in MEFs with different genetic background treated with hypoxia alone and a combination of 20 μ M Nutlin-3 with hypoxia. VEGF lack of repression can be observed in p21 $-/-$ cells after 24h of hypoxia and Nutlin-3 treatment (B) Relative pg VEGF protein measured by ELISA and normalized against mg of cell lysate. p21 $-/-$ cells have higher VEGF levels their WT and p53 $-/-$ counterparts.

Supplemental Figure 2. (A) R1 displays a 950 bp region upstream of the promoter where the HIF-1a and p53 site are adjacent. (B) R2 is a region within the first intron where the HIF-1a and p53 sites are overlapping. (C) R3 is a double p53 site with a 9 bp spacer sequence.

Supplemental Figure 3. (A) Relative mRNA levels measured by q-RT-PCR. p21 mRNA expression is induced in WT cells when treated with doxorubicin or Nutlin-3 in combination with hypoxia. (B) Western blot on WT cells treated with hypoxia alone and in combination with doxorubicin or Nutlin-3. (C) Relative mRNA levels measured by q-RT-PCR. mRNA expression in Mdm2 $-/-$ p53 $lsl/-$ cells after Cre excision and re-activation of p53. (D) Western blot confirming ectopic expression of p21. (E) Relative mRNA levels measured by q-RT-PCR. VEGF expression in parental p21 $-/-$ cells and p21 $-/-$ cells expressing ectopic 3xHA-tagged human p21. At 24h of hypoxia in cell expressing ectopic p21 VEGF is repressed compared to the parental counterpart.

Supplemental Figure 4. (A) HCT116 injected with WT MEFs displaying more hypoxia and less vessels. Necrotic region shown with asterisk. (B) HCT116 injected with p21 $-/-$ MEFs displaying less hypoxia and more vessel formation. Bright field 40X and boxed inserts of 100X images of tumour sections stained with PECAM and hypoxyprobe

Supplemental Figure 5. (A) Y79 shMX displaying less hypoxia and more vessels. (B) Y79 displaying more hypoxia and less vessel formation. Necrotic region shown with asterisk. Bright field montaged 40X (left) and 100X images (right) of tumour sections stained with PECAM and hypoxyprobe

Supplemental Figure 6. (A) Western blot displaying knockdown of p53 in WERI cells with shp53. (B-C) Bright field 100X of tumour sections stained with PECAM and hypoxyprobe.

(B) WERI shMX displaying less hypoxia and more vessels. (C) WERI shp53 displaying more hypoxia and less vessel formation. Necrotic region shown with asterisk.

Supplemental Table 1.

Primer sequences used in q-RT-PCR for CHIP analysis.

	forward primer	reverse primer
VEGF R1	5'-GGAACAAGGGCCTCTGTCTG-3'	5'-GTGAGACGACCTGTGGAAACC-3'
VEGF R2	5'-CCCTCTGTCGTCGTACGTG-3'	5'-ATCGTACGTGCGGTGACTCT-3'
VEGF R3	5'-CCTTTGGCAGGATCCCTTGT-3'	5'-TGGGCAAGTTCGCAGTAAA-3'
beta-actin	5'-TGGGCCGTTAGCTAGTGTCT-3'	5'-CAGCTGTGGCTGCACATAAT-3'
Gapdh	5'-CTCCTGGCTTCTGTCTTTGG-3'	5'-TGGCGTAGCAATCTCCTTTT-3'
HMBS	5'-CCCCTCACCTGGCTATTTTA-3'	5'-GGACATAATGGAGGGCAAGA-3'

