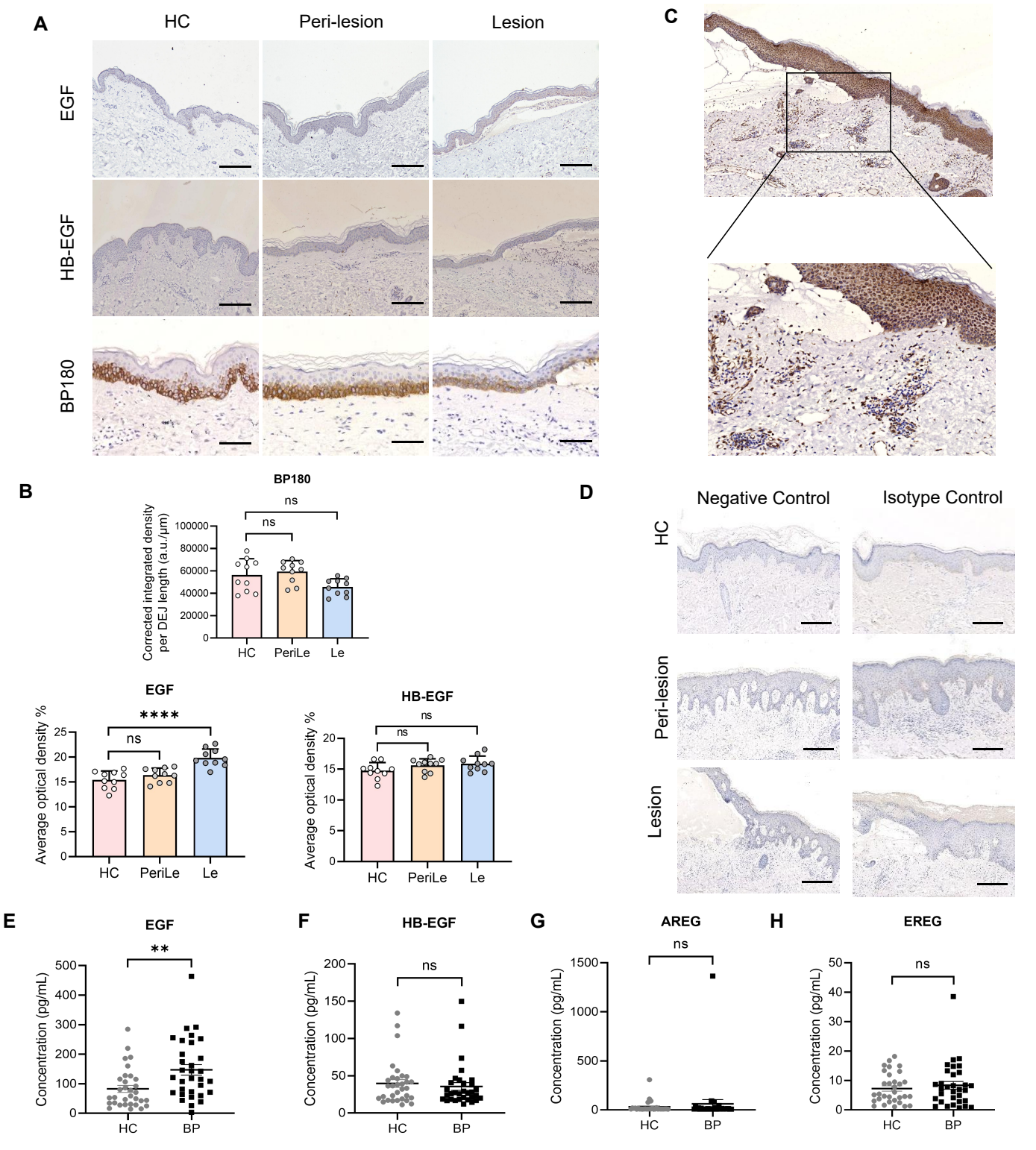

Figure S1. Expression of EGF family ligands in BP lesions. (**A**) Immunohistochemistry analysis of EGF, HB-EGF, and BP180 in skin biopsies from healthy controls (HC) and BP patients (peri-lesion and lesion). Scale bar = 100 μm. (**B**) Quantification of corrected integrated optical density for BP180 per DEJ length, and average optical density (%) for EGF and HB-EGF. (**C**) Representative high-magnification image of TGF-α in BP lesional skin. (**D**) Negative and isotype control staining in HC and BP tissues. (**E–H**) ELISA quantification of serum levels of EGF, HB-EGF, AREG, and EREG in HC and BP patients. Data are presented as mean ± SEM. $^{**}P < 0.01$, $^{****}P < 0.0001$.

