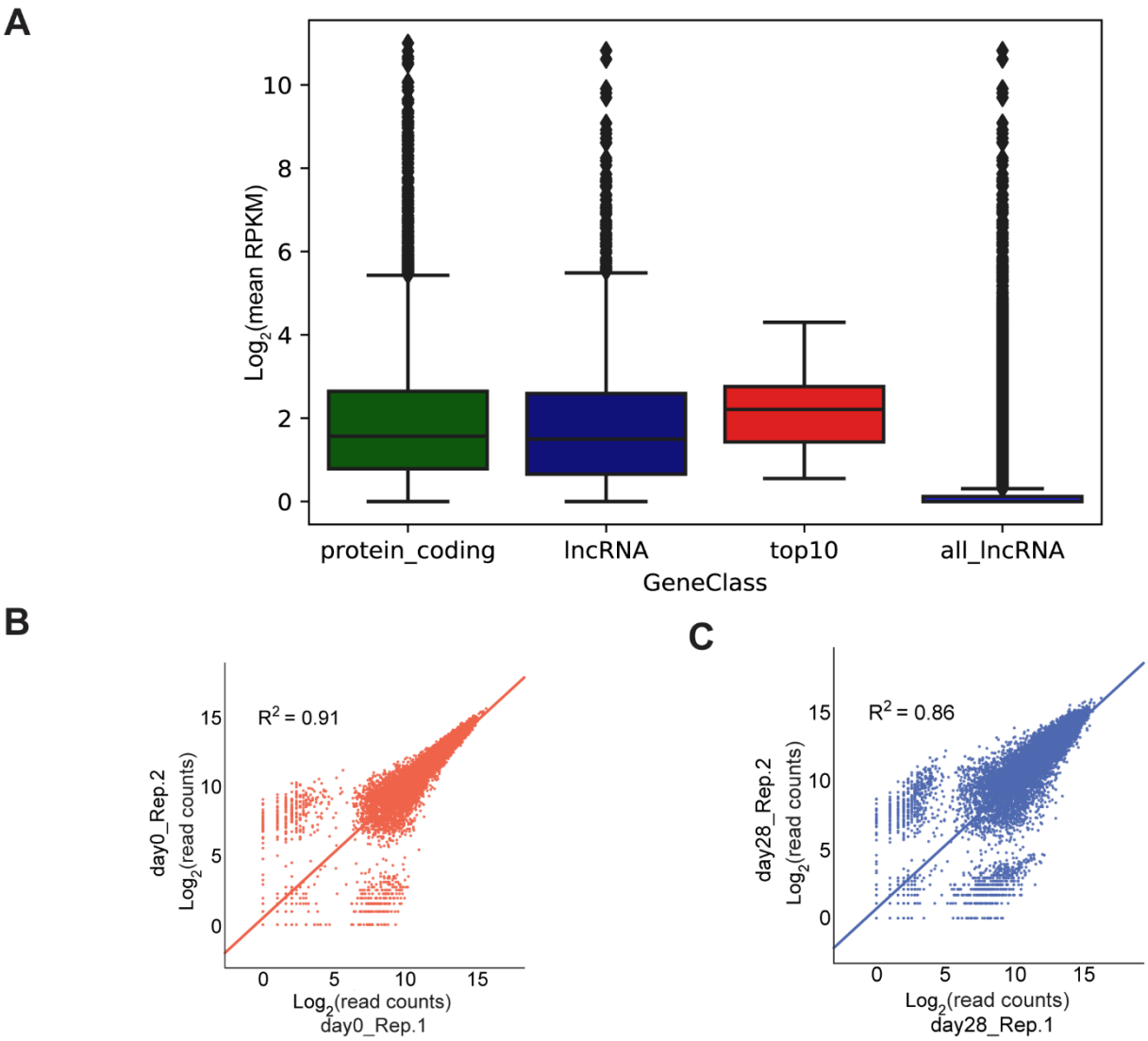
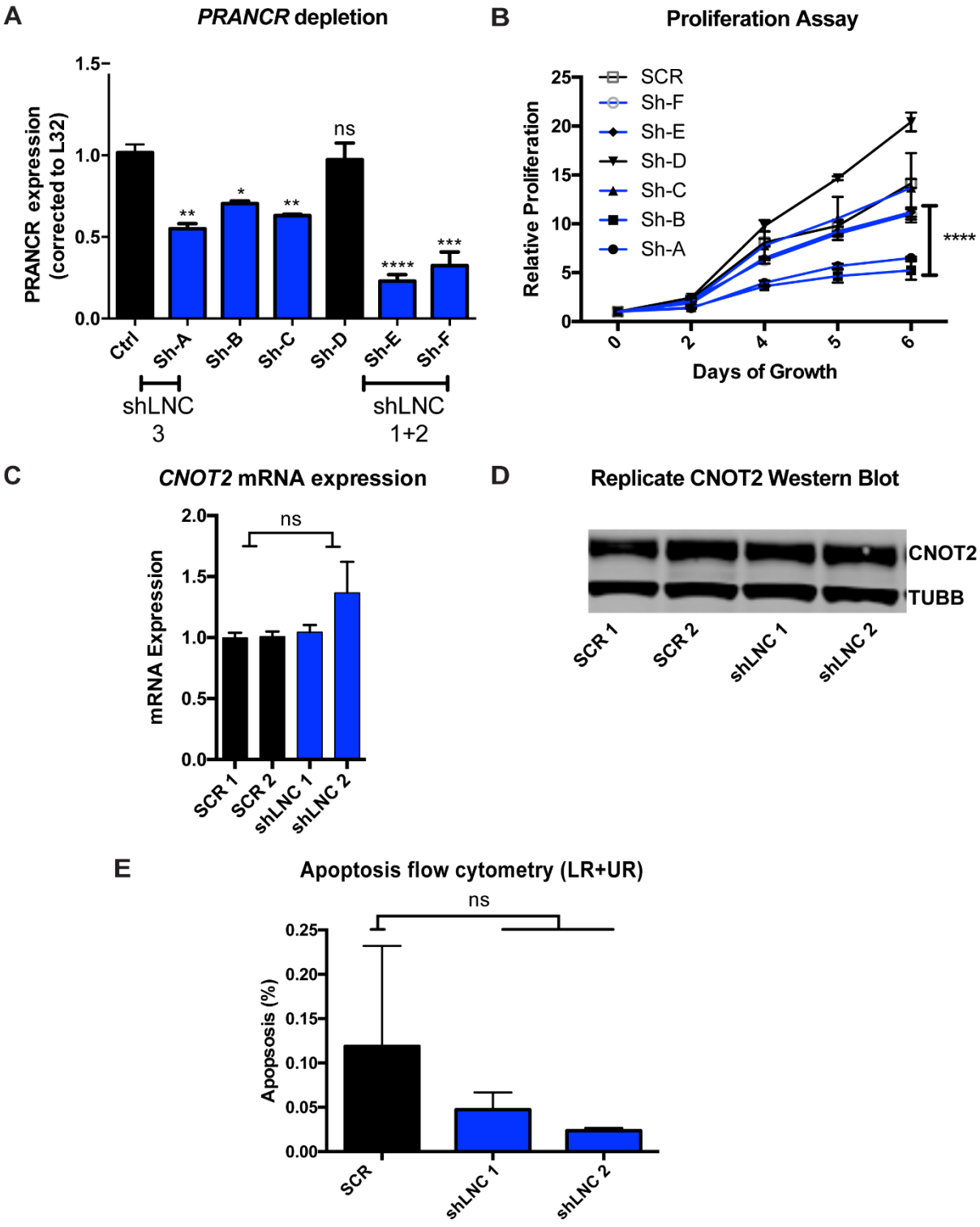
Supplemental Figures

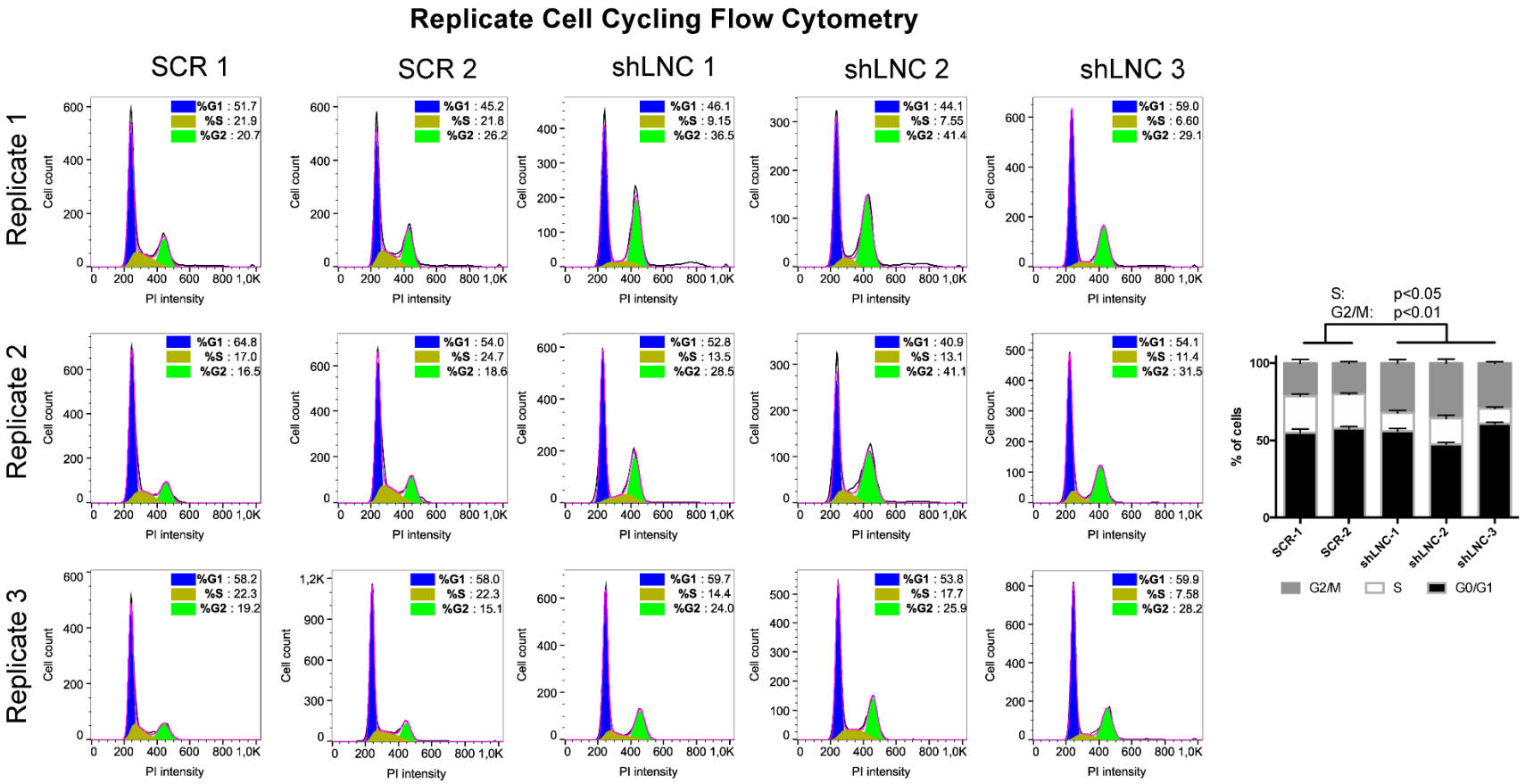


Supplemental Figure S1: The average expression of lncRNAs included in the CRISPRi screen and reproducibility of the screen. A) Box plots of average expression levels of protein-coding genes (6,305 genes; protein_coding), screen-included and all lncRNA genes (2,263; lncRNA and all_lncRNA GeneClass) and the top-10 CRISPRi screen hits (top10; see main Figure 1D-E). Only lncRNA genes with an RPKM > 1 were included. Center lines represent median values; box limits represent the interquartile range; whiskers extend 1.5 times the interquartile range; dots represent outliers. n = 4 (2 basal and 2 suprabasal expression values from 2 independent epidermal biopsies). Scatter plot of normalized read counts of all sgRNA in two replicates at B) day 0 and C) day 28, indicating high technical and biological reproducibility respectively. Each dot represents the abundance of a single sgRNA in two replicate samples.