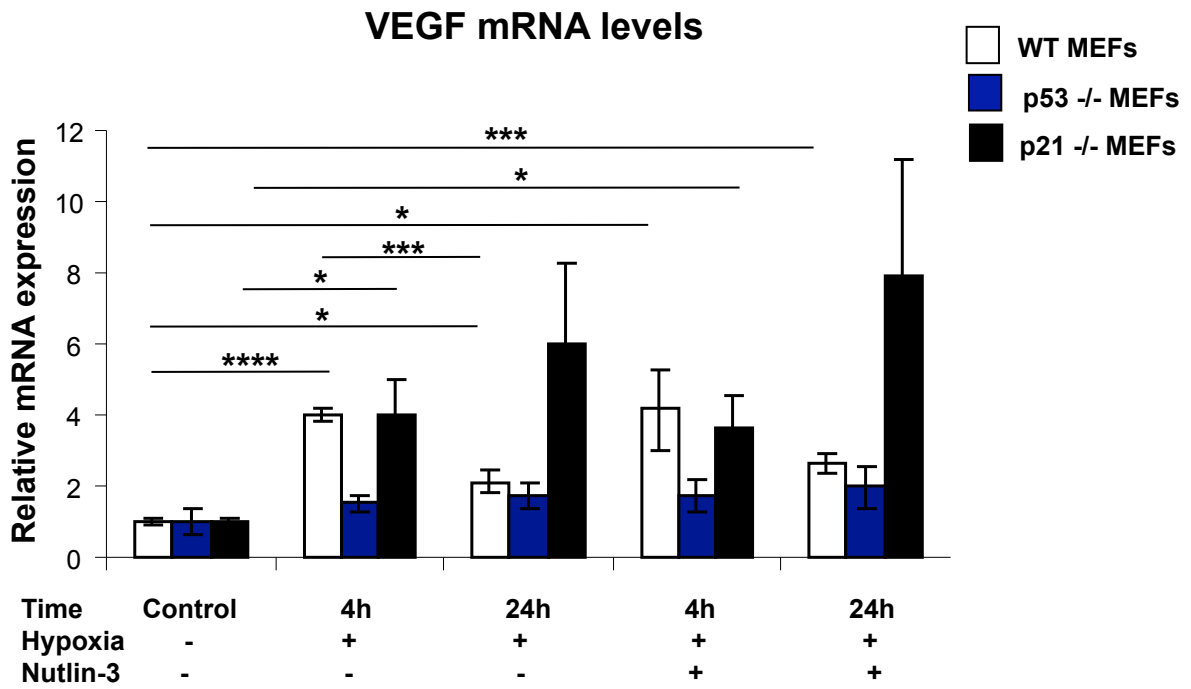
Supplemental Table 2.

Primer sequences used in q-RT-PCR for mRNA expression.

