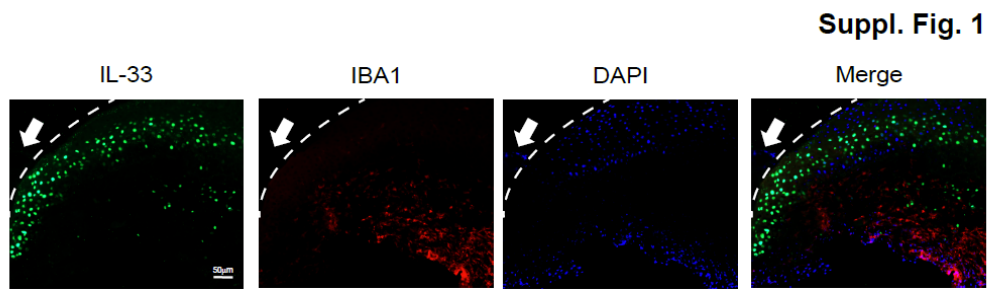


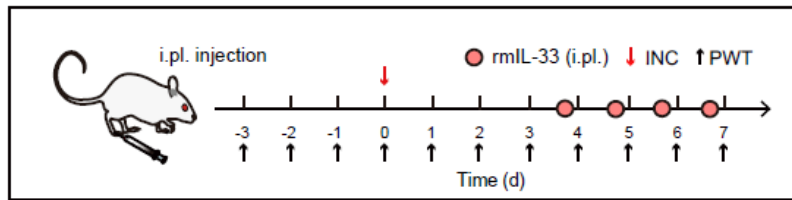
Supplementary figure legends



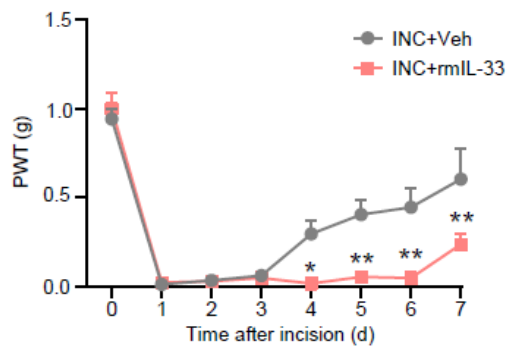
Suppl. Fig. 1 IL-33 was not expressed in skin infiltrating macrophages. Representative immunofluorescence pictures showing IL-33 (in green) and Iba-1 (in red, a macrophage marker) immunostaining in the incised skin of INC pain model mice. DAPI is shown in purple. Scale bar indicates 50 μm . White line denotes stratum corneum of epidermis. White arrows indicate the direction of the incision made.