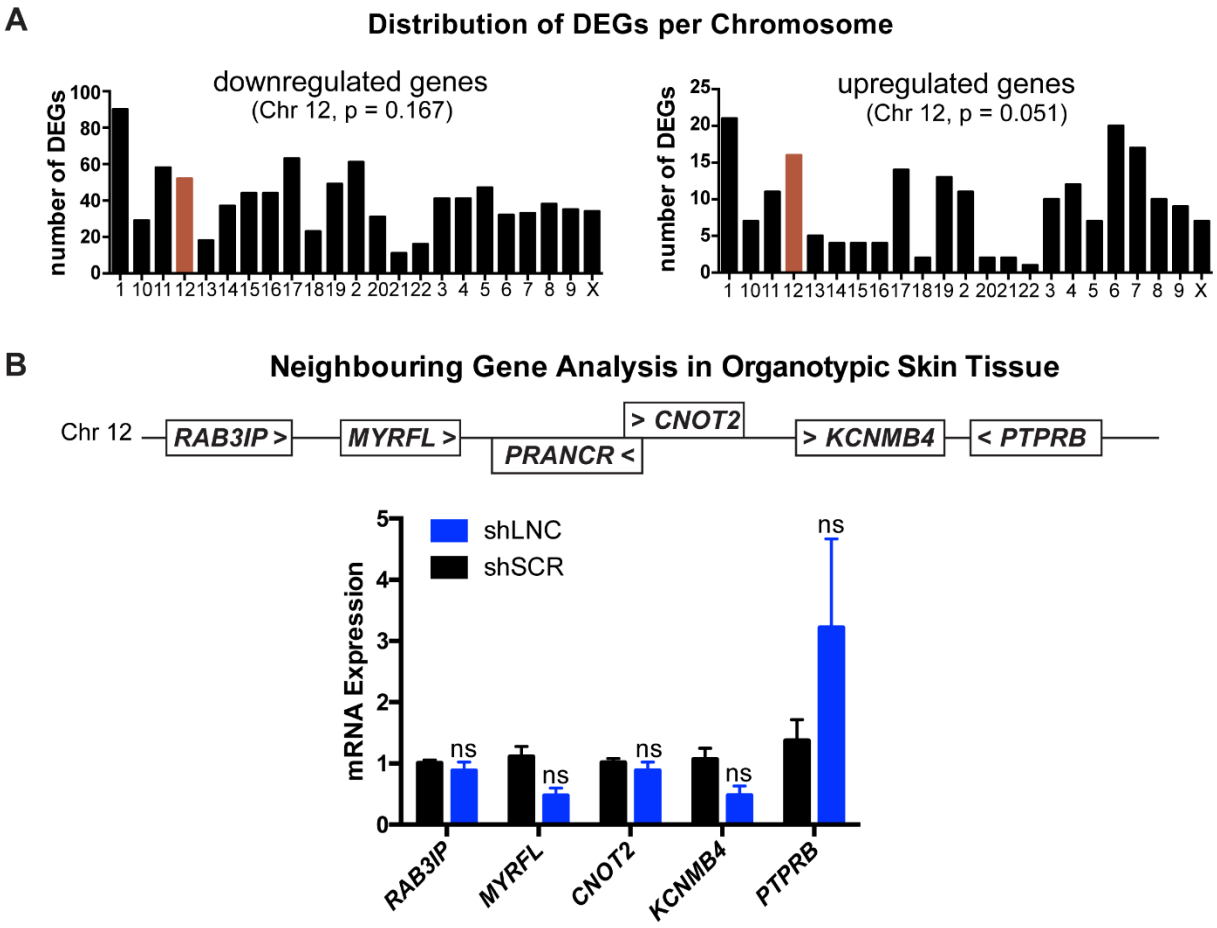


Supplemental Figure S2: Selection of shRNAs targeting *PRANCR*, results of replicate *CNOT2* expression experiments and flow cytometric apoptosis assay. A) Results of RT-qPCR assessing *PRANCR* expression for six independent short hairpin RNAs (shRNAs; sh-A-F), as compared to a scrambled shRNA (Ctrl). The two shRNAs attaining the highest degree of lncRNA depletion (sh-E and sh-F) were used in downstream experiments, and in the main document referred to as shLNC1 and shLNC2. Sh-A (referred to as shLNC3) was used in replicate flow cytometric cell cycle experiments, as displayed in Supplemental Figure S3. B) Proliferation assay of control

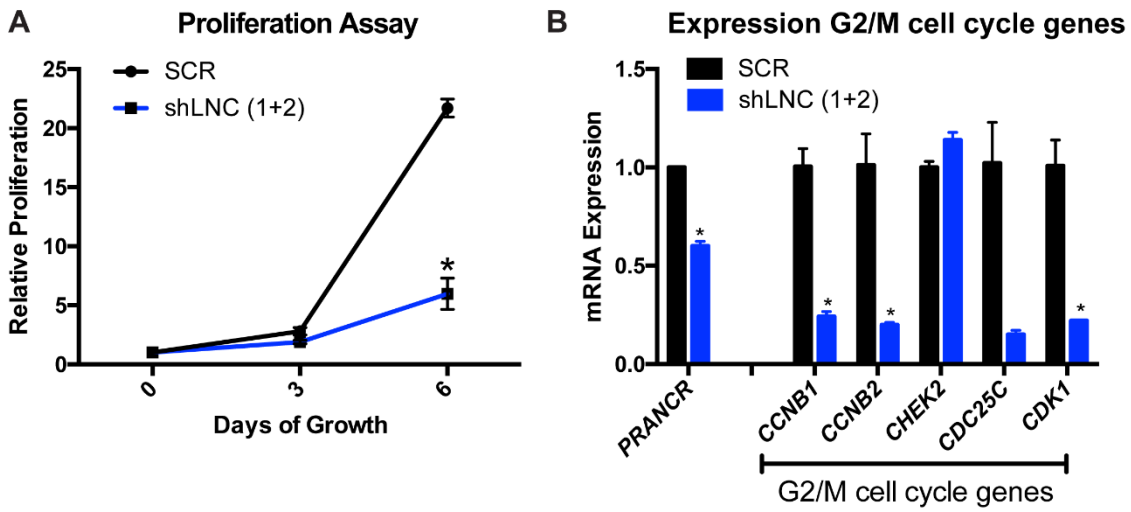
(scrambled shRNA; SCR) vs epidermal progenitors infected with six independent shRNAs (sh-A-F; as indicated in A), quantitated using the fluorescence-based alamarBlue assay. Plotted values represent the relative increase in fluorescence at each time point relative to the starting point (day 0). n = 2, dots represent mean value with SEM. Comparisons performed by 1-way ANOVA. C) Expression of *CNOT2* mRNA using RT-qPCR in control and *PRANCR*-depleted epidermal progenitors. Bars represent mean values with SEM, n = 4, expression levels compared by 1-way ANOVA. D) Western blot analysis of CNOT2 protein levels in whole cell protein lysate of control and *PRANCR*-depleted epidermal progenitor keratinocytes. Image represent a replicate experiment to the one shown in main Figure 1D. TUBB = Beta-Tubulin. E) Flow cytometric analysis of apoptosis, comparing control and *PRANCR*-depleted epidermal progenitor keratinocytes. Values are presented as the percentage of cells in the Lower Right (LR) and Upper Right (UR) of the Scatter Plots (FSC on y-axis, Annexin-V on x-axis), which were considered apoptotic. Bars represent mean values with SEM, n = 2, 10,000 cells per measurement. SCR1/2 = Scrambled short hairpin 1 or 2, shLNC1/2 = short hairpin RNA 1 or 2 targeting *PRANCR*.



