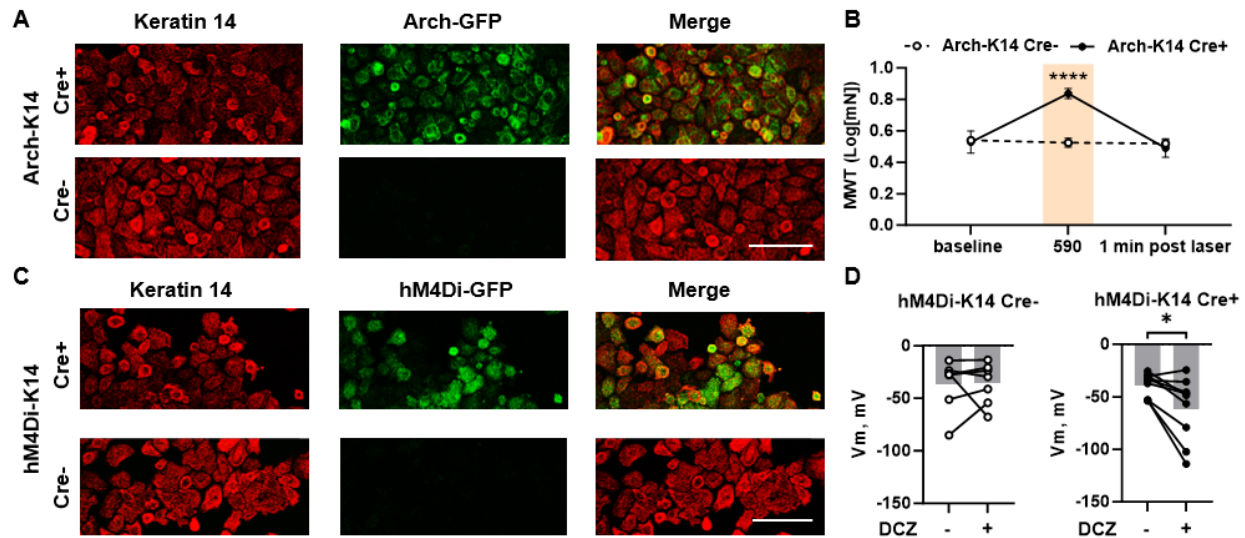
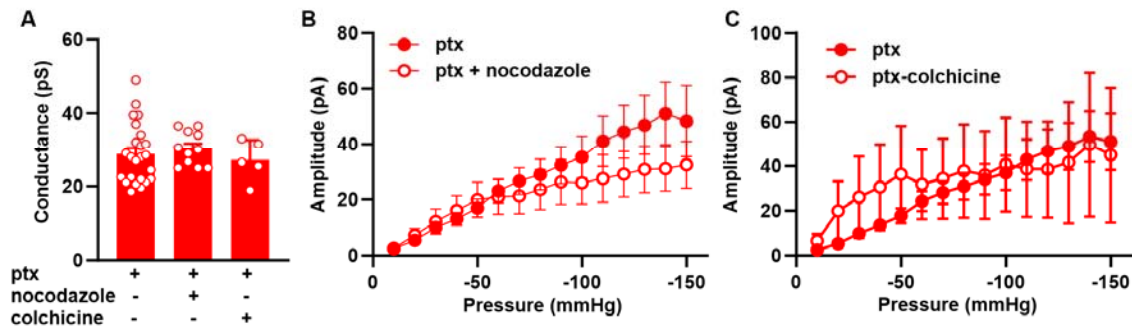


## SUPPLEMENTAL MATERIALS



**Supplementary Fig. 1. Validation of optogenetic and chemogenetic mouse lines.** (A) Cultured mouse keratinocytes from Arch-K14 Cre<sup>-</sup> and Arch-K14 Cre<sup>+</sup> animals. Immunoreactivity to keratin 14 is shown in red, while immunoreactivity for GFP is shown in green. Overlay data shows that the Arch-K14 Cre<sup>-</sup> animal has no GFP expression in K14-expressing keratinocytes. (B) Withdrawal thresholds of naïve Arch mice return to baseline levels 1 min after 590 light is removed; n = 4-5 animals. (C) Cultured mouse keratinocytes from hM4Di-K14 Cre<sup>-</sup> and hM4Di-K14 Cre<sup>+</sup> animals. Immunoreactivity to keratin 14 is shown in red, while immunoreactivity for GFP is shown in green. Overlay data shows that the Arch-K14 Cre<sup>-</sup> animal has no GFP expression in K14-expressing keratinocytes. (D) Changes of hM4Di-K14 Cre<sup>-</sup> and hM4Di-K14 Cre<sup>+</sup> keratinocytes' membrane potential upon 10 min treatment with deschloroclozapine (DCZ, 0.5  $\mu$ M). Dots represent individual cells; n = 3 animals. Statistical analysis for (C) was performed using 2way ANOVA with Tukey's multiple comparisons tests; for (D) using paired Student's *t* test. Error bars,  $\pm$  SEM. \*P < 0.05, \*\*P < 0.01.



**Supplementary Fig. 2. Nocodazole and colchicine do not reverse the paclitaxel-induced sensitization of Piezo1 currents.** (A) Summary data of the effect of pretreatment of Piezo1 expressing HEK-P1KO cells with paclitaxel, paclitaxel + nocodazole, and paclitaxel + colchicine on Piezo1 conductance. Current-pressure relationship of stretch-activated currents recorded at a  $V_{\text{hold}} = -80$  mV from paclitaxel (n=39), paclitaxel + nocodazole (B, n=21), and paclitaxel + colchicine (C, n=6) treated HEK-P1KO cells expressing Piezo1. Error bars,  $\pm$  SEM.