Supplementary Information

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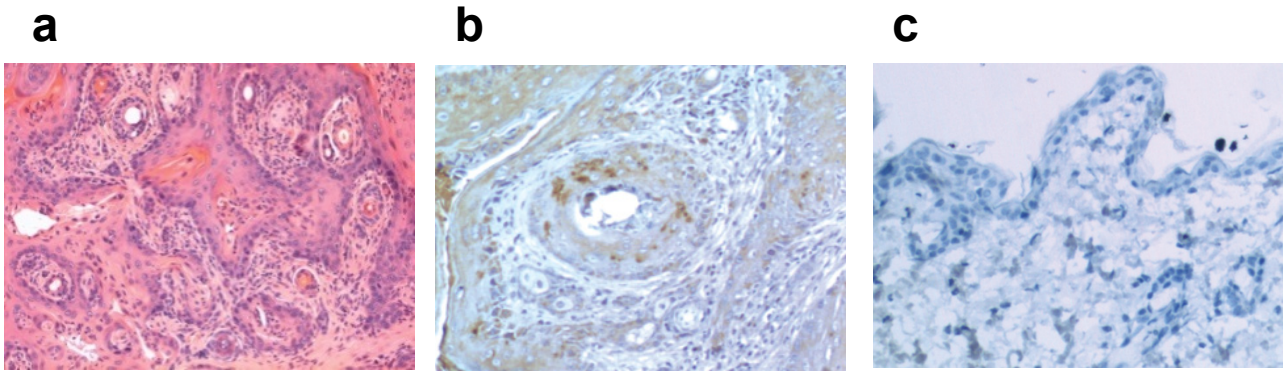
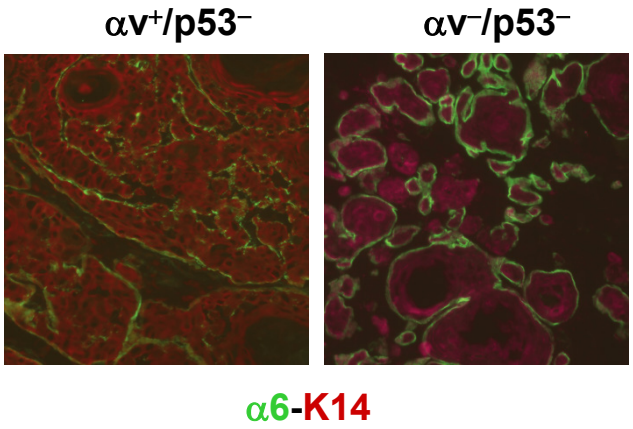
Supplementary Figure S1