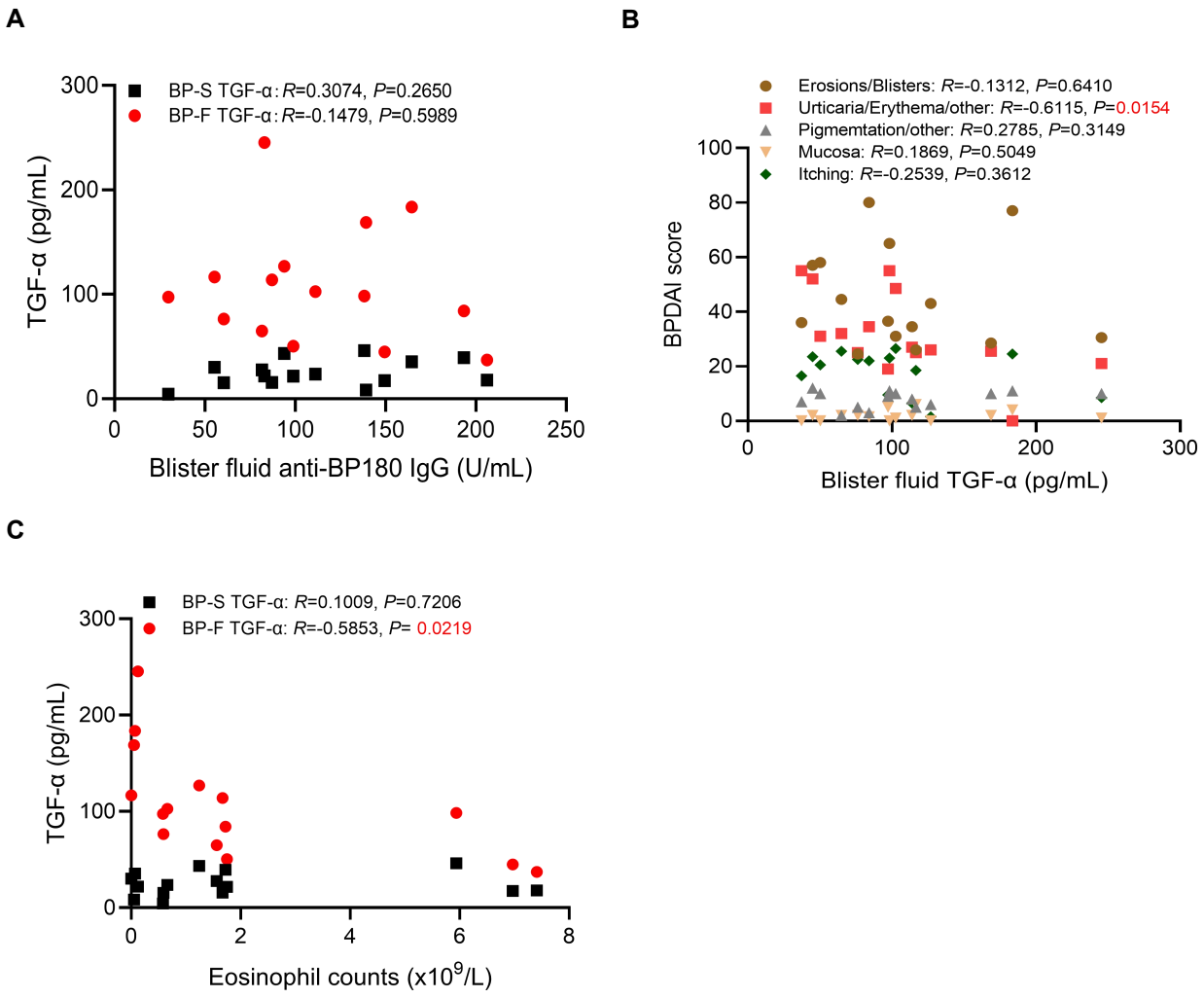

Figure S2. Correlation of TGF-α with BP clinical features. (**A**) Correlation between blister fluid anti-BP180 IgG levels and TGF-α levels in serum (BP-S) and blister fluid (BP-F). (**B**) Correlation of blister fluid TGF-α levels with BPDAI subscores (erosions/blisters, urticaria/erythema, pigmentation, mucosa, and itching). (**C**) Correlation between TGF-α levels and peripheral blood eosinophil counts. Pearson correlation coefficients (*R*) and *P*-values are indicated. Each dot represents one patient.

