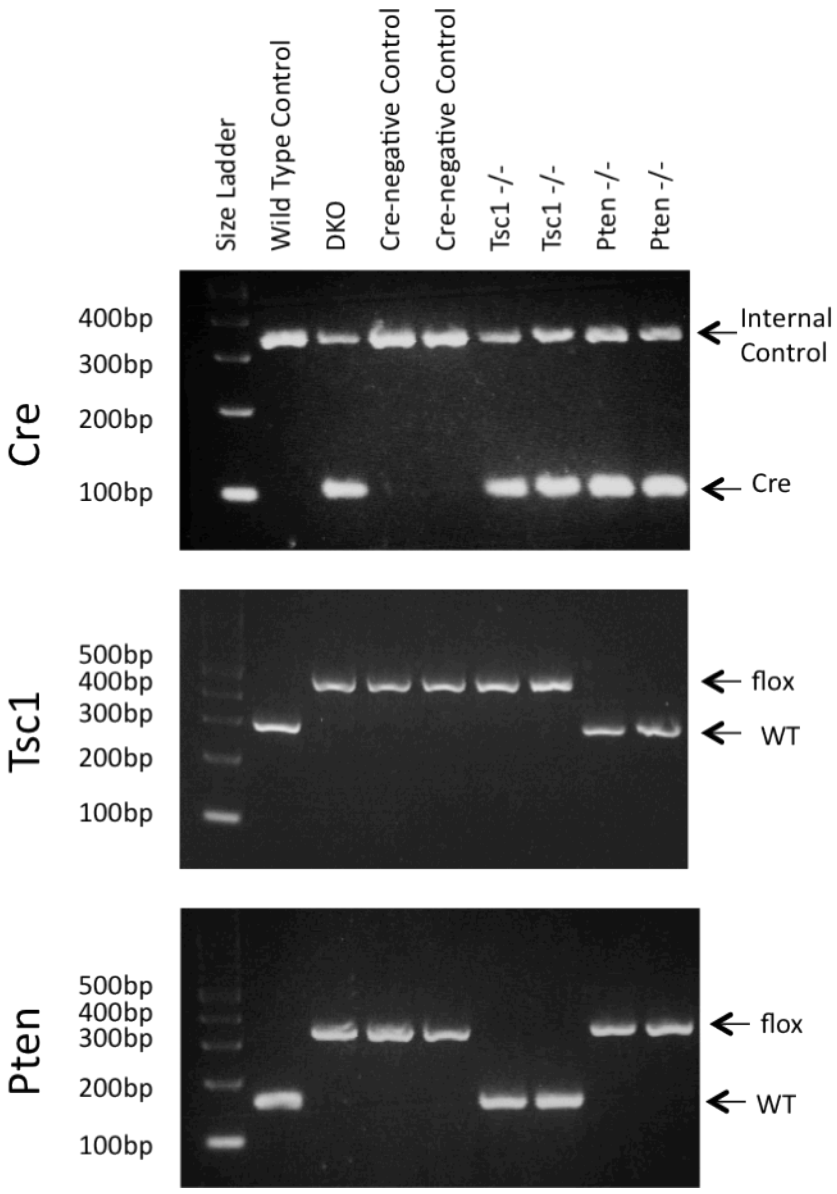
Supplemental Table 1. Liver:body weight ratios*

	Tsc1				**Pten**				**Tsc1;Pten**	
Age (weeks)	12		60		12		45		10	
Genotype	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-	+/+	-/-
Male	3.82 ±0.12	4.33 ±0.16	3.37 ±0.11	5.65 ±0.6	3.68 ±0.11	7.39 ±0.62	3.71 ±0.22	14.63 ±0.92	3.97 ±0.14	12.64 ±0.95
p-value (+/+ vs. -/-)	0.02		0.01		0.001		2×10^{-6}		0.0008	
p-value	9×10^{-6}				0.003					
	2×10^{-7}									
Female	3.6 ±0.14	3.75 ±0.14	3.13 ±0.05	3.83 ±0.22	3.56 ±0.08	6.48 ±0.24	3.35 ±0.14	10.99 ±0.7	4.07 ±0.18	8.61 ±0.54
p-value (+/+ vs. -/-)	0.5		0.007		.000003		3×10^{-6}		0.001	
p-value	N.S.				2×10^{-5}					
	5×10^{-7}									
p-value (male -/- vs. female -/-)	0.02		0.003		0.15		0.005		0.02	

*ratio expressed as percentage.