Suppl. Fig. 2

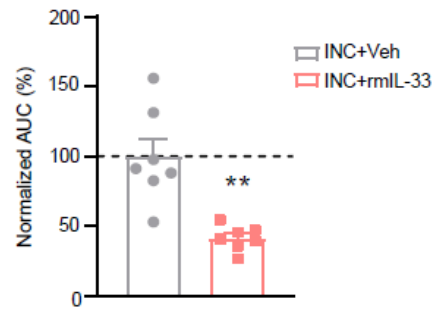
A



B

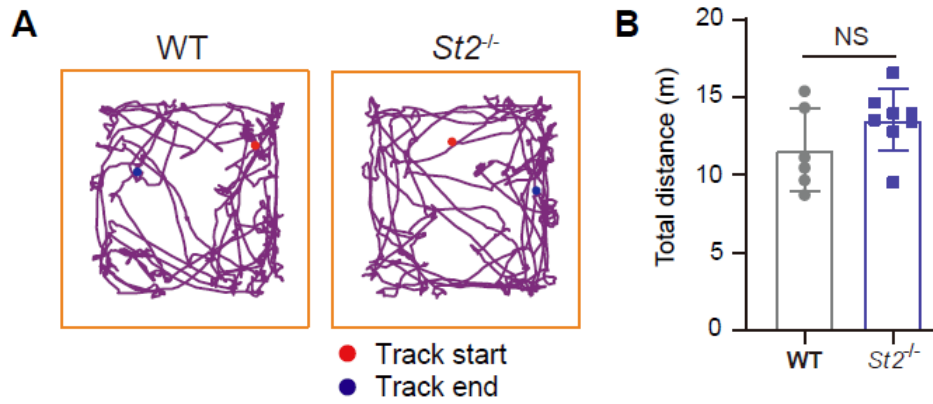


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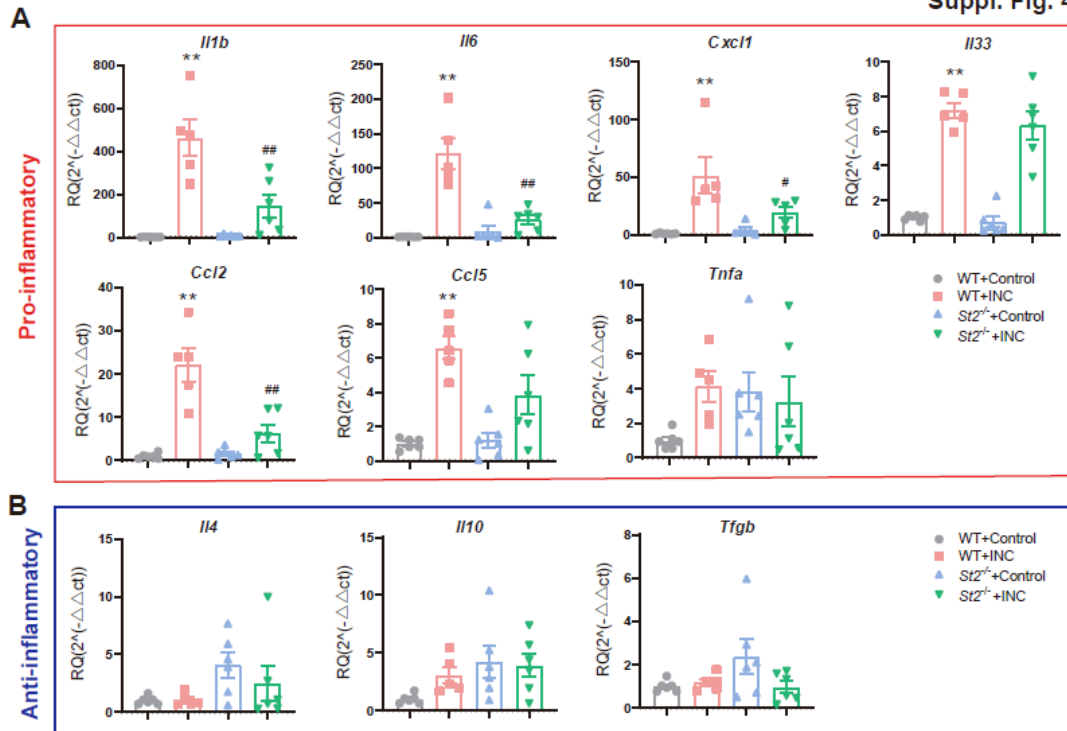


Suppl. Fig. 2 Recombinant mouse IL-33 (rmIL-33) injection into the incised tissues worsened mechanical allodynia of INC model mice. (A) Schematic picture showing time points for INC model establishment, rmIL-33/vehicle application and behavioral assay. (B) Time course showing PWT changes of INC pain model mice receiving either rmIL-33 (300 ng/site) or corresponding vehicle (0.1% BSA in PBS) injection into the incised tissues. (C) Summary of AUC of curves as shown in panel A. * $p < 0.05$ and ** $p < 0.01$ vs. INC+Veh group. $n = 7$ mice/group. Two-way ANOVA followed with Tukey's post-hoc test in panel A. Student's unpaired t test for panel B.