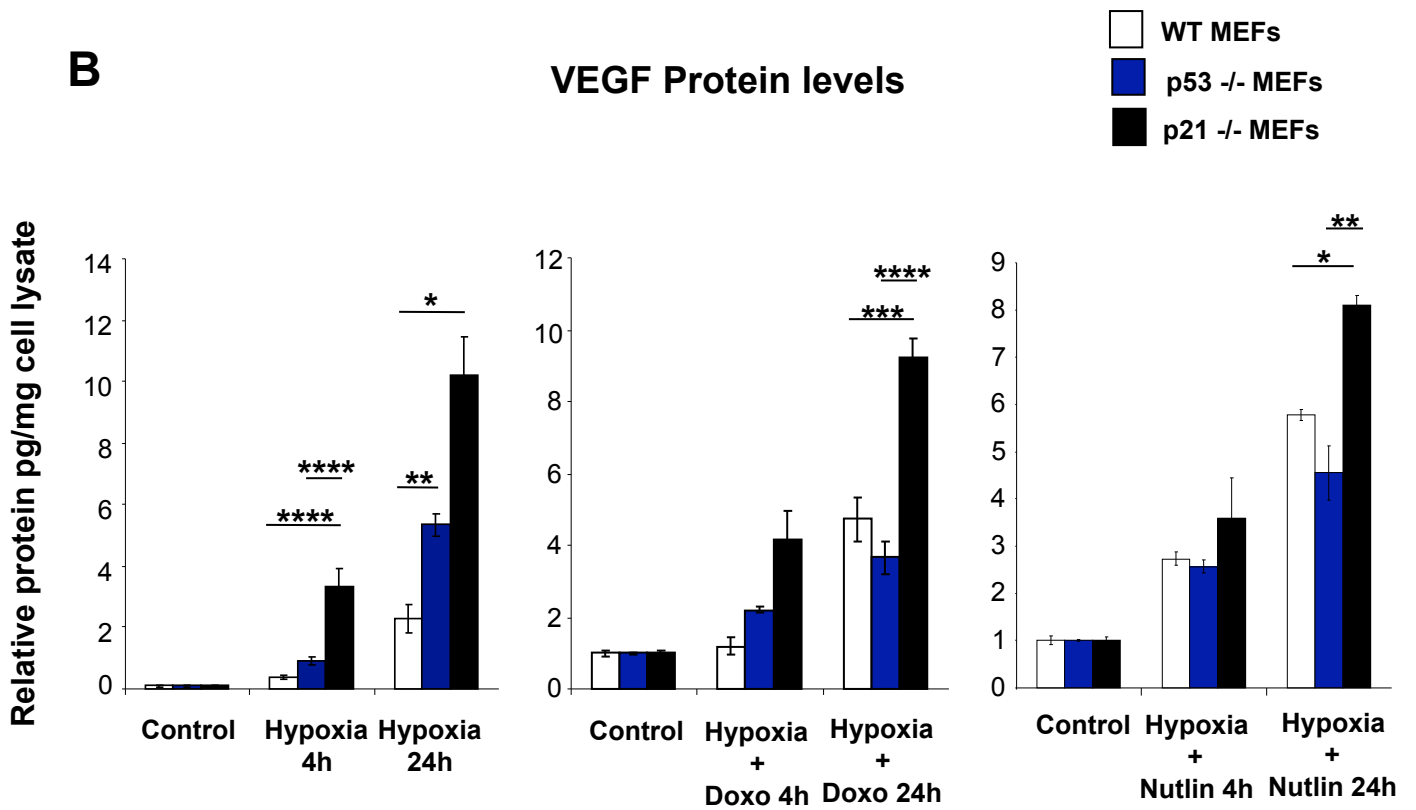
	forward primer	reverse primer
VEGF	5'-CTTGTTTCAGAGCGGAGAAAGC-3'	5'-ACATCTGCAAGTACGTTTCGTT-3'
Gapdh	5'-AGGTTGTCTCCTGCGACTTCA-3'	5'-GGTGGTCCAGGGTTTCTTACTC-3'
HMBS	5'-TCGGGGAAACCTCAACACC-3'	5'-CCTGGCCCACAGCATAACAT-3'
beta-actin	5'-AGTGTGACGTTGACATCCGTA-3'	5'-GCCAGAGCAGTAATCTCCTTCT-3'
p21	5'-CCTGGTGATGTCCGACCTG-3'	5'-CCATGAGCGCATCGCAATC-3'
PFKB3	5'-CCCAGAGCCGGGTACAGAA-3'	5'-GGGGAGTTGGTCAGCTTCG-3'