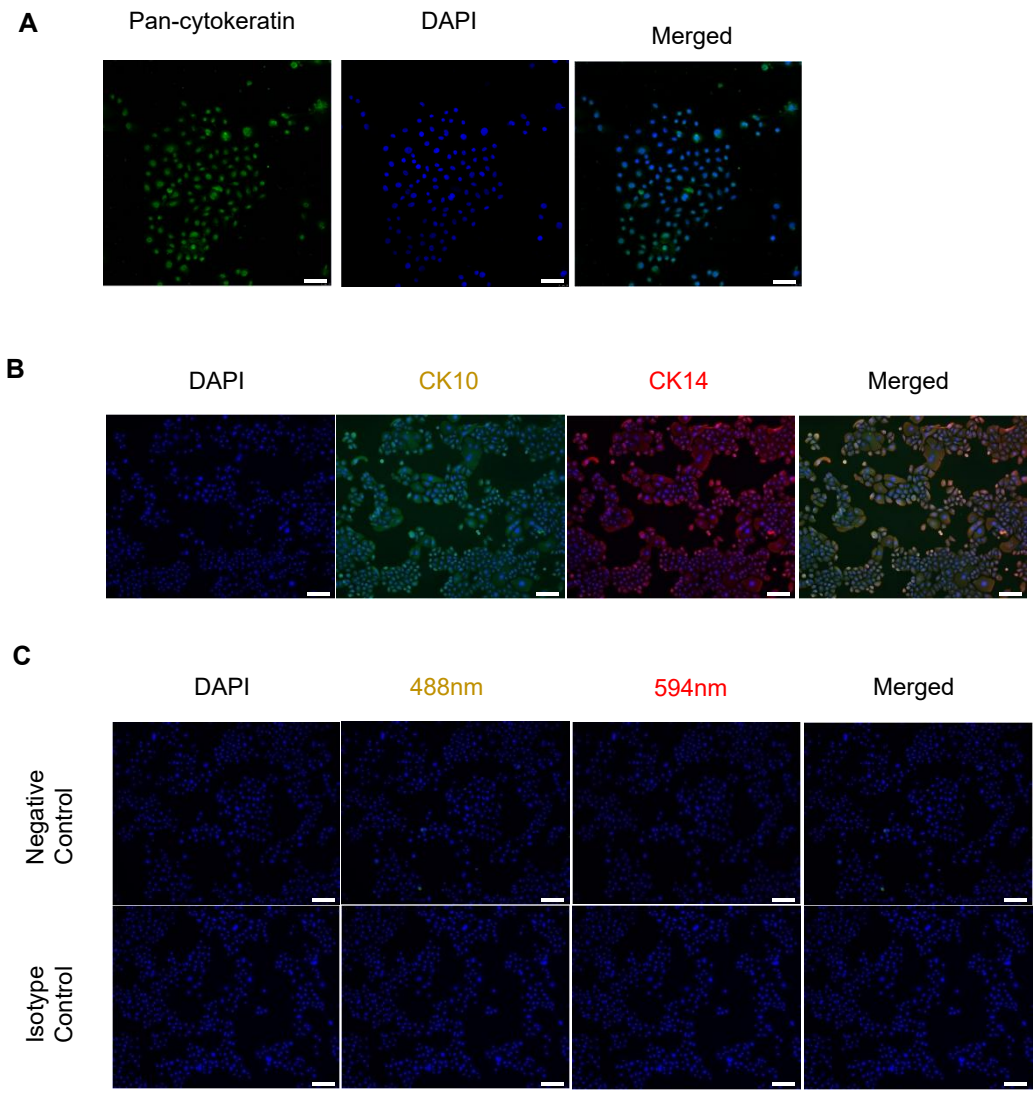

Figure S3. Characterization of cultured keratinocytes. (**A**) Immunofluorescence staining for pan-cytokeratin in cultured keratinocytes. (**B**) Co-staining of keratinocyte markers CK10 and CK14 with DAPI. (**C**) Negative and isotype control staining for keratinocyte immunofluorescence imaging. Scale bars = 100 μm.