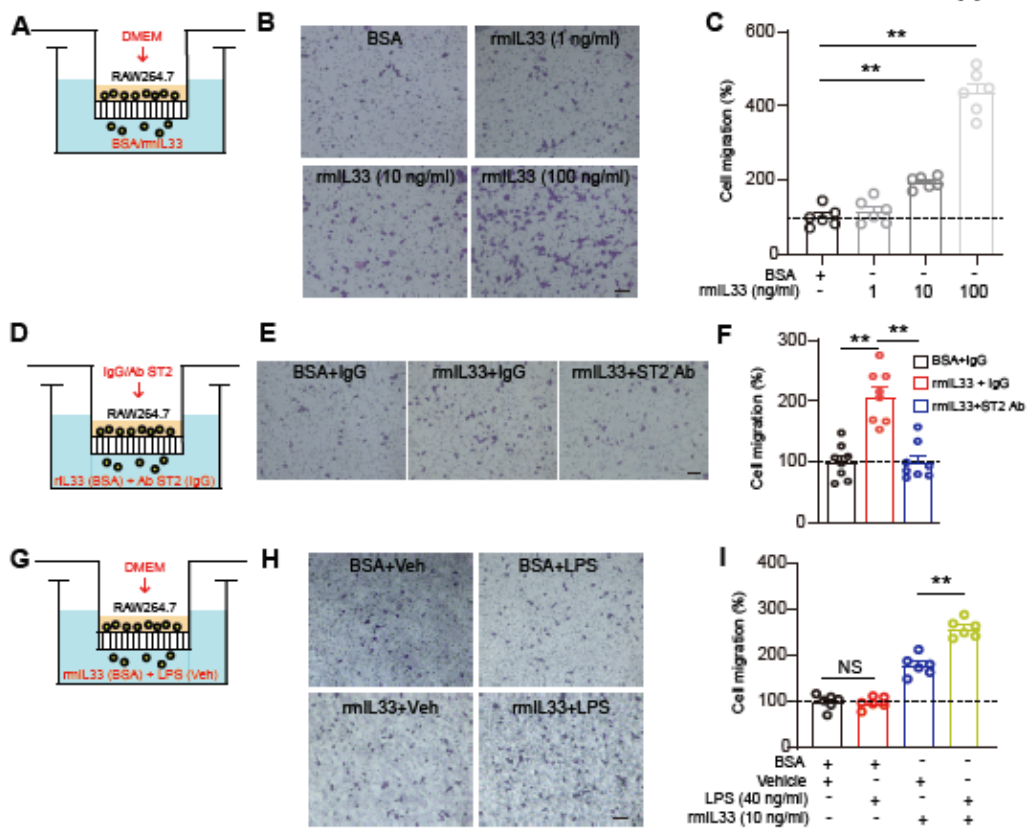
Suppl. Fig. 3



Suppl. Fig. 3 $St2^{-/-}$ mice displayed normal locomotor activity. (A) Representative movement traces of WT and $St2^{-/-}$ mouse in the open field test. (B) Summary of the total distance travelled by two groups of mice. n=6-8 mice/group. NS: no significance. Student's unpaired *t* test for panel B.



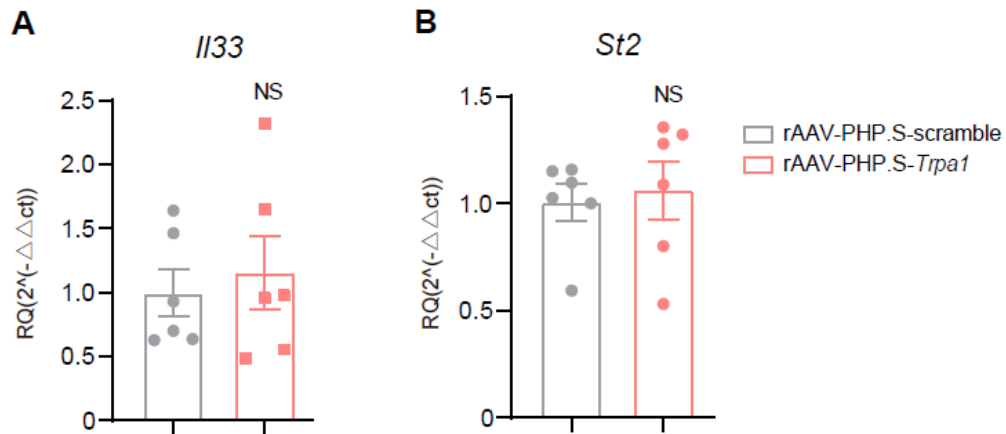
Suppl. Fig. 4 Expression changes of certain pro-inflammatory and anti-inflammatory genes in WT and $St2^{-/-}$ mice upon incision. (A) Expression changes of some typical pro-inflammatory genes in skin tissues of WT+Control, WT+INC, $St2^{-/-}$ +Control and $St2^{-/-}$ +INC groups of mice. (B) Expression changes of some typical anti-inflammatory genes in skin tissues of WT+Control, WT+INC, $St2^{-/-}$ +Control and $St2^{-/-}$ +INC groups of mice. n=5-6 mice/group. **p<0.01 vs. WT+Control group. #p<0.05, ##p<0.01 vs. WT+INC group. One-way ANOVA followed with Tukey's post-hoc test.



