



Fig. S3. STAT3 signaling pathway is crucial for histamine- and serotonin-induced intracellular calcium increase in keratinocytes. (a) Images of keratinocytes from control mice (Ctrl) and keratinocyte-specific STAT3-depleted mice (cKO) at pretreatment, after stimulation with histamine and after applying ionophore. Bars indicate 100 μ m. (b-d) Histamine (b) and serotonin (c) were able to induce intracellular calcium increase in keratinocytes from Ctrl mice, but these responses were significantly impaired in keratinocytes from cKO mice. Two-way repeated-measures ANOVA followed by Bonferroni test, $F(1,58) = 7.67$, $p < 0.01$ for histamine; $F(1,58) = 30.0$, $p < 0.01$ for serotonin. (d) Chloroquine could not induce intracellular calcium increase in keratinocytes from Ctrl or cKO mice. $F(1,58) = 0.854$, $p = 0.362$. (e, f) Intracellular calcium increase in keratinocytes from Ctrl mice induced by histamine (e) or serotonin (f) application was significantly attenuated by treatment with STA-21, a STAT3 inhibitor, or GSK205, a selective TRPV4 inhibitor. $*p < 0.05$ versus Ctrl mice. The two-tailed t -test was used for statistical analysis. For d-h, values indicate mean + SEM. Thirty regions (100 μ m diameter) containing at least ten keratinocytes per each were analyzed.