Supplemental Figure 1

A

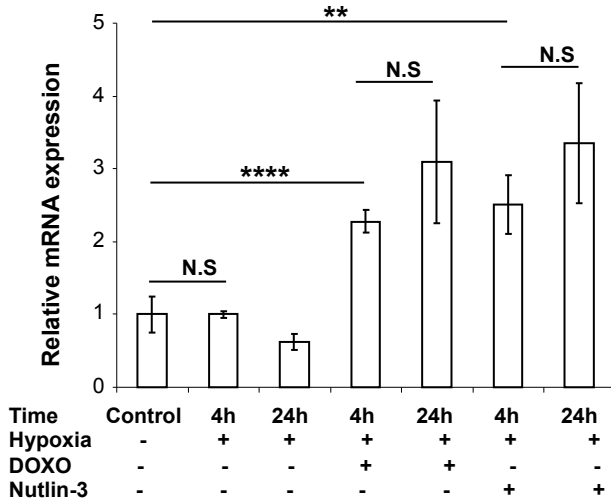


B

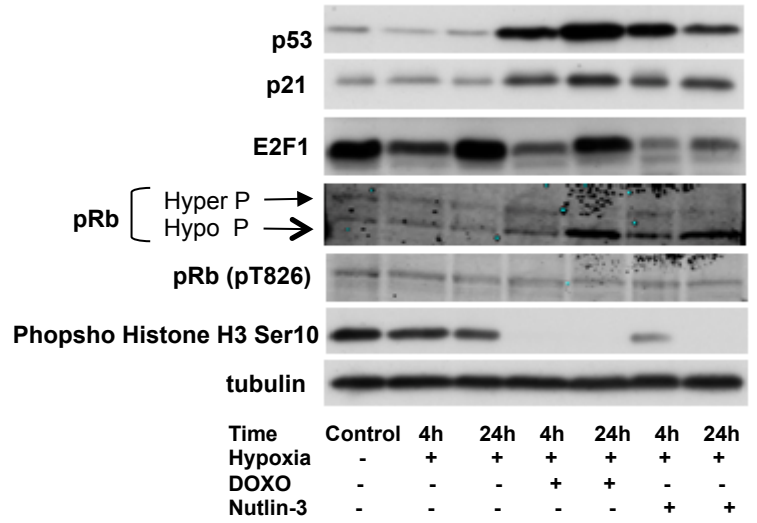


Supplemental Figure 3

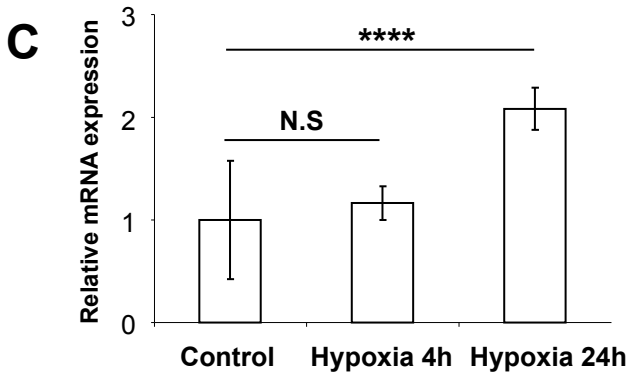
A WT MEFs – p21 mRNA levels



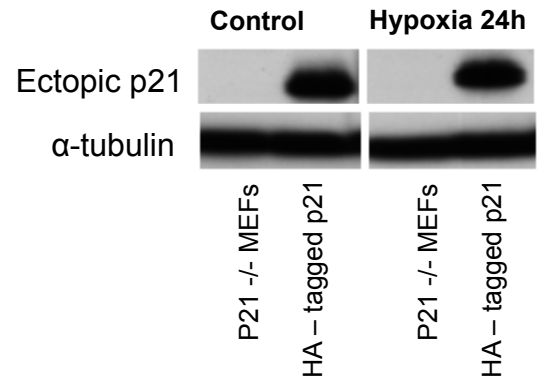
