

Supplementary figure

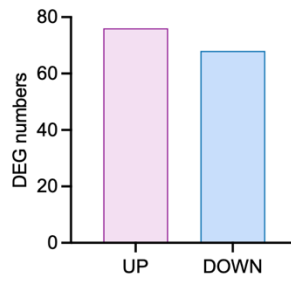


Fig. S1 Number of differentially expressed genes in mice induced by MC903 treatment.

Numbers of up-regulated and down-regulated genes identified through RNA-seq.

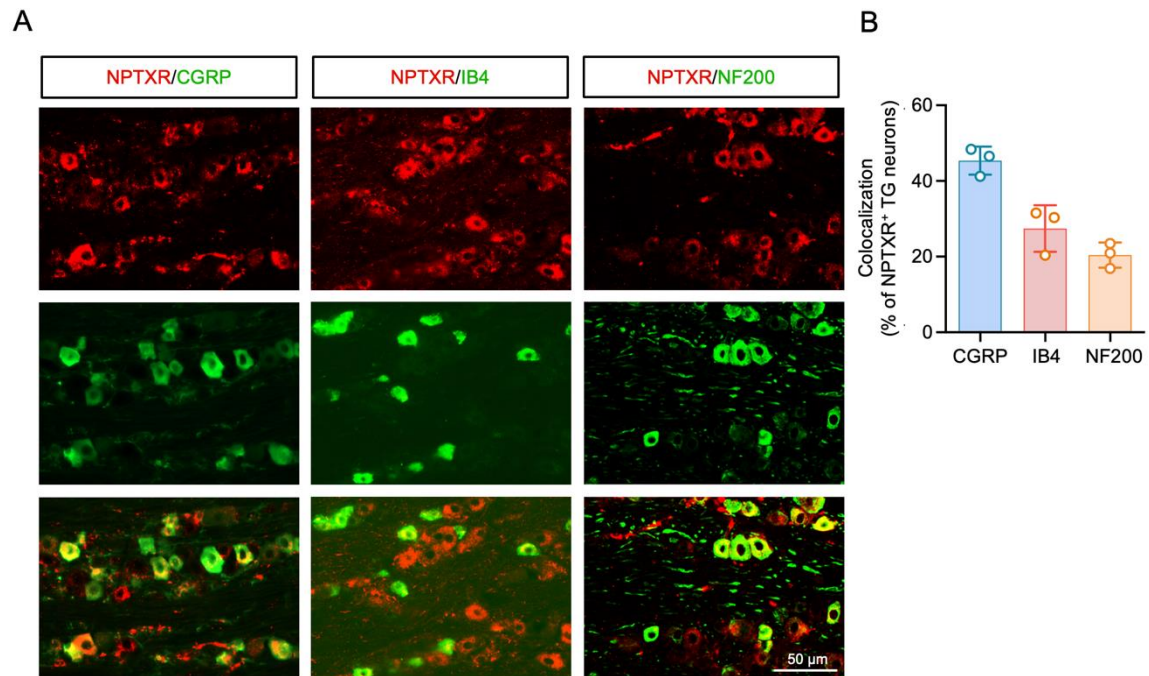


Fig. S2 NPTXR is mainly distributed in CGRP⁺ neurons.

(A) Representative images of double staining of NPTXR with CGRP, IB4, and NF200 in TG of MC903 10 d mice. Scale bar = 50 μ m. (B) Statistical chart of the images in (A).

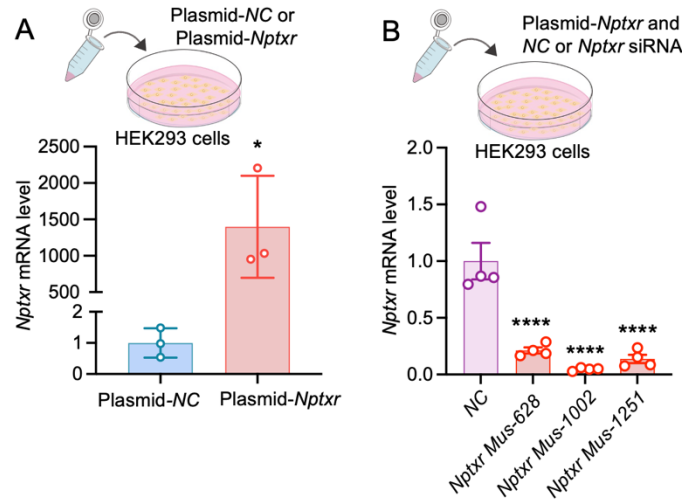


Fig. S3 Validation of *NPTXR* overexpression and knockdown efficacy *in vitro*.

