Supplementary Table 1: List of antibodies used in immunoblotting and immunohistochemical assays

antibody	clone / term	host	Company
HIF-1α	54	mouse	BD Transduction Laboratories (San Jose, USA)
HIF-1α	-	rabbit	Cayman Chemicals (Ann Arbor, USA)
HIF-2α	VNC01	goat	R&D Systems (Minneapolis, USA)
HIF-2α	NB100-480	rabbit	Novus Biologicals (Littleton, USA)
ARNT	2B10	mouse	Acris Antibodies (Hiddenhausen, Germany)
p70S6K	cH-9	mouse	Santa Cruz Biotechnology (Heidelberg, Germany)
p70S6K-P (Thr389)	-	rabbit	Cell Signaling (Danvers, USA)
rpS6	5G10	rabbit	Cell Signaling (Danvers, USA)
rpS6-P (Ser235/236)	-	rabbit	Cell Signaling (Danvers, USA)
ß-actin	AC-15	mouse	Sigma (St. Louis, USA)
PCNA	PC10	Mouse	Cell Signaling (Danvers, USA)
PECAM-1 (M-20)	Sc-1506	goat	Santa Cruz Biotechnology (Heidelberg, Germany)
(HRP)-conjugated sec. mouse antibodies	-	goat	DAKO (Hamburg, Germany)
(HRP)-conjugated sec. rabbit antibodies	-	swine	DAKO (Hamburg, Germany)

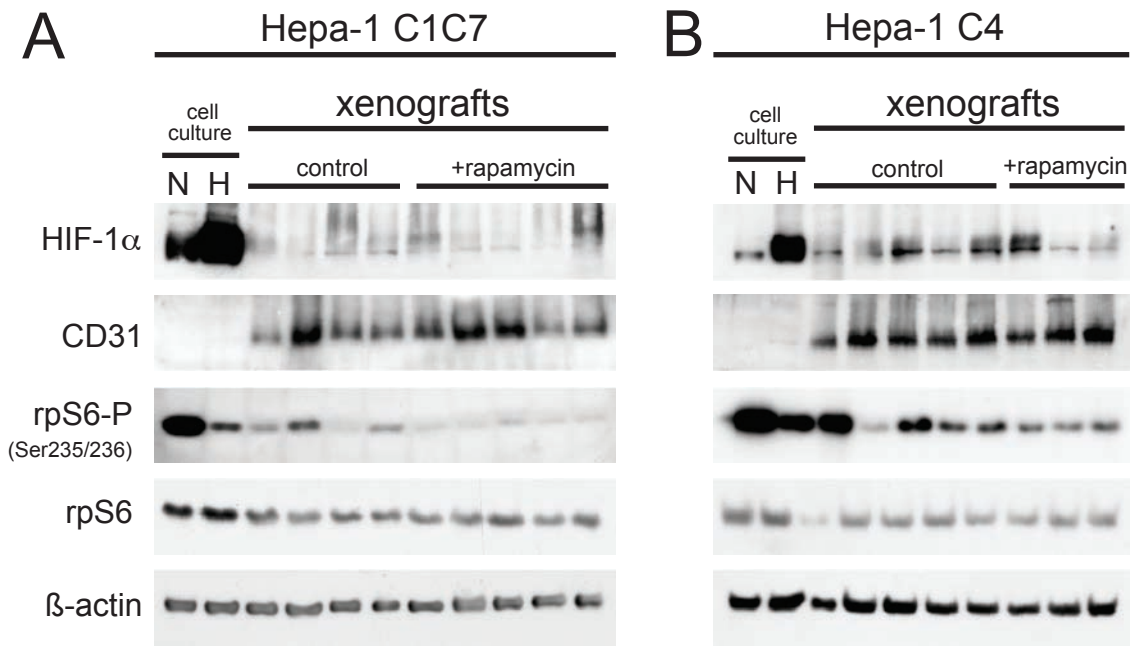
Suppl. Figure 1
30µg of total xenograft tumor lysates from Hepa-1 C1C7 (A) and Hepa-1 C4 (B) cells were immunoblotted for the following proteins: HIF-1α, CD31, rpS6-P (Ser235/236), rpS6 and ß-actin. As controls, total cell lysates from Hepa-1 cell culture experiments (N, normoxia; H, hypoxia, 1%O_2) were added.