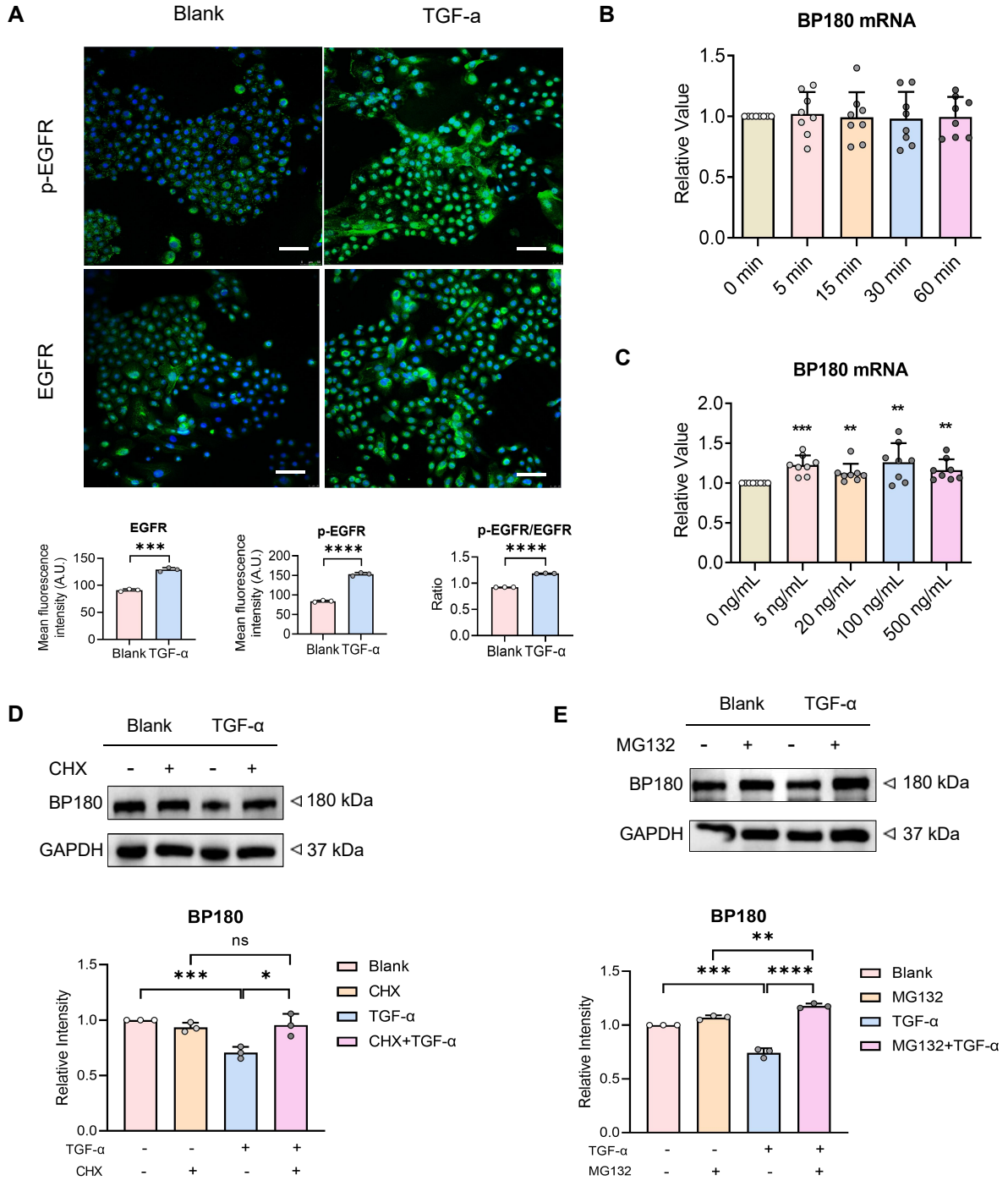

Figure S4 Effects of TGF-α on EGFR signaling and BP180 stability in keratinocytes. (A) Immunofluorescence staining of p-EGFR and EGFR in keratinocytes treated with TGF-α (100 ng/mL, 1 h). Quantification of fluorescence intensity and p-EGFR/EGFR ratio is shown. (**B**) BP180 mRNA levels in keratinocytes treated with 100 ng/mL TGF-α over various time periods (0, 5, 15, 30, 60 min). (**C**) BP180 mRNA levels in keratinocytes treated with escalating concentrations of TGF-α (0, 5, 20, 100, 500 ng/mL) for 1 hour. (**D**) Western blot analysis of BP180 protein in keratinocytes treated with 100 ng/mL TGF-α for 1 hour, with or without cycloheximide (CHX, 10 μg/mL, 1h). (**E**) Western blot analysis of BP180 protein in