(A) qPCR showing *Nptxr* mRNA expression at 6 h after transfection of the plasmid in HEK293 cell line. * $P < 0.05$, compared to plasmid-NC group. Student's test. $n = 3$ mice per group. (B) Down-regulation of *Nptxr* mRNA by treatment with three pairs of *Nptxr* siRNAs in HEK293 cell line. **** $P < 0.0001$, compared to NC group, One-way ANOVA followed by Bonferroni's tests. $n = 4$ mice per group.

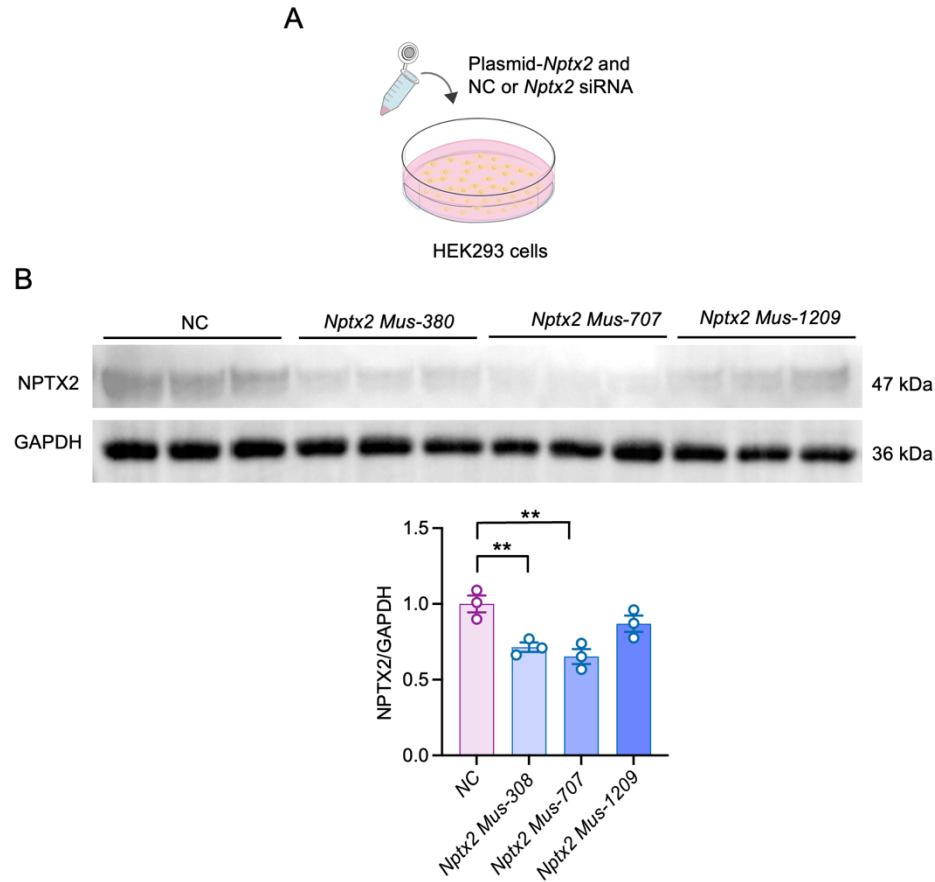


Fig. S4 NPTX2 protein expression is significantly reduced at 48 h after transfection three pairs of *Nptx2* siRNAs in HEK293 cell line.

(A) NPTX2 expression 48 h after transfection three pairs of *Nptx2* siRNAs in HEK293 cells. (B) Statistical chart of the western blot bands in (A). ** $P < 0.01$, compared to NC group. One-way ANOVA followed by Bonferroni's test. $n = 3$ mice per group. NC, negative control. Data are presented

as means \pm SEM.

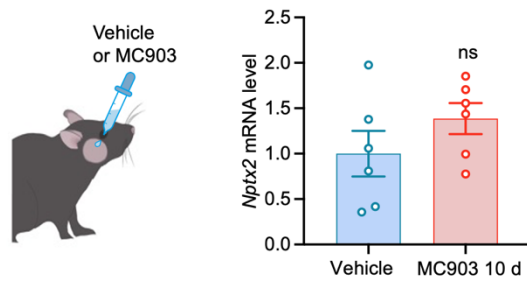


Fig. S5 *Nptx2* mRNA does not change in the facial skin at MC903 10 d.

Nptx2 mRNA expression in facial skin at MC903 10 d. Compared to vehicle group. ns, not significant.

Data are presented as means \pm SEM.