B



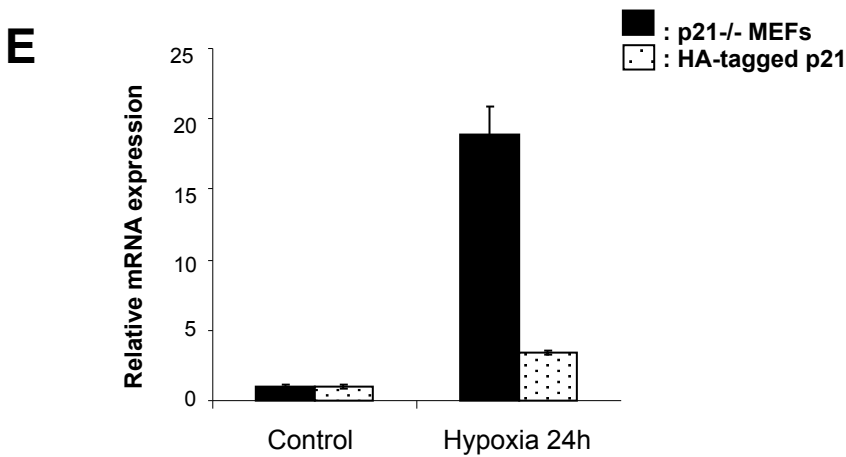
2KO+C – p21 mRNA levels



D



VEGF mRNA levels

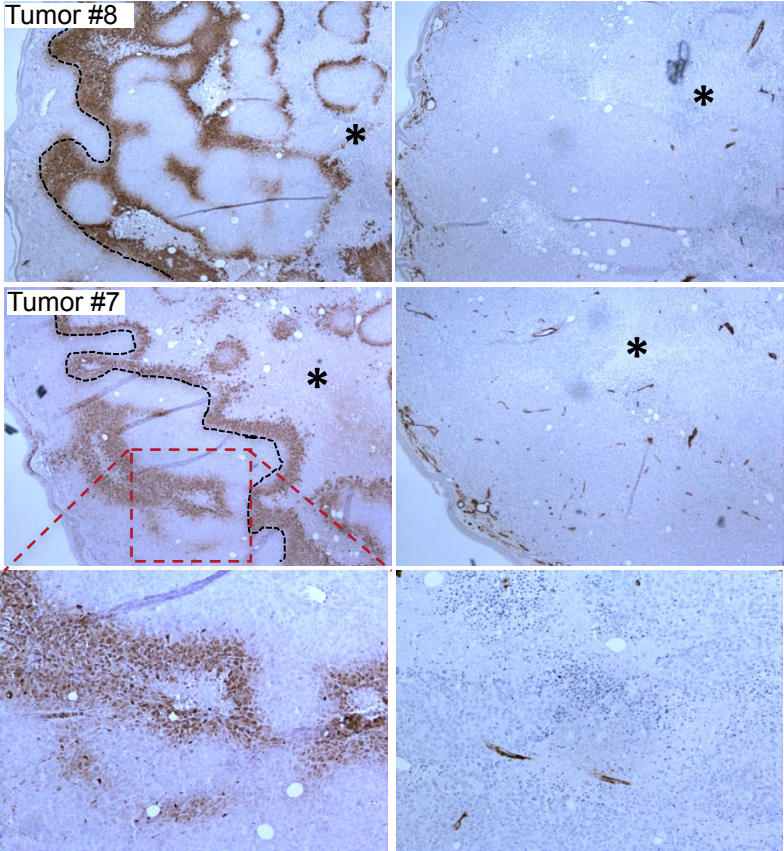


Supplemental Figure 4

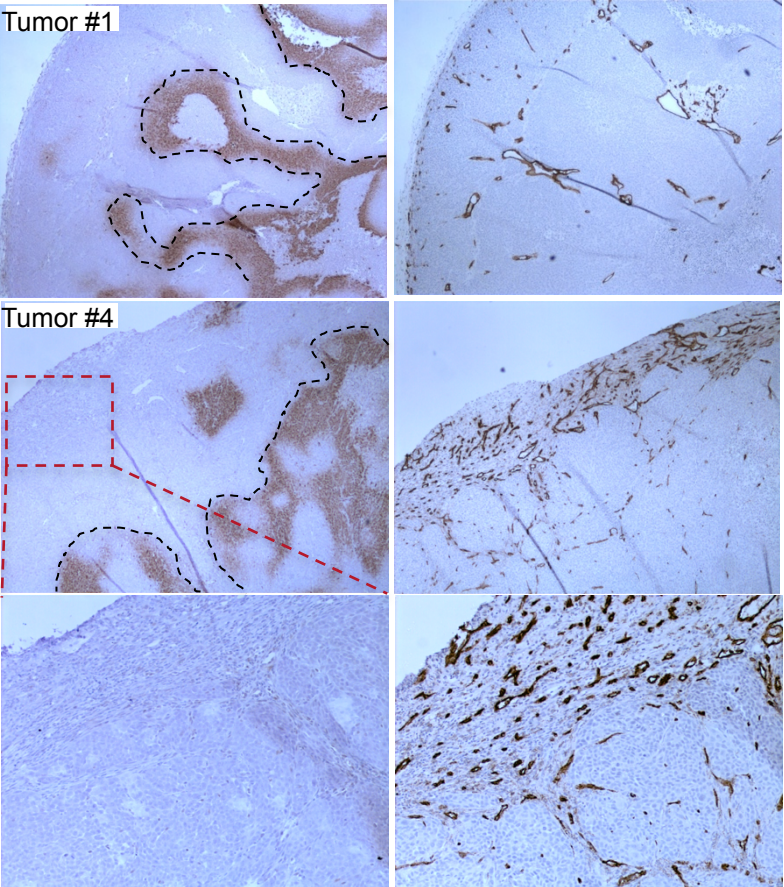
A

Hypoxyprobe

PECAM



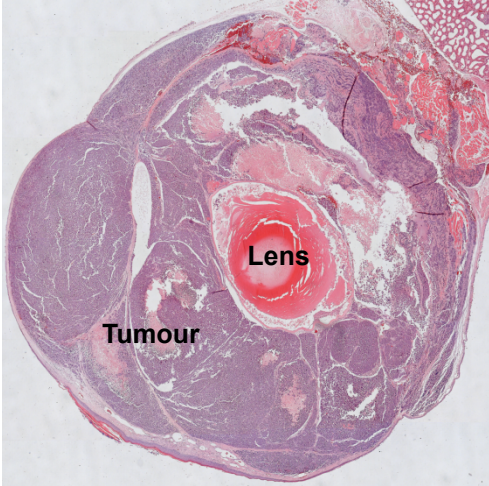