keratinocytes treated with 100 ng/mL TGF-α for 1 hour, with or without MG132 (10 μM, 1h). Data in all panels represent three independent experiments. Representative images are shown, scale bar = 100 μm. Data are presented as the mean ± SEM. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.

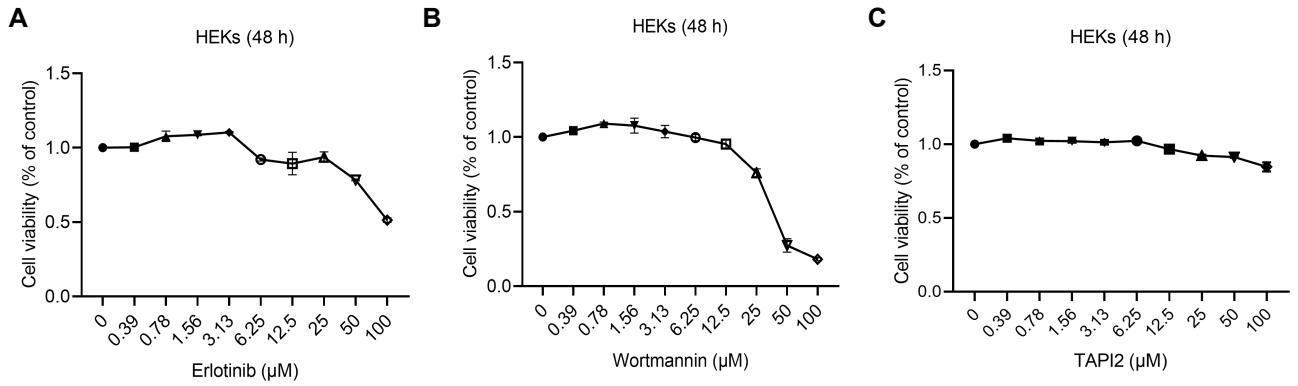

Figure S5 Cytotoxicity of Erlotinib, Wortmannin, and TAPI2 in keratinocytes. Human epidermal keratinocytes (HEKs) were exposed to escalating concentrations of each inhibitor for a duration of 48 hours. Cell viability was assessed using the MTT assay across varying concentrations of (**A**) Erlotinib, (**B**) Wortmannin, and (**C**) TAPI2. Error bars denote the mean ± SEM from a minimum of three independent experiments.