Suppl. Figure 2
(A) For the initiation of xenograft tumors, BalbC nu/nu mice were injected subcutaneously with 4x10^6 HeLa cells. Animals were sacrificed when tumors reached a maximal size conforming to animal rights. (B) When the tumors initiated sufficient growth, rapamycin was applied via oral gavage daily at a concentration of 1.5 mg/kg

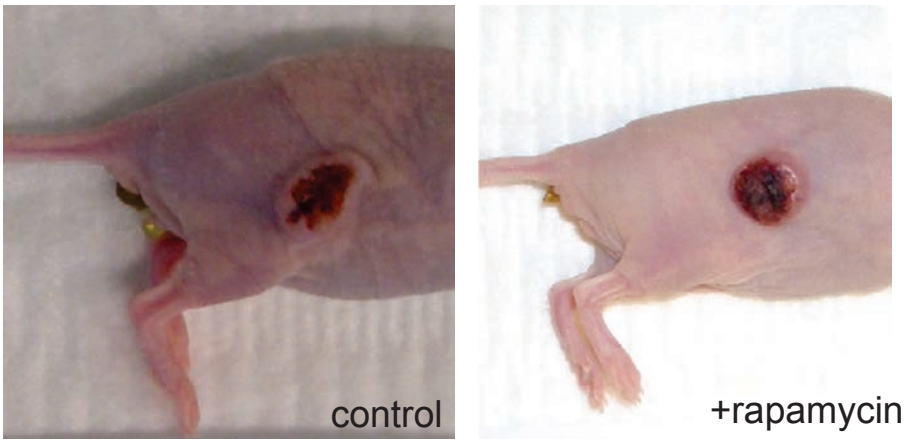
bodyweight. Tumor size was monitored by measurement of length and width every two days.

Suppl. Figure 3
(A) Immunohistochemical staining of PCNA and phospho rpS6 (Ser/Thr 235/236) in paraffin embedded serial sections of Caki-1 xenograft tumors. (B) Immunohistochemical analyses of PCNA in paraffin embedded Caki-1 xenografts either treated with rapamycin (1.5mg/kg bodyweight) or control group (C) Western blot analysis of the expression levels of PCNA in total xenograft cell lysates from both control and rapamycin treated animals.

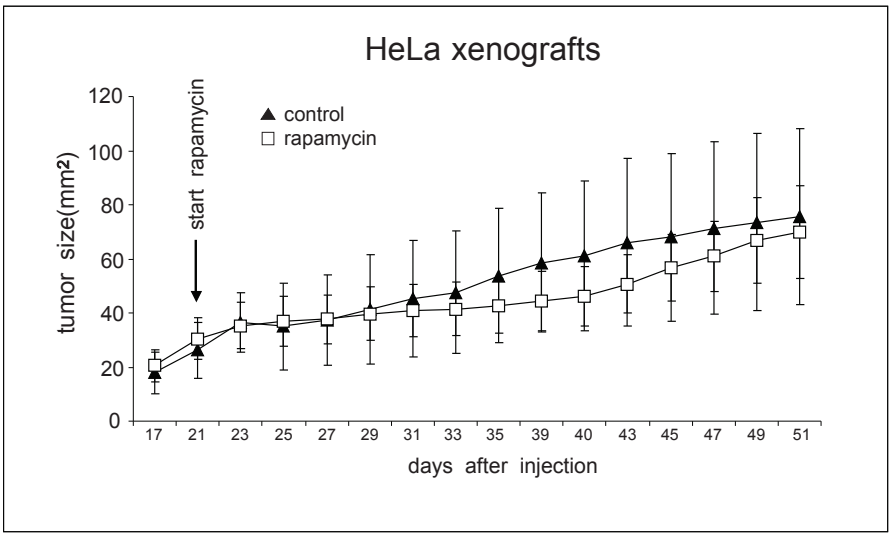
Suppl. Figure 4
Immunohistochemical staining for HIF-1α and HIF-2α in serial sections of either Caki-1 or HeLa tumor xenografts. Magnifications as indicated (10x or 20x).

