Figure legends

Supplementary Figure 1

Activation of the K-*ras*$^{G12D\ in}$ the skin.

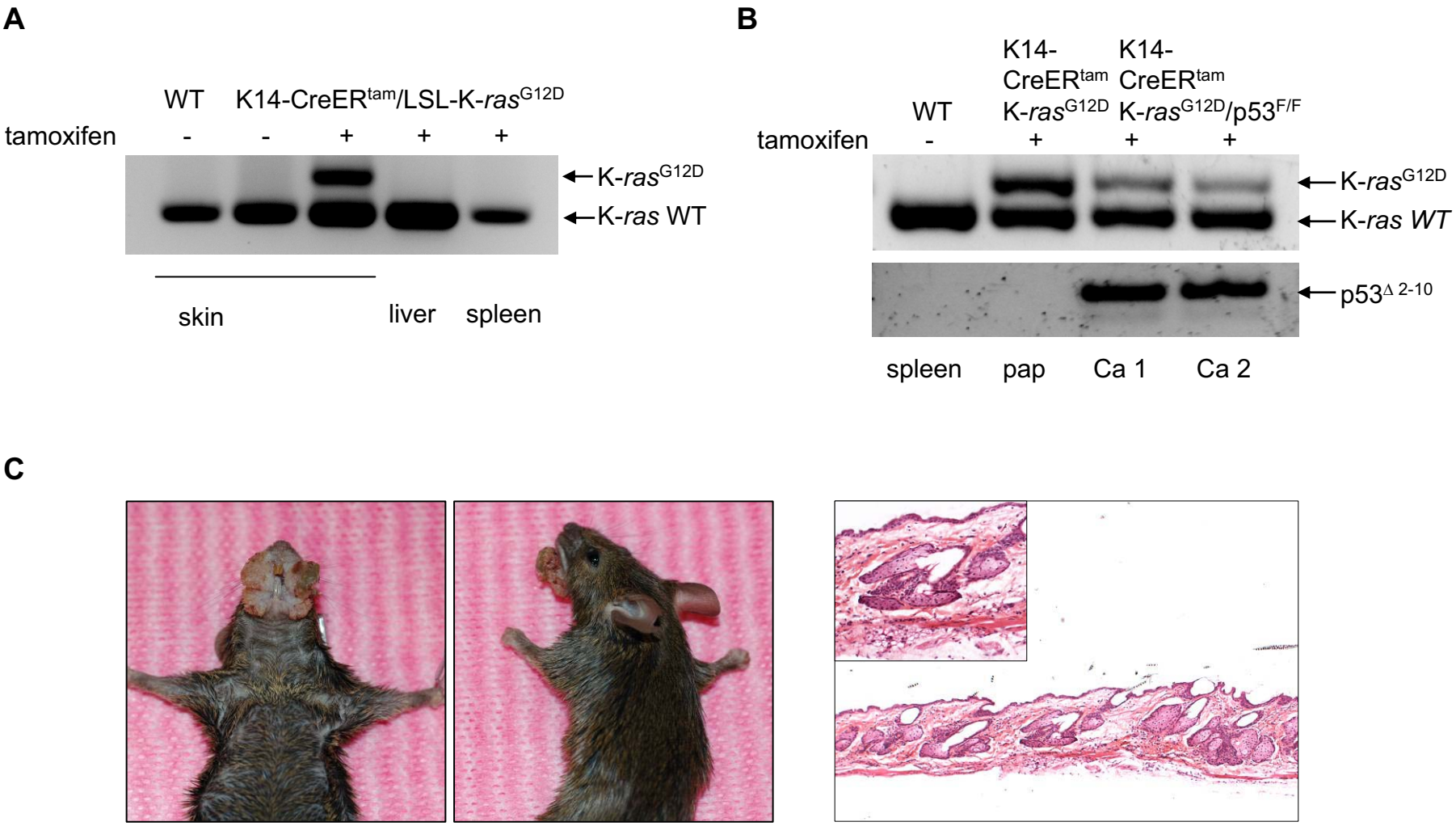
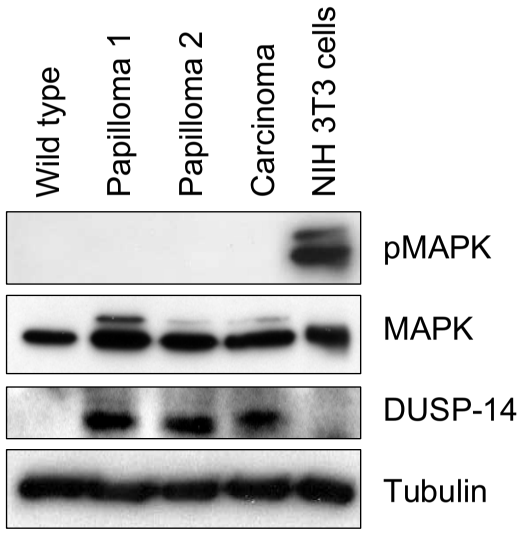
(A) The excision of the stop cassette after Cre activation by tamoxifen treatment in the skin of K14-CreER^{tam}/LSL-K-*ras*^{G12D} mice was analyzed by PCR. Wild type skin and the skin of K14-CreER^{tam}/LSL-K-*ras*$^{G12D/+}$ mice without induction with tamoxifen did not show K-*ras*^{G12D} recombination. Lack of K-*ras*^{G12D} expression in liver and spleen from K14-CreER^{tam}/LSL-K-*ras*$^{G12D/+}$ mice induced with tamoxifen reflect the tissue specificity of K14-Cre-driven genetic recombination. (B) The tongue carcinomas from K14Cre-ER^{tam}/LSL-K-*ras*$^{G12D/+}$/p53$^{flox/flox}$ mice show K-*ras*^{G12D} activation as well as *p53* excision. Excision of the *lox*P-flanked sequences from the floxed *p53* allele in tongue carcinomas was examined by PCR using loxP flanked sequences, and activation of the K-*ras*^{G12D} allele was analyzed as above using DNA purified from carcinomas. DNA purified from spleen of wild type mice was used as negative control, and DNA purified from K-*ras*^{G12D} papillomas was used as positive control. (C) *Left panels*, normal gross appearance of the skin from K14-CreER^{tam}/LSL-K-*ras*$^{G12D/+}$ mice 60 days after treatment with tamoxifen. At this time, most animals have developed oral papillomas. *Right panels*, the picture shows representative non-neoplastic mouse skin in K14-CreER^{tam}/LSL-K-*ras*$^{G12D/+}$ mice treated with tamoxifen, depicting the typical epithelial structures of the epidermis, hair follicles and sebaceous glands. There were no signs of neoplastic or preneoplastic disease or hyperproliferation in the skin. At high magnification, the epidermis is composed of two or three layers of normal-looking squamous epithelium. The slightly dilated hair shaft is surrounded by fully differentiated sebaceous glands.

Supplementary Figure 2

Lack of pMAPK activation and upregulation of DUSP-14 in K-*ras*^{G12D} induced lesions.

Samples of total cell lysates from papillomas and carcinomas from of K14-CreER^{tam}/LSL-K-*ras*$^{G12D/+}$ and K14-CreER^{tam}/LSL-K-*ras*^{G12D}/+/*p53*$^{flox/flox}$ mice respectively were used. Oral mucosa from wild type mice was used as normal control and NIH-3T3 cells stimulated with PDGF during 5 minutes were used as positive control for pMAPK expression. Both papillomas and carcinomas do not show increased levels of pMAPK, but they show upregulation of DUSP-14, a MAPK phosphatase.

Supplementary Figure 1



Supplementary Figure 2