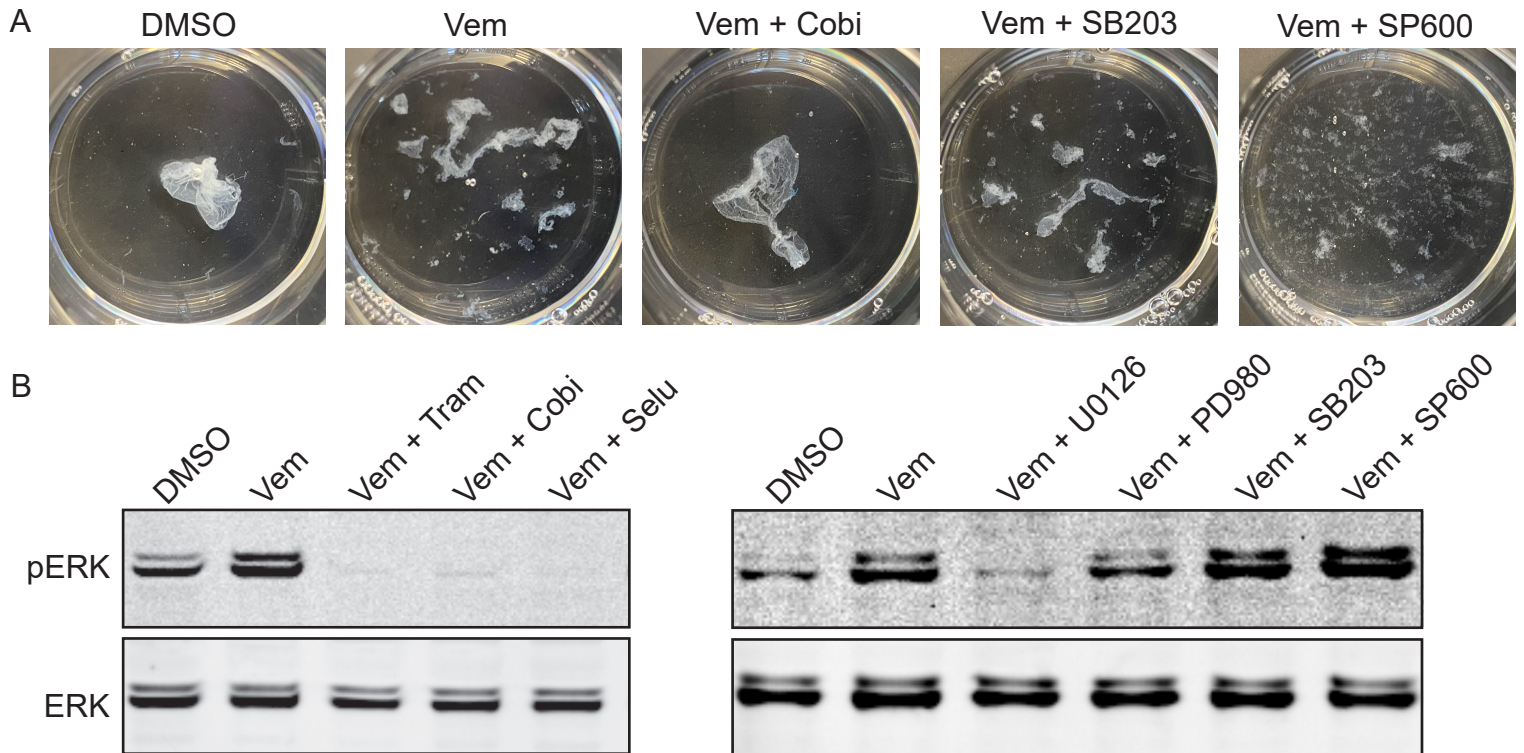