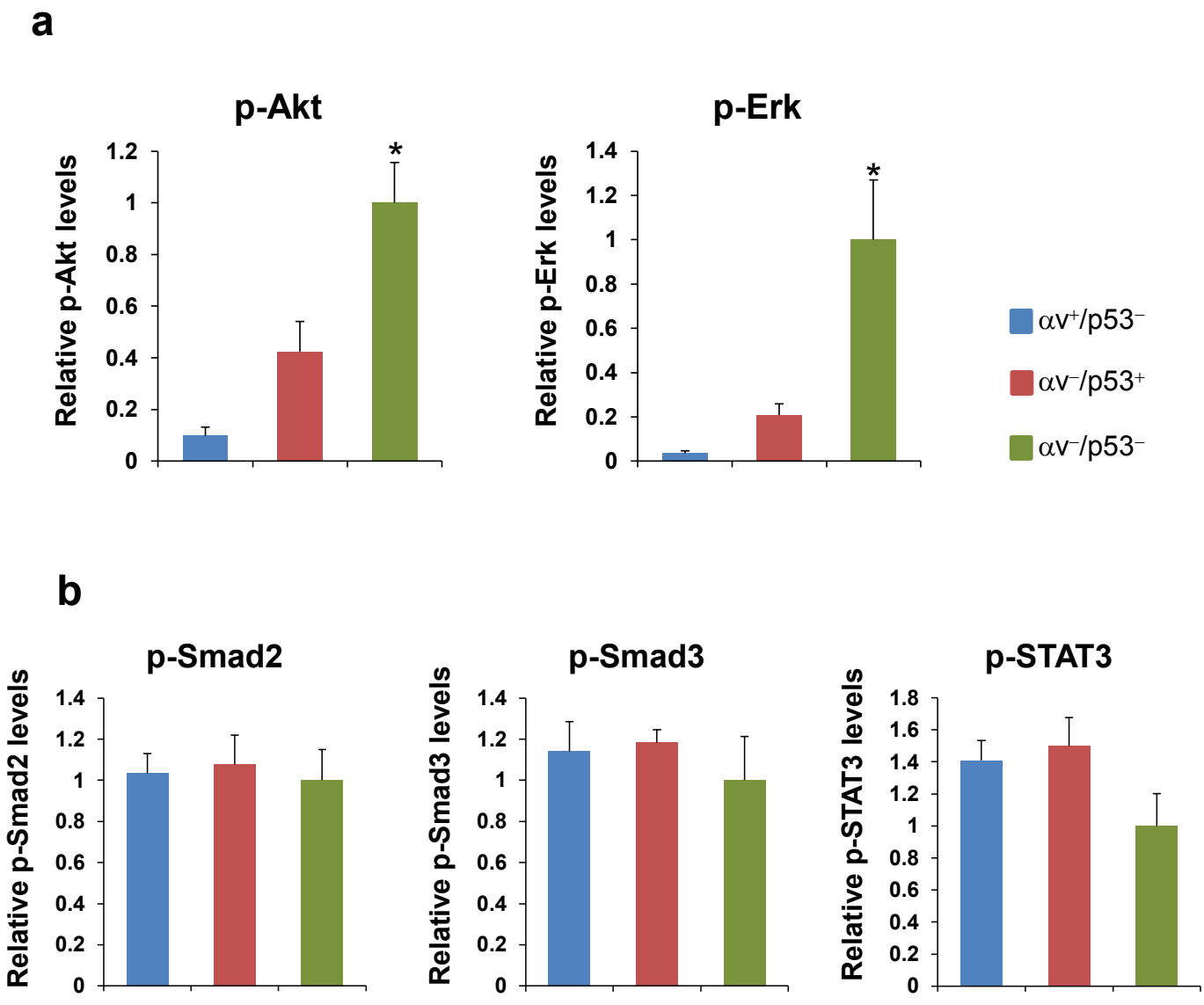
Supplementary Figure S1. Induction of p53 in SCCs generated by αv deletion. (**a**) Histology of an SCC that developed in an $av^{f/f}$-$p53^{wt/wt}$ mouse. (**b,c**) immunohistochemistry for p53 in the tumor shown in A (b) and control skin (c).

Supplementary Figure S2



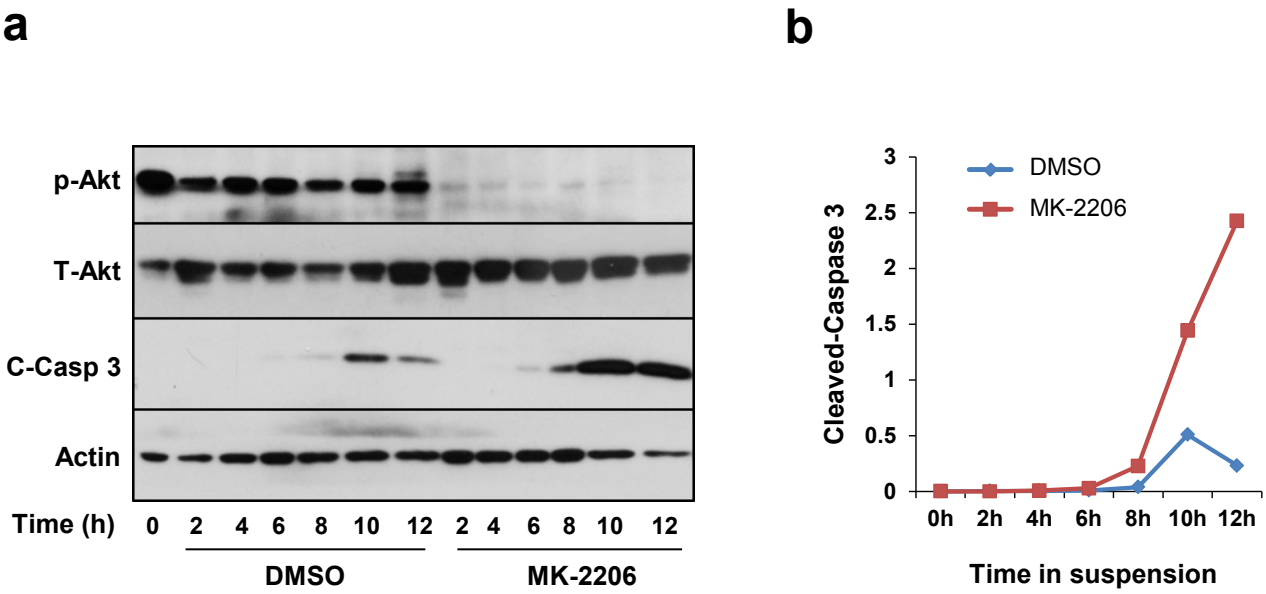
Supplementary Figure S2. Integrin α6 expression in SCCs. Double immunofluorescence for α6 and K14 in a conventional $\alpha v^{+}/p53^{-}$ SCC (left panel) and a pseudoglandular/acantholytic $\alpha v^{-}/p53^{-}$ SCC (right panel). Note that α6 lines the basal layer of basal epithelial cells in both SCC phenotypes.