B



Supplemental Figure 5

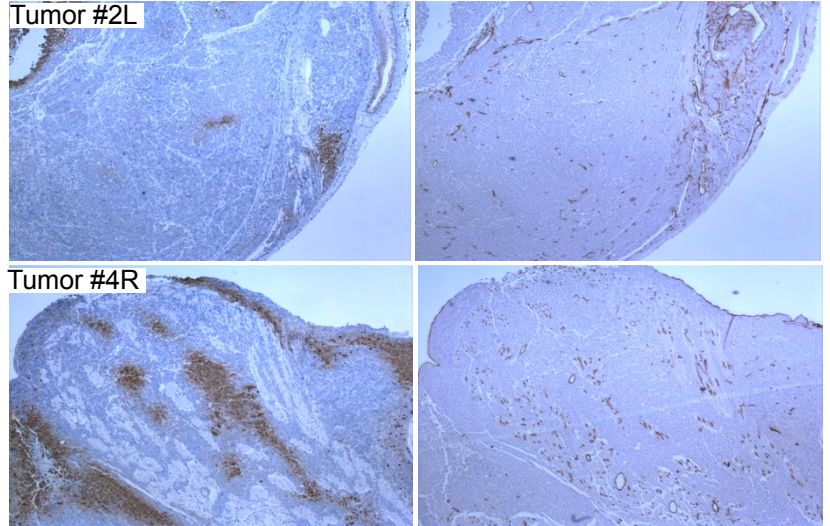
A

Y79-shMX



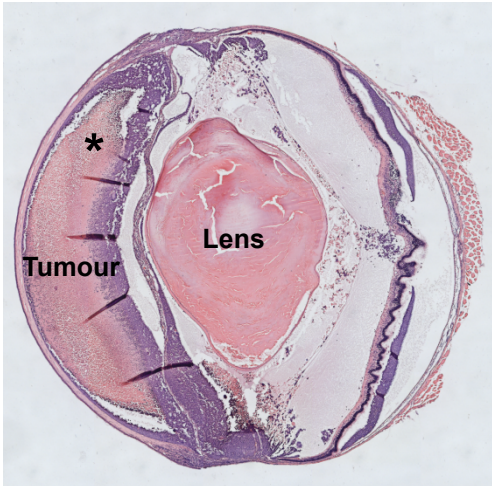
Hypoxyprobe

PECAM



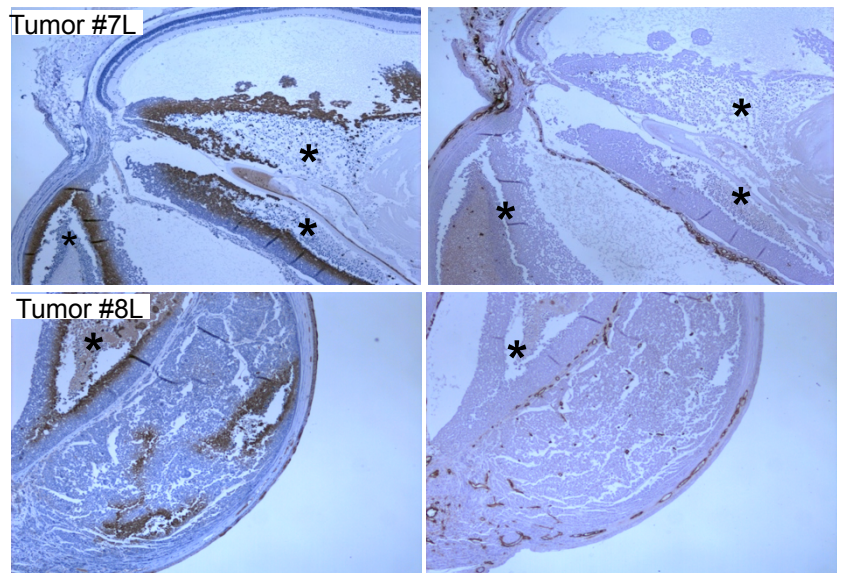
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Y79-shp53