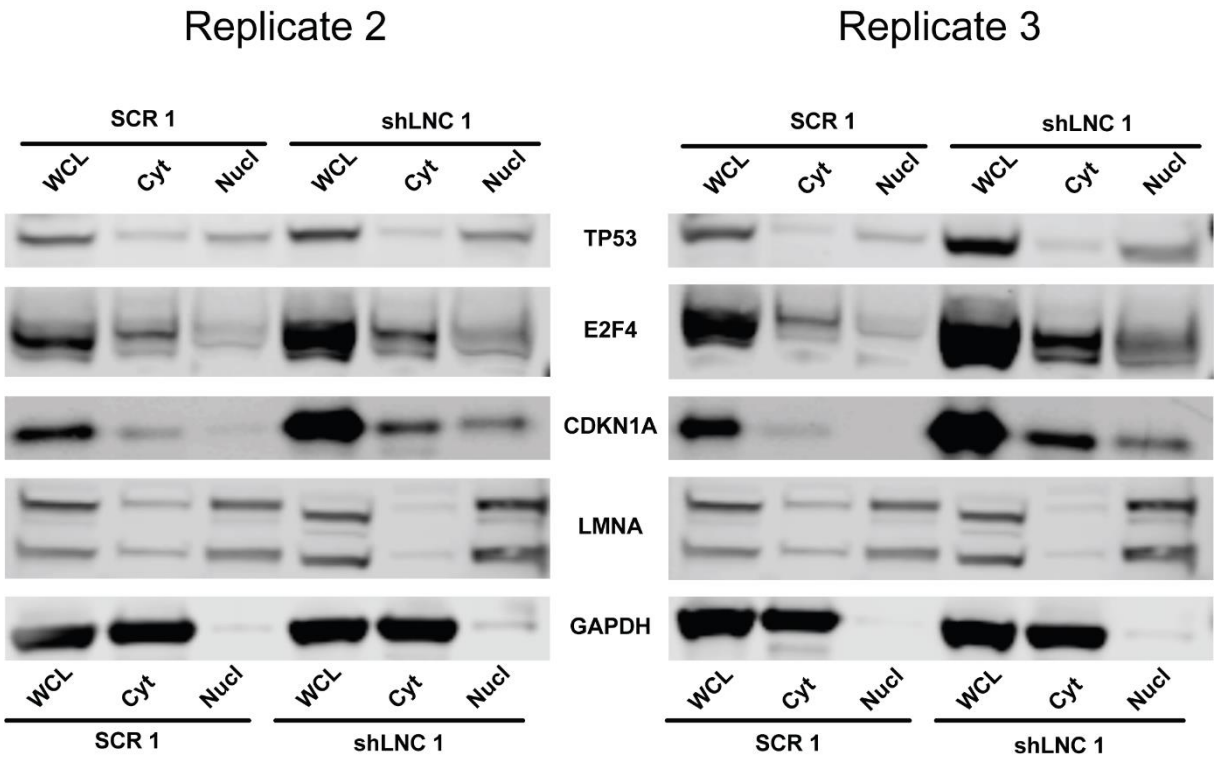
Supplemental Figure S3: Overview of replicate flow cytometric analyses of cell cycle based on propidium iodide DNA staining. Graphs are derived by FlowJo software using the built-in Dean-Jett-Fox univariate model to fit the data. Each graph represents ≥ 10,000 cells. Each replicate represents an independent biological epidermal progenitor keratinocyte line infected with the indicated shRNA. The graphs of biological replicate #1 are also displayed as representative results in Figure 2H. The right panel displays average cell cycle phases based on all replicates, as shown upper right of each graph. Bars represent mean with SEM, n = 3 independent biological keratinocyte lines. Comparisons performed by 1-way ANOVA followed by Dunnett's Multiple Comparisons test. SCR1/2 = Scrambled shRNA 1 or 2, shLNC1/2/3 = shRNA 1, 2 or 3 targeting *PRANCR*.



Supplemental Figure S4: Distribution of differentially expressed genes and expression of *cis* genes in organotypic epidermal tissue. A) Distribution of differentially expressed genes (DEGs) upon *PRANCR* knockdown, classified by their chromosomal location. Hypergeometric mean was calculated to test for potential enrichment of differentially expressed genes *in cis* (Chr. 12; the location of *PRANCR*) after *PRANCR* knockdown. For both downregulated (left) and upregulated (right) genes, the p-values > 0.05 indicate that genes differentially expressed upon *PRANCR* loss were not enriched on Chr. 12. B) Expression levels of five genes adjacent to *PRANCR* in control and *PRANCR*-depleted