Suppl. Fig. 5 IL-33/ST2 signaling induces macrophage chemoattraction in vitro. (A) Schematic picture showing transwell migration assay using murine macrophage cell line RAW264.7 cell with Boyden chamber. Recombinant IL-33 (rIL-33) or vehicle (BSA) was added in the medium as indicated. (B) Representative photos showing migration of Raw264.7 cells in medium containing BSA or different concentrations of rmIL-33 (1, 10 or 100 ng/ml). (C) Summary of cell migration % as in panel B. Results from BSA-treated group was taken as 100% and all others were normalized. (D) Schematic picture of RAW264.7 cell in Boyden chamber. Recombinant mouse IL-33 (rmIL-33, 10 ng/ml)/BSA and ST2 neutralizing antibody (ST2 Ab, 30 μ g/ml)/ isotype control IgG was added in the medium as indicated. (E) Representative photos showing migration of Raw264.7 cells towards medium containing BSA+IgG, rmIL-33+IgG or rmIL-33+ST2 Ab. (F) Summary of cell migration % as in panel E. Results from BSA+IgG group was taken as 100% and all others were normalized. (G) Representative photos showing migration of Raw264.7 cells in medium containing rmIL-33/BSA and LPS/Veh (DMEM). (H) Representative photos showing migration of Raw264.7 cells towards medium containing rmIL-33 (10 ng/ml)/BSA and LPS (40 ng/ml)/Veh. (I) Summary of cell migration % as in panel H. Results from BSA+Veh group was taken as 100% and all other were

normalized. Scale bar=100 μ m. n=6-8 tests/group. **p<0.01. NS: no significance. One-way ANOVA followed with Tukey's post-hoc test was used.

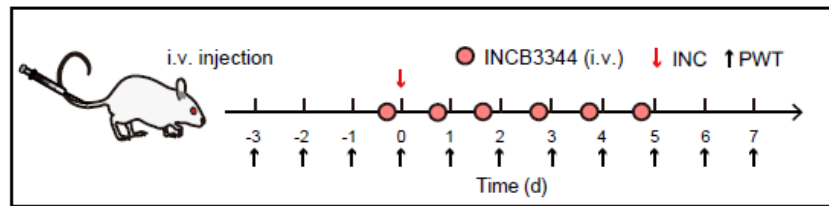
Suppl. Fig. 6



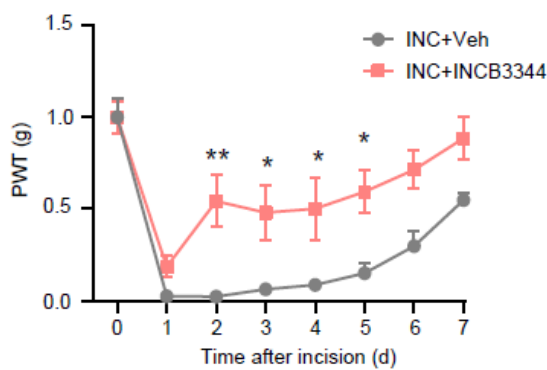
Suppl. Fig. 6 *Il33* and *St2* gene expression in the incised tissues of *Trpa1* knockdown mice.

(A&B) qPCR examination of *Il33* and *St2* gene expression in the incised tissues of mice with *Trpa1* knockdown. n=6 mice/group. NS: no significance. Student's unpaired *t* test.

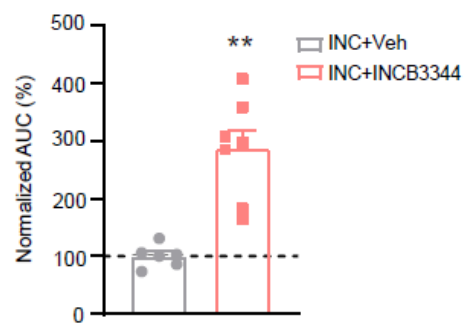
A



B



C



Suppl. Fig. 7 Blocking CCR2 signaling reduces mechanical allodynia in INC pain model mice.

(A) Schematic picture showing time points for INC model establishment, INCB3344/vehicle application and behavioral assay. (B) Time course showing PWT changes of INC pain model mice receiving either INCB3344 (a CCR2 specific antagonist) or corresponding vehicle (0.3% DMSO in PBS) treatment (i.v.). (C) Summary of AUC of curves as shown in panel A. * $p < 0.05$ and ** $p < 0.01$ vs. INC+Veh group. $n = 6-7$ mice/group. Two-way ANOVA followed with Tukey's post-hoc test in panel A. Student's unpaired t test for panel B.