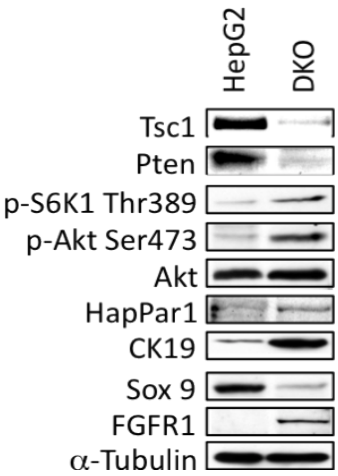
Supplemental Figure 1

PCR genotyping illustrating the detection of *Cre*, *Tsc1*^{fl} and *Pten*^{fl} alleles in offsprings. The DKO mice carry the *Tsc1*^{fl}, *Pten*^{fl} and Cre alleles, whereas the Cre-negative controls contain the *Tsc1*^{fl} and *Pten*^{fl}, but not the Cre, alleles.

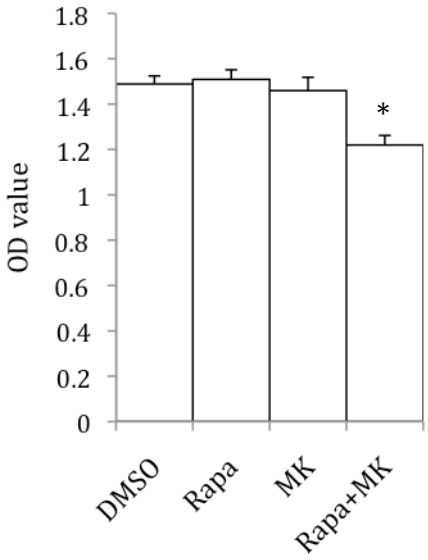


Supplemental Figure 2

A. Biochemical profile of DKO primary cells (passage 4). Immunoblot analysis of cell lysates using indicated antibodies.

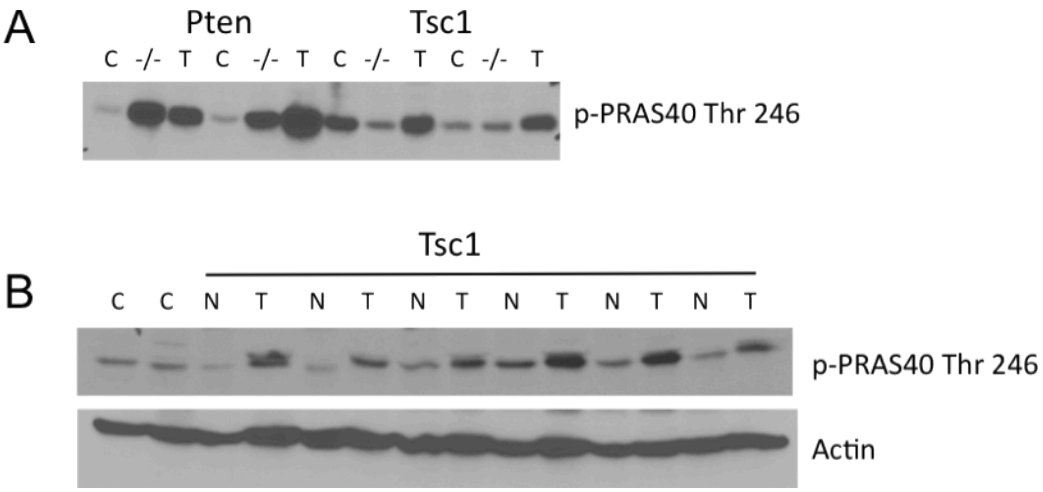


B. Effects of rapamycin and MK2206 on HepG2 cells. MTT assay was performed after 3 days of treatment with rapamycin (50nM) and/or MK2206 (500nM). * $p<0.01$ compared to all other groups.



Supplemental Figure 3

Activation of Akt in *Tsc1*-/- tumors. A) Expression of phospho-PRAS40(Thr246) by Western blot analysis of liver and tumor lysates from *Pten*-/- and *Tsc1*-/- mice along with their respective control (C) livers. *Pten*-null livers (-/-) and tumors (T) serve as positive controls for Akt activity. Comparatively, Akt activity in the *Tsc1*-/- tumors (T) was less than the Pten counterparts but higher than the *Tsc1*-/- livers (-/-). B) Additional examples of *Tsc1*-/- tumors (T) paired with adjacent non-tumor livers (N) highlighting the consistent increase in tumor phosphorylation of PRAS40(Thr246). C, control mouse livers. Actin serves as loading control.



Supplemental Figure 4

Immunohistochemical analyses of Pten expression in liver tissues. Formalin-fixed paraffin-embedded tissue sections were processed for Pten immunostaining in non-tumor liver tissues from *Pten*$^{fl/fl}$ (Cre-negative), *Pten*$^{fl/fl}$*;Alb-Cre* (Pten-/-) and *Tsc1*$^{fl/fl}$*;Alb-Cre* (Tsc1-/-) mice. While most cells in the Cre-negative and *Tsc1*-/- livers expressed Pten, only the non-parenchymal cells in the *Pten*-/- stained positively with Pten antibody. (Note that some biliary epithelia express Pten in the *Pten*-/- livers – see Figure 4A)