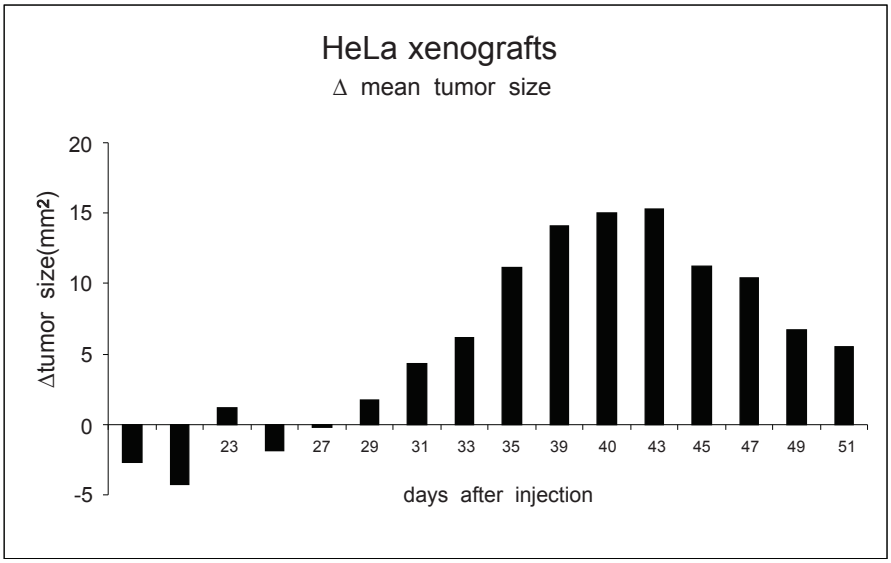

A
Hepa-1 C1C7
cell culture
xenografts
N H
control
+rapamycin
HIF-1α
CD31
rpS6-P
(Ser235/236)
rpS6
ß-actin
B
Hepa-1 C4
cell culture
xenografts
N H
control
+rapamycin

