Supplementary Information:

Figure S1.
Keratinocyte proliferation is required for tissue regeneration. Primary cultures of newborn Nagy-GFP mouse keratinocytes were harvested and irradiated (5000 rads) to induce growth arrest, mixed with primary dermal fibroblasts and implanted onto Nude mice. Grafted skin was analyzed for GFP expression and hair formation. (A) Light images of grafts at 6 weeks post-grafting indicate a lack of hair formation and re-epithelialization of graft bed with host keratinocytes, (B) Fluorescent images of graft surface demonstrating no surface GFP indicating lack of skin regeneration by implanted cells, (C) histological examination of grafted skin confirm re-epithelialization by invading host keratinocytes. Bar= 50 μm.

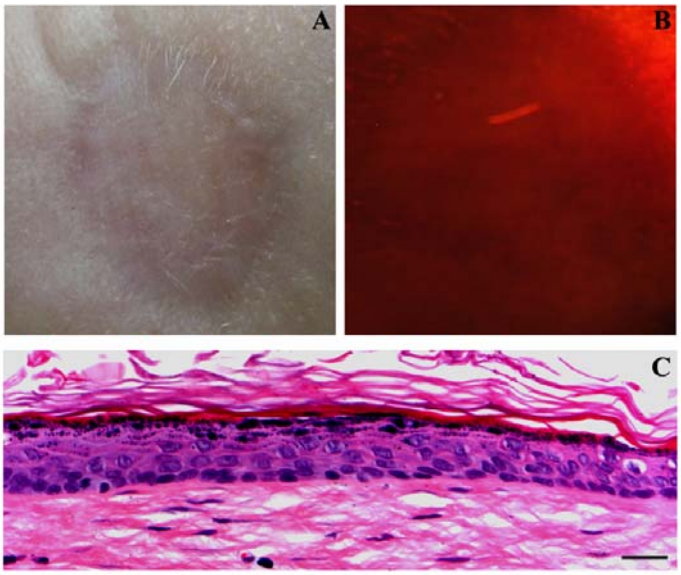

Figure S2.
The size of reconstituted skin is directly correlated with the number of implanted proliferating keratinocytes. Images of skin reconstituted from mixtures of GFP- expressing proliferating keratinocytes and γ-irradiated non-labeled keratinocytes at ratios of 2% (A), 10% (B) and 100% (C) at 6 weeks post-grafting demonstrating the GFP-expressing area of grafts. The graduations on the ruler are in millimeters.

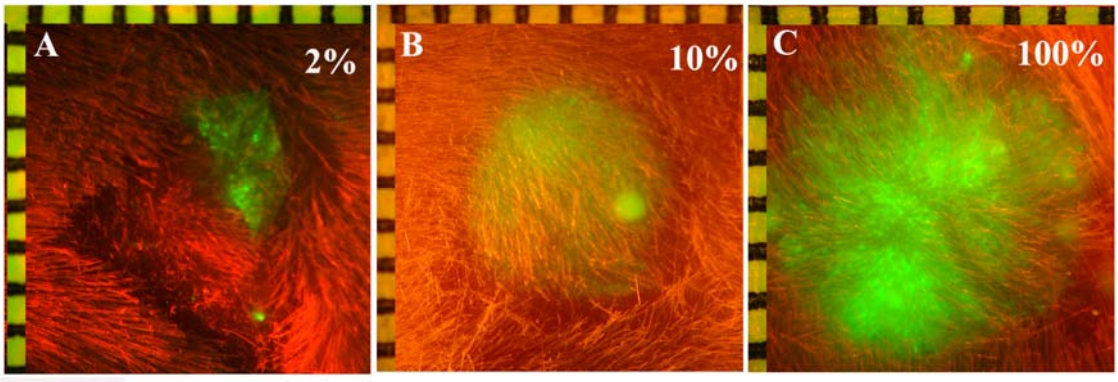

Figure S3.

Tissue regenerative efficiency of differentiated keratinocytes in the presence of proliferating keratinocytes. Non-labeled proliferating keratinocytes and GFP+ differentiated mouse keratinocytes were mixed at ratios indicated in the figure, combined with fibroblasts and grafted onto mice. Light and fluorescent images of representative skin reconstituted from mixtures at the ratio 1:0 (A- C), 3:1 (D-F) and 1:1(G-I) are shown at 6 weeks post-grafting. Analysis of GFP-expressing cells in grafted skin showed a significant contribution of differentiated cells (GFP+) to skin regeneration even in the presence of equal numbers of proliferating keratinocytes. The reconstituted follicles at equal or higher ratios of differentiated keratinocytes were occasionally chimeric and composed of a mixture of GFP+ and non-labeled keratinocytes indicating that, at least in some instances, differentiated and proliferating cells contributed to the formation of a single follicle (F, I and I*). At lower ratios (1 differentiated to 3 proliferating keratinocytes) however, there was very little contribution from differentiated keratinocytes. Tissue sections were counterstained with DAPI for nuclear staining (blue in C, F, I). Bar =100 μm for C, F, I and 20 μm for I*.