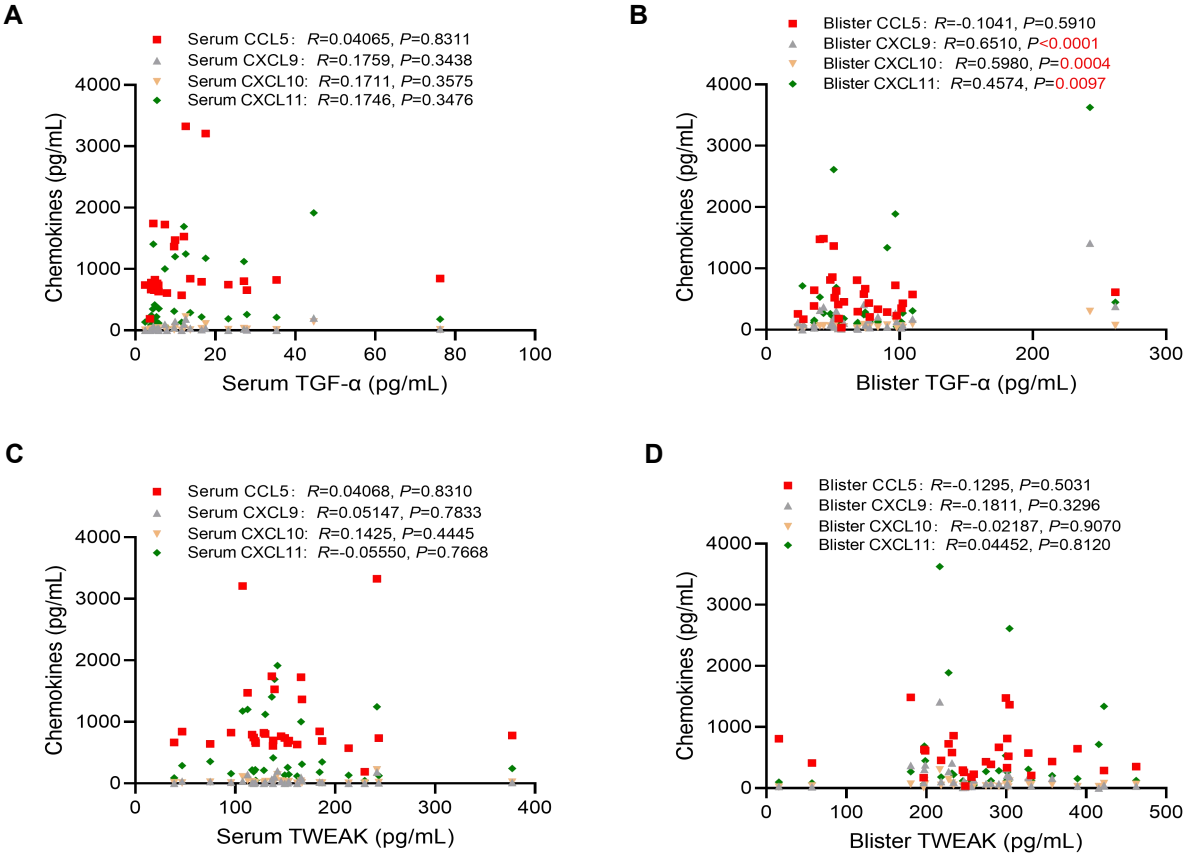

Figure S6 Correlation of TGF-α/TWEAK with chemokine levels in BP patients. (**A–B**) Correlation analysis of serum (**A**) and blister fluid (**B**) TGF-α levels with chemokines CCL5, CXCL9, CXCL10, and CXCL11. (**C–D**) Correlation analysis of serum (**C**) and blister fluid (**D**) TWEAK levels with the same chemokines. Pearson correlation coefficients (*R*) and *P*-values are indicated. Each dot represents one patient.