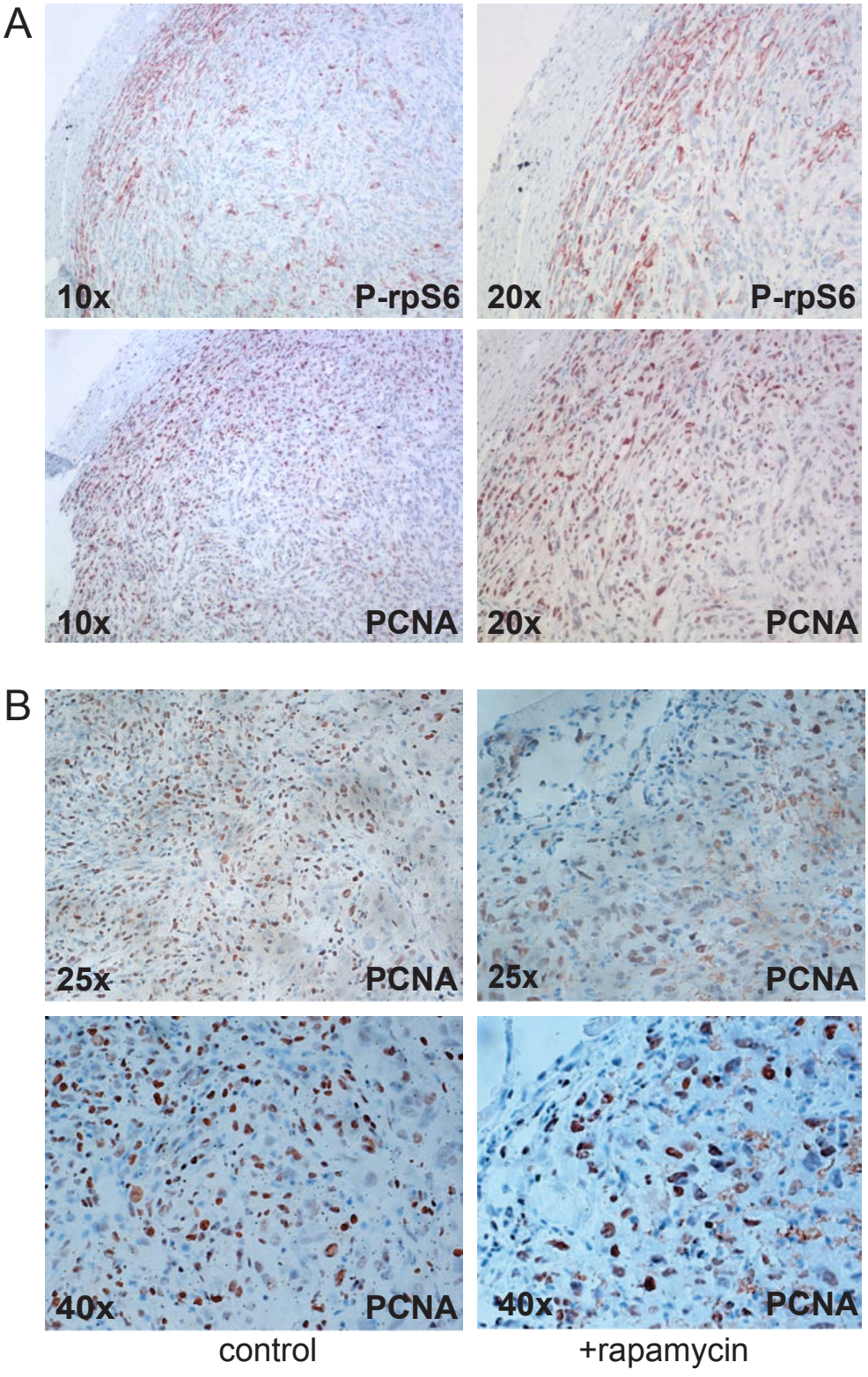
A

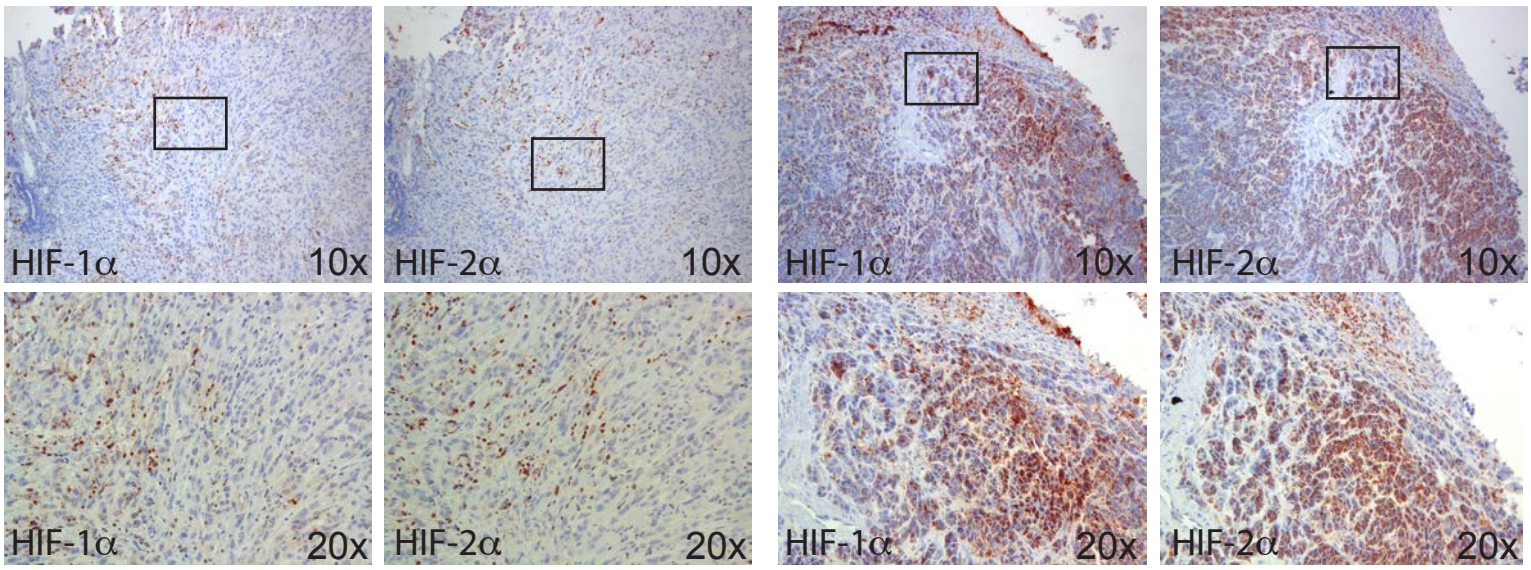

control
+rapamycin

B


HeLa xenografts
tumor size(mm²)
start rapamycin
control
rapamycin
120
100
80
60
40
20
0
17
21
23
25
27
29
31
33
35
39
40
43
45
47
49
51
days after injection


HeLa xenografts
Δ mean tumor size
Δtumor size(mm²)
20
15
10
5
0
-5
23
27
29
31
33
35
39
40
43
45
47
49
51
days after injection


A
10x
P-rpS6
20x
P-rpS6
10x
PCNA
20x
PCNA
B
25x
PCNA
25x
PCNA
40x
PCNA
40x
PCNA
control
+rapamycin
C
cell culture
control
+ rapamycin
Caki-1 xenografts
control
+ rapamycin
ß-actin
PCNA


Caki-1 xenograft
HeLa xenograft
HIF-1α
10x
HIF-2α
10x
HIF-1α
10x
HIF-2α
10x
HIF-1α
20x
HIF-2α
20x
HIF-1α
20x
HIF-2α
20x