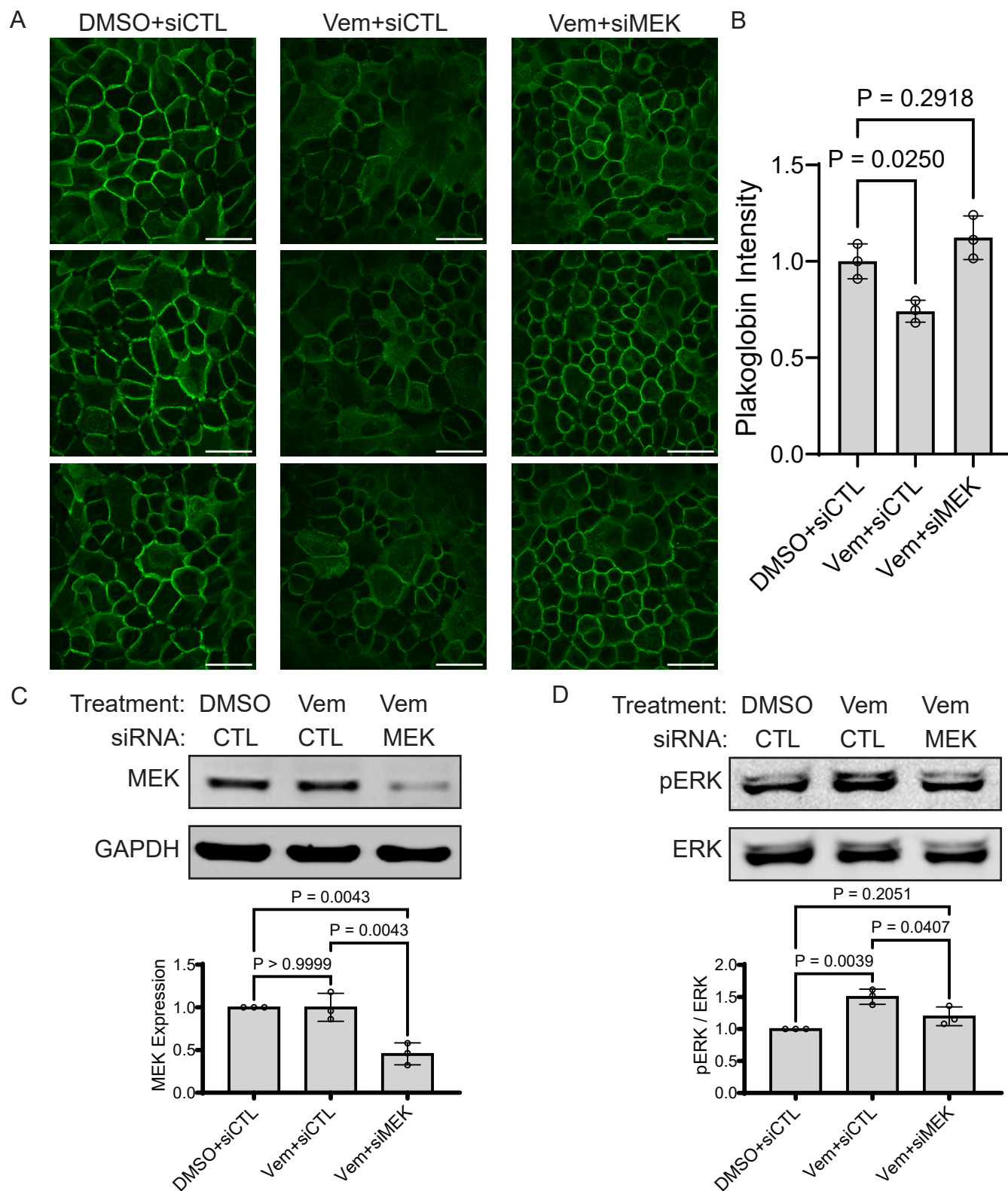


