Supporting Information

Arwert et al. 10.1073/pnas.1007404107

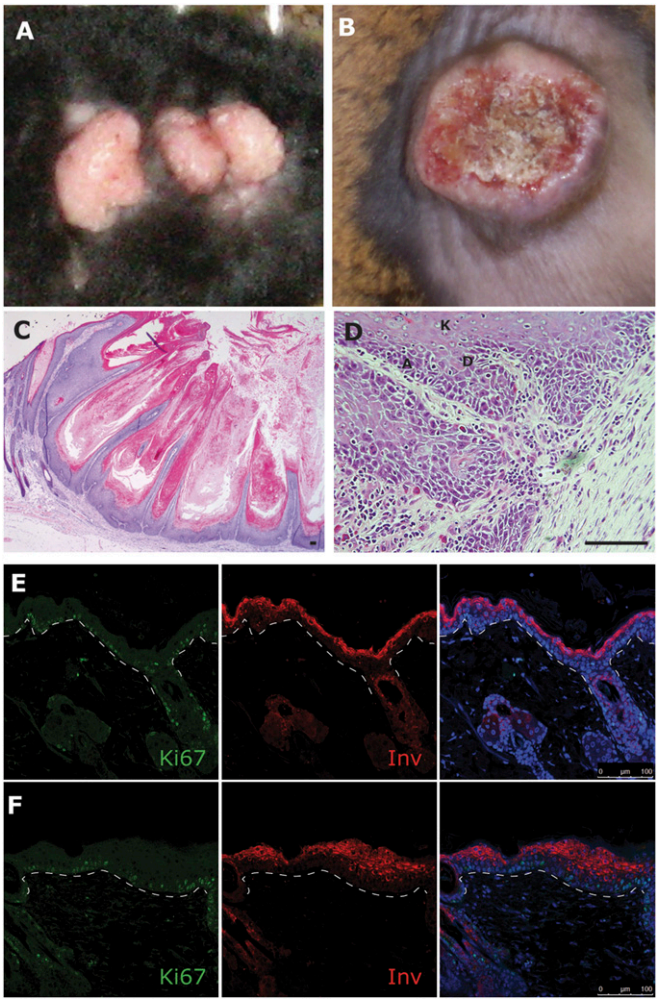

Fig. S1. Keratoacanthomas and wound healing in InvEE mice. (*A* and *B*) Macroscopic appearance of (*A*) papillomas and (*B*) keratoacanthoma. Note that, whereas papillomas have a cauliflower-like appearance, the center of the keratoacanthoma has collapsed to form a crater. (*C* and *D*) H&E sections of keratoacanthomas. (*D*) Disorganization of the epithelial-stromal interface, atypical keratinocytes (A), koilocytosis (K), and dyskeratosis (D). (*E* and *F*). Unwounded (*E*) and hyperproliferative, wounded (*F*) InvEE skin labeled with Ki67 (green) and involucrin (red). DAPI nuclear counterstain is shown in blue. Dotted line indicates epidermal-dermal boundary. [Scale bars: 200 μm (*C*); 100 μm (*D*–*F*).]