Supplementary Figure S3



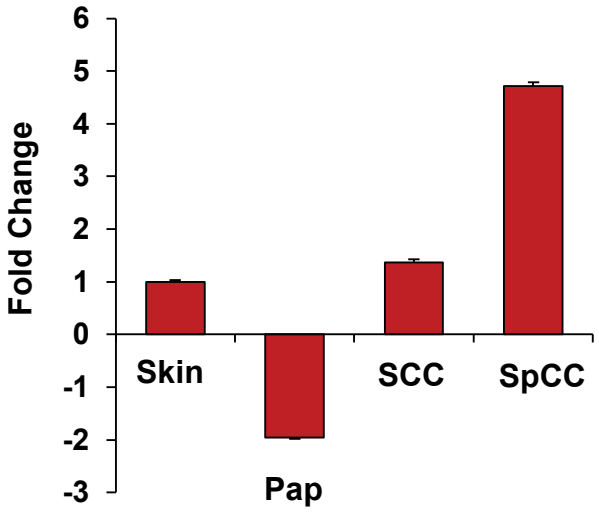
Supplementary Figure S3. (a) Quantification of p-Akt and p-Erk in tumors with the indicated genotypes in western blots shown in Figure 2a, top panel. The phosphorylated levels of Akt (p-Akt) and Erk (p-Erk) were determined as the ratio p-Akt/T-Akt (left) and p-Erk/T-Erk (right) after normalization of the expression levels of T-Akt and T-Erk with Actin. Data is represented as the fraction of p-Akt (left) and p-Erk (right) levels in tumors with the indicated genotypes relative to those in $\alpha v^{-}/p53^{-}$ tumors. **(b)** Quantification of the normalized levels of p-Smad2, p-Smad3 and p-STAT3 in the western blots shown in Figure 2a, bottom panel. Data is represented as the fraction of p-Smad2 (left), p-Smad3 (middle) and p-STAT3 (right) levels in tumors with the indicated genotypes relative to those in $\alpha v^{-}/p53^{-}$ tumors. *p< 0.05 for comparisons with each of the other two groups.