Hypoxyprobe

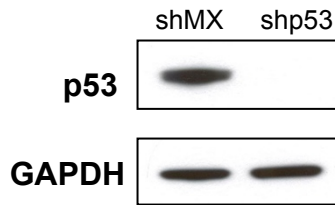
PECAM



Supplemental Figure 6

A

WERI cells – p53 levels

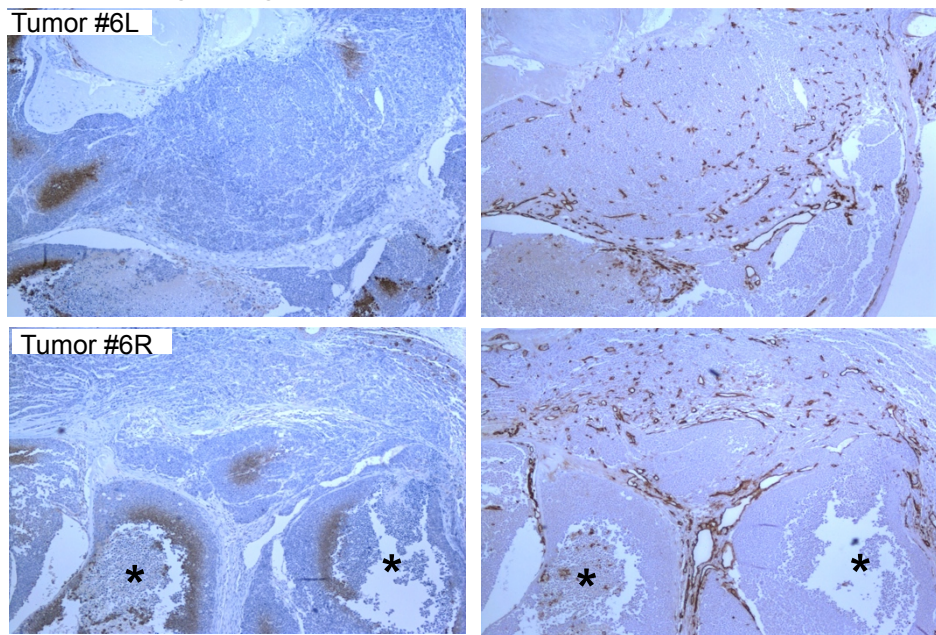


B

Hypoxyprobe

PECAM

**WERI
shMX**



C

Hypoxyprobe

PECAM

**WERI
shp53**