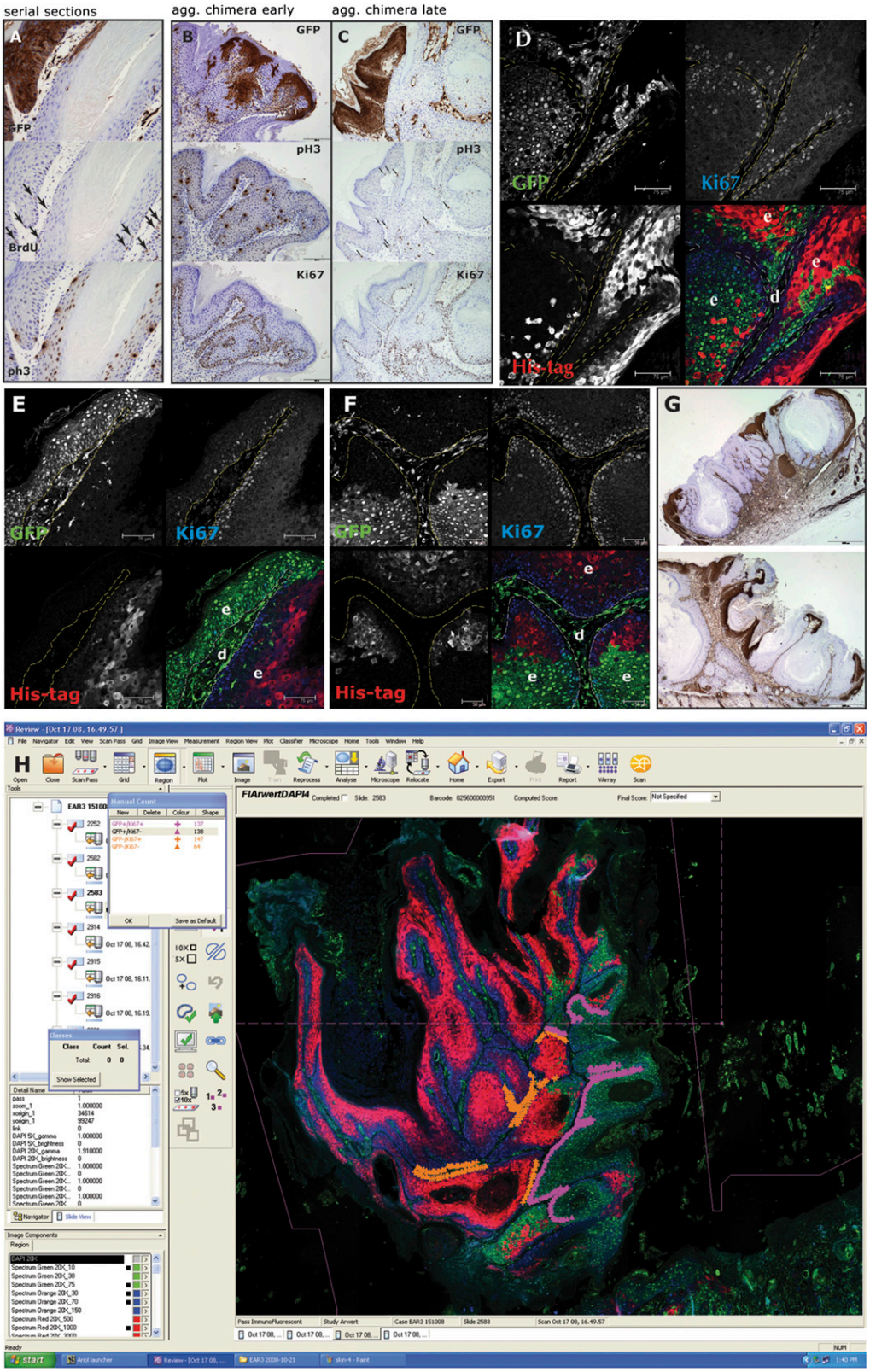

Fig. S2. Proliferation in GFP/InvEE chimeric epidermis and papillomas. (*A–C*) Serial sections of papillomas stained for GFP and the proliferation markers shown. pH3: phospho-histone H3. Arrows indicate positively labeled basal layer cells. Note absence of suprabasal proliferation. Papillomas were compared at early (d = 15 in *B*) and late (d = 60 in *C*) time points after wounding. GFP contribution and tumor histology were indistinguishable at the two time points. (*D–F*) Sections of chimeric papillomas labeled with antibodies to GFP (green), Ki67 (blue), and MEK1 transgene His tag (red); in *D–F Bottom Right*, panels show merge of other panels. e: epithelium; d: dermal stroma. (*G*) Additional examples of GFP/InvEE papillomas stained with GFP antibody. (*H*) Screen shot of chimeric papilloma stained as in *D–F* and scanned using the Ariol review program showing how Ki67 labeling was quantitated (Fig. 2*G*). Pink areas denote basal layer of GFP-positive zones; orange areas denote basal layer underlying MEK1-positive suprabasal cells.

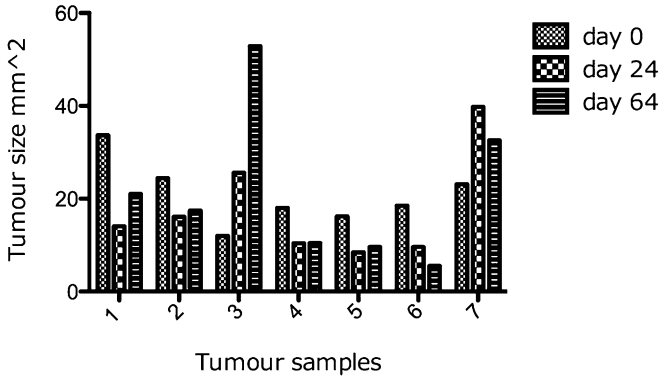

Fig. S3. Treatment of existing tumors with dexamethasone. Seven InvEE mice, each with one spontaneous papilloma (numbered 1–7), received daily s.c. injections of dexamethasone for 30 d and were left untreated for another 34 d. Tumor size was recorded before treatment (day 0) and on days 24 and 64.