Supplementary Figure S4



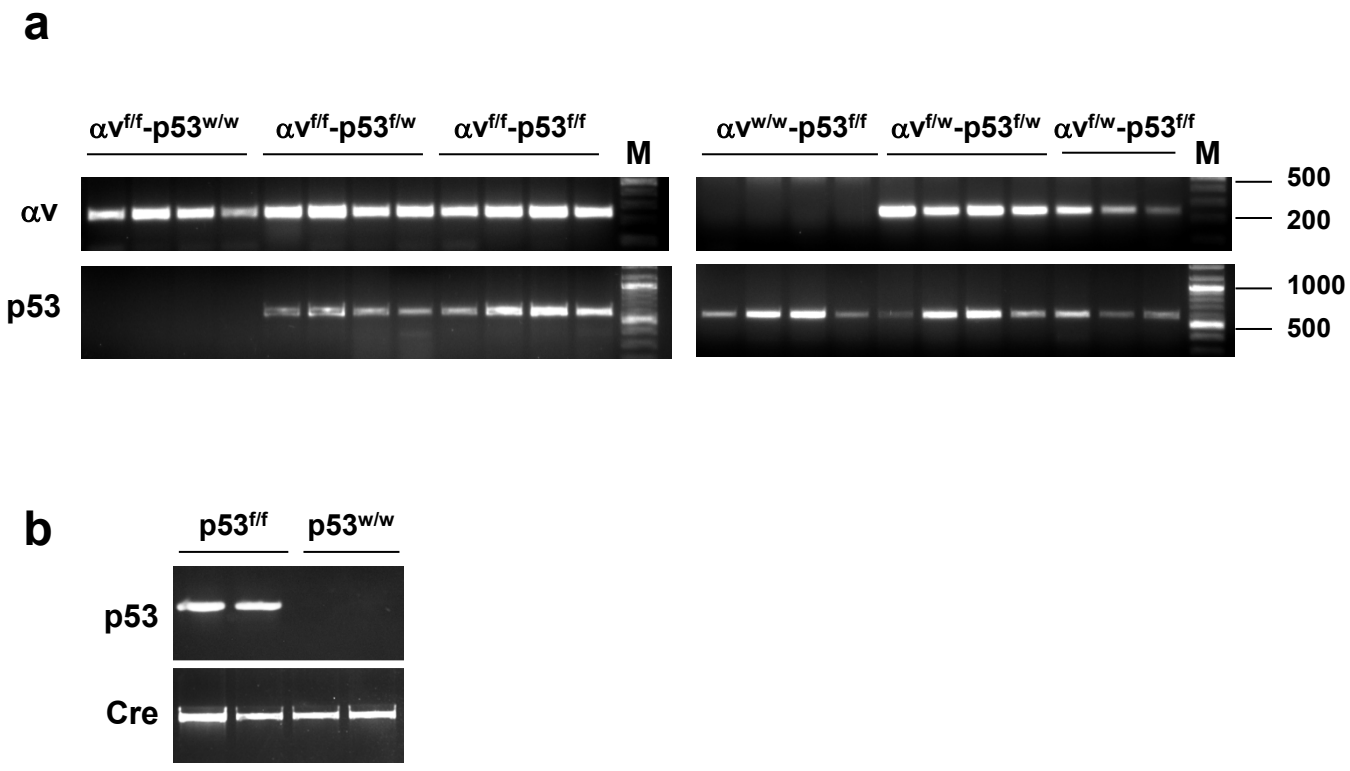
Supplementary Figure S4. Akt protects αv⁻/p53⁻ cells from anoikis. (a) 5x 10^6 cells from a cell line established from an αv⁻/p53⁻ SCC were detached from the tissue culture dish and placed in suspension for the indicated times, in the presence of the Akt inhibitor MK-2206 (2μM) or solvent (DMSO). Akt activation was analyzed by western blot using an antibody for phosphorylated Akt (p-Akt), and apoptosis was determined using an antibody for cleaved caspase 3 (C-Casp3). Total Akt (T-Akt) was analyzed as control for the presence of Akt protein in the lysates, and actin was used a loading control. A western blot analysis representative of three independent experiments is shown. **(b)** Quantification of the levels of caspase 3 cleavage band shown in panel a after normalization with actin.

Supplementary Figure S5



Supplementary Figure S5. Expression of αv integrin in skin tumors. Quantitative real-time PCR for the expression of αv in mouse skin and skin tumors induced by activation of K-ras and p53 mutations (Caulin et al. 2007, Torchia et al, 2011). Note that αv expression decreases in benign papillomas (Pap), but increases in spindle cell carcinomas (SpCC), the most aggressive tumors that developed in this model.

Supplementary Figure S6



Supplementary Figure S6. Activation of conditional alleles in the skin of mice with the indicated genotypes. **(a)** PCR analysis designed to identify deletion of the conditional αv and p53 alleles (250bp and 612bp, respectively), using specific primers for each allele, following PCR conditions described in Lacy-Hulbert et al., 2007 and Jonkers et al., 2001. DNA was purified from tail snips collected from 4-6 week-old mice. **(b)** Persistent activation of conditional alleles in the skin was confirmed in 2-year-old $p53^{f/f}$ mice (top panel). Activation of the p53 allele was analyzed as indicated in a. Amplification of Cre with specific primers was used as control (bottom panel).

Supplementary Table S1

Supplementary Table S1. Prevalence of tumors arising from different sites. Data is represented as a percentage of mice with tumors in the indicated locations relative to the total number of mice that developed tumors for each of the indicated genotypes. The number of mice analyzed in each genotypic group is indicated.

	$\alpha v^{f/f}$-$p53^{f/f}$ (n=26)	$\alpha v^{f/f}$-$p53^{f/wt}$ (n=25)	$\alpha v^{f/wt}$-$p53^{f/f}$ (n=13)	$\alpha v^{f/wt}$-$p53^{f/wt}$ (n=10)	$\alpha v^{wt/wt}$-$p53^{f/f}$ (n=7)
Skin	92	88	70	70	100
Oral	17	28	23	10	14
Ano-rectal	14	12	8	10	0
Periorbital	6	8	8	10	0