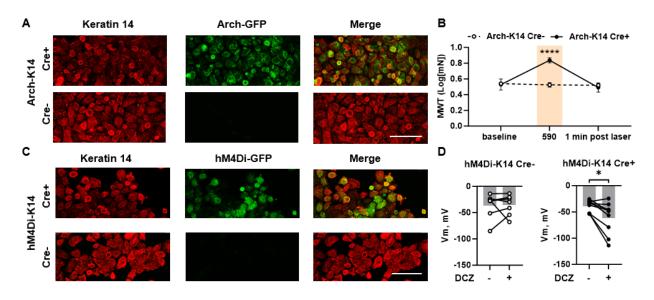
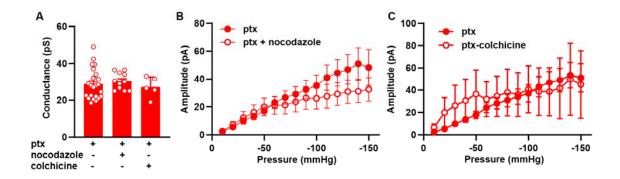
## SUPPLEMENTAL MATERIALS



Supplementary Fig. 1. Validation of optogenetic and chemogenetic mouse lines. (A) Cultured mouse keratinocytes from Arch-K14 Cre- and Arch-K14 Cre+ 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- 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- and hM4Di-K14 Cre+ 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- animal has no GFP expression in K14-expressing keratinocytes. (D) Changes of hM4Di-K14 Cre- and hM4Di-K14 Cre+ animals has no GFP expression in K14-expressing keratinocytes. (D) Changes of hM4Di-K14 Cre- and hM4Di-K14 Cre+ 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.

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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  $V_{hold} = -80$  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.