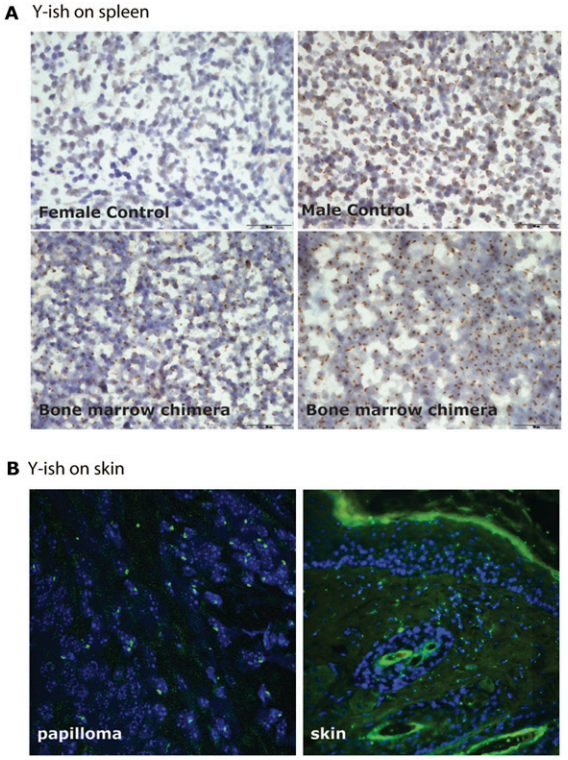

Fig. S4. Confirmation of bone marrow chimerism. (*A*) Y-chromosome in situ hybridization on spleens of female (negative control) and male (positive control) mice and two female spleens collected more than 14 wk after transplantation with male bone marrow. Brown: Y-chromosome labeling; blue: hematoxylin counter-stain. (*B*) Fluorescent Y-chromosome (green) in situ hybridization on papilloma and skin from female mice after transplantation with male bone marrow. DAPI nuclear counterstain is shown in blue. (Scale bars: 50 μm.)

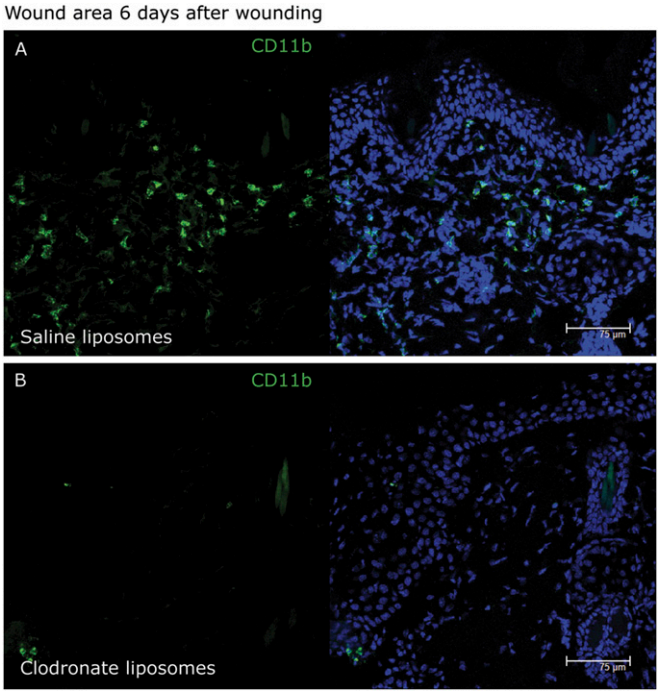

Fig. S5. Macrophage depletion by clodronate liposomes. Immunofluorescence detection of CD11b-positive cells (green) in InvEE skin 6 d after wounding. Nuclei were counterstained with DAPI (blue). Mice were injected with saline (*A*) or clodronate liposomes (*B*). (Scale bars: 75 μm.)