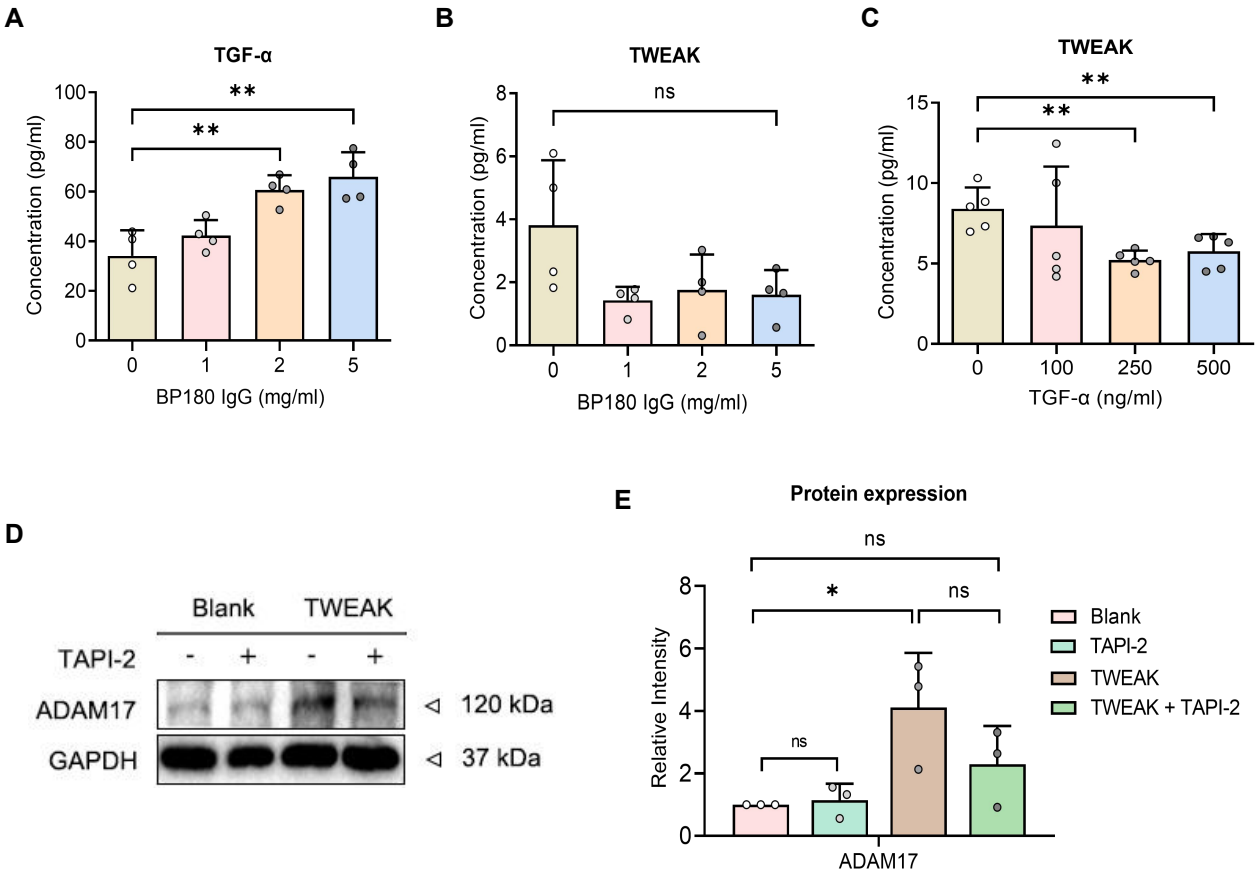

Figure S7 Crosstalk among BP180 IgG, TGF-α, TWEAK, and ADAM17 in keratinocytes. (**A–C**) ELISA analysis of TGF-α and TWEAK concentrations in the supernatants of keratinocytes stimulated for 48 hours. Keratinocytes were treated with purified human BP180 IgG (0, 1, 2, 5 mg/mL) (**A, B**) or TGF-α (0, 100, 250, 500 ng/mL) (**C**). **(D-E)** Western blotting analysis depicting ADAM17 expression in keratinocytes treated with blank control, TAPI-2 (10 μM), TWEAK (100 ng/mL), or their combination for 48 hours. Representative blots and quantification of relative intensity are shown. Data are presented as the mean ± SEM. *$P <$ 0.05, **$P < 0.01$.