Supplemental Figure S1

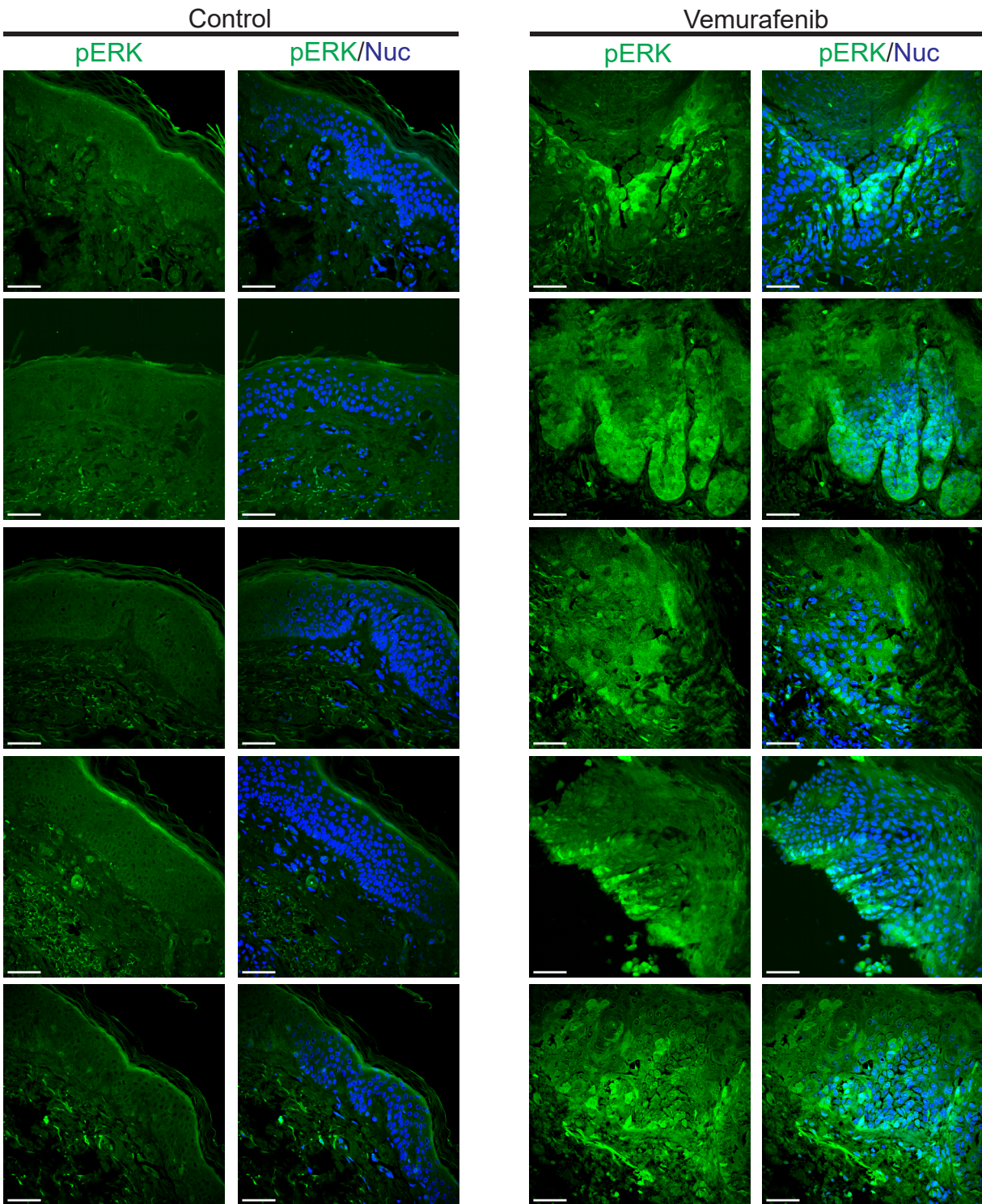


**Supplemental Figure S1: MEK inhibition dampens ERK hyper-activation and restores integrity of vemurafenib-treated keratinocyte sheets.** (A) Images of drug-treated keratinocyte monolayers after a mechanical dissociation assay; representative images of fragmented cell sheets transferred into 6-well cell culture plates are shown. (B) Immunoblot of total and phosphorylated ERK (pERK) in lysates from NHEKs treated for 24 h with vemurafenib (Vem, 10  $\mu$ M) +/- MEK inhibitors trametinib (Tram, 1  $\mu$ M), cobimetinib (Cobi, 1  $\mu$ M), selumetinib (Selu, 1  $\mu$ M), U0126 (10  $\mu$ M), PD98059 (PD980, 20  $\mu$ M), a p38 inhibitor SB203580 (SB203, 10  $\mu$ M), or the JNK inhibitor SP600125 (SP600, 25  $\mu$ M).

Supplemental Figure S2



**Supplemental Figure S2: Silencing of MEK enhances desmosomal protein localization in vemurafenib-treated keratinocytes.** NHEKs were transfected with control siRNA (siCTL) or siRNA against MEK1/2 (siMEK) for 48 hrs then were treated with DMSO or vemurafenib (10  $\mu$ M) for 24 h prior to fixation or lysis. (A) Confocal immunofluorescence images of plakoglobin; scale bar = 50  $\mu$ m. (B) Bar graph displays the mean  $\pm$  SD of normalized plakoglobin intensity (mean of DMSO+siCTL set to 1) from  $\geq 10$  images across each treatment group with data points plotted for N=3 experimental replicates. (C) Immunoblot of MEK (GAPDH loading control); bar graph displays the mean  $\pm$  SD of the ratio of MEK/GAPDH band intensities (DMSO+siCTL set to 1) with data points plotted for N=3 experimental replicates. (D) Immunoblot of pERK and ERK; bar graph displays the mean  $\pm$  SD of the ratio of pERK/ERK band intensities (DMSO+siCTL set to 1) with data points plotted for N=3 experimental replicates. All P-values are from one-way ANOVA using the Bonferroni adjustment for multiple comparisons.



**Supplemental Figure S3: Additional biopsies of B-RAF inhibitor-induced Grover disease display epidermal hyperactivation of ERK.** Immunostaining of pERK and Hoechst to stain nuclei (Nuc) in tissue cross-sections from patient biopsies; images shown are from 5 control biopsies and from 5 patients with vemurafenib-induced Grover disease; scale bar = 50  $\mu$ m.