**SUPPLEMENTARY MATERIALS AND METHODS**

**Fluorescence-activated cell sorting**

To purify TOM-expressing cells, newborn back skin of *Prss56Cre,R26tdTom,Nf1flox/flox* mice was dissected free of other tissues and digested with collagenase/dispase type I (Sigma/Roche) for 2 h at 37°C, followed by mechanical dissociation and filtration. The resulting cell suspension was purified on a FacsVantage (Becton Dickinson) equipped with an argon laser tuned to 561 nm. Dead cells and doublets were excluded by gating on a forward-scatter and side-scatter area versus width. Log RFP fluorescence was acquired through a 530/30 nm band pass. Internal TOM-negative cells served as negative controls for FACS gating. Equal number of TOM-positive and TOM-negative cells were sorted directly into RNAlater (Ambion) and stored at -80°C until further processing.

**Histology and immunohistochemistry**

Mice were perfused with 4% PFA (Electron Microscopy Sciences) in 0.1 M phosphate buffer. Dorsal skin, subcutaneous nerves and nerve roots were immersed in the same fixative overnight at 4°C and cryopreserved in 30% sucrose prior to embedding in OCT (Sakura). 12 µm- (nerves) and 20 µm- (skin) thick sections were cut on a Leica cryostat. Immunofluorescence was performed as previously described (4). The cell nuclei were counterstained with Hoechst (Life Technologies). For whole-mount immunolabelling, dorsal skin of E13.5 and E15.5 embryos and DRGs from newbornpups were dissected and fixed in 4% PFA. Samples were blocked overnight in 4% bovine serum albumin (BSA) (Sigma Aldrich) in PBS containing 0.3% Triton-X-100 (PBST) (Sigma Aldrich), then incubated for 48h with the primary antibody/BSA/PBST solution at 4°C. After rinsing, secondary antibodies were applied overnight at room temperature. Samples were then washed and flat-mounted in Fluoromount-G (SouthernBiotech). Whole-mount immunostaining and clarification of adult skin was performed using the iDISCO+ method, as described (<https://idisco.info/idisco-protocol/>). Z-stacks were acquired using Leica TCS SP5 and TCS SP8 laser-scanning confocal microscopes and assembled in ImageJ and Photoshop CS6 (Adobe).

The following primary antibodies were used: rat anti-tdTOM (1:500, Kerafast #EST203), rabbit anti-dsRED (1:500, Clontech #632496) and goat anti-mCherry (1:500, Sicgen #AB0040-200) for detection of TOM, rabbit anti-S100 (1:400, Dako # Z0311), rabbit anti-βIII-tubulin (clone TUJ-1) (1:1000, BioLegend #801201), chicken anti-βIII-tubulin (1:500, Synaptic Systems #302306), goat anti-SOX10 (1:100, Santa Cruz #sc-17342), goat anti-SOX2 (1:100, R&D #AF2018), goat anti-KIT (1:100, R&D #AF1356), rabbit anti-IBA1 (1:400, Wako #019-19741), goat anti-PDGFR⍺ (1:100, R&D #AF1062), rabbit anti-PDGFRß (1:100, Abcam #ab32570), goat anti-MITF (1:300, R&D #AF5769), goat anti-TRP2 (1:100 Santa Cruz #sc-10451), rabbit anti-CGRP (1:1000, ImmunoStar #24112), rabbit anti-NCAM (1:100, Merck #AB5032), rabbit anti-L1 (1:100, Merck #MAB5272), rabbit anti-P75NTR (1:500, Merck #07-476), rabbit anti-PHH3 (1:400, Abcam #ab5176), rabbit anti-ERK1/2 (1:250, Cell Signaling #9101), rat anti-PECAM (1:100 BD Biosciences #553370), rabbit anti-NG2 (1:200, Merck #AB5320), chicken anti-VIM (1:200, Merck #AB5733), chicken anti-K15 (1:100 , BioLegend #833901), rat anti-MBP (1:80, Merck #MAB386). Alexa 549-, Alexa 488- and Alexa 647-conjugated secondary antibodies were from Jackson Immuno Research.

**RNA extraction and semi-quantitative RT-PCR**

Total RNA was isolated from FACS-sorted TOM-positive and TOM-negative cell fractions using the RNAqueous-Micro kit (Thermo Fisher Scientific) according to the manufacturer's instructions. Adult *Nf1*-KO mutant skin and E12.5 neural tube (with BCs) were mechanically dissociated using a MM300 TissueLyser (Qiagen) and RNA was extracted using the RNeasy Fibrous Tissue kit (Qiagen) according to the manufacturer's instructions. Total RNA (100 ng) was reverse transcribed using pSuperscript III Rnase H reverse transcriptase (Invitrogen) and a mix of oligo-dT and random primers (Invitrogen), according to the manufacturer's instructions. PCR was performed as follows: 2 min at 94°C; 30 cycles of 2 min at 94°C, 1 min at the primer-specific annealing temperature, 1 min at 72°C; and 10 min at 72°C. The sequences of forward (F) and reverse (R) primers, primer annealing temperature (°C) and expected product size (bp) are as follows: β-actin (F: TGTTACCAACTGGGACGACA/ R: GGGGTGTTGAAGGTCTCAAA, 60°C, 165 bp), Prss56 (F: GGTCTTCAGTGGCCTAGTGG/ R: AGCCTCTGTCCTTGATCAGC, 58°C, 151 bp),  Nf1 (F: GCTTCCCTCAGAACAGCATC/ R : GCCCCTTTCAATTCTAGGTGG, 58.5°C, 128 bp). For each RNA sample, two independent PCR amplifications were performed.

**Sirius red staining of collagen**

For collagen staining, fixed dorsal skin was embedded in paraffin and 