organotypic epidermis, as measured by RT-qPCR. Schematic shows the location of these genes with respect to *PRANCR* on Chr. 12 (diagram not to scale). Bars represent mean with SEM, n = 7 in both control and *PRANCR* knockdown. Differences were evaluated using Student's *t*-test with multiple hypothesis testing correction, ns = not significant. High variation (SEM) is due to low expression of these genes in keratinocytes (high Cq values). SCR = scrambled short hairpin, shLNC = biological replicates of shRNAs targeting *PRANCR*.



Supplemental Figure S5: *PRANCR* knockdown in primary dermal fibroblasts. A) Proliferation assay of control vs *PRANCR*-depleted fibroblasts; quantitated by the fluorescence-based alamarBlue assay. Plotted values represent the increase in fluorescence at each time point relative to the starting point (day 0). n = 2, dots represent values with SEM. Comparisons at day 6 performed by Student's *t*-test. B) Expression of *PRANCR* and five G2/M cell cycle genes, as measured by qRT-PCR, in control and *PRANCR*-depleted fibroblasts. Bars represent values with SEM. Comparisons performed by Student's *t*-test with multiple hypothesis testing corrections. SCR = Scrambled short hairpin, shLNC = shRNAs 1 or 2 targeting *PRANCR*. * indicates p-values < 0.05.



Supplemental Figure S6: Replicate Western Blot analysis of TP53, E2F4 and CDKN1A in whole cell lysates (WCL), cytoplasmic cell fractions (Cyt) and nuclear cell fractions (Nucl) in control (SCR) and *PRANCR*-depleted (shLNC1) keratinocytes. Shown are two biological replicates in addition to the one shown in Figure 5I. All replicates are summarized in the graph in the lower panel of Figure 5I. Successful fractionation is confirmed by LMNA/C (nuclear abundance) and GADPH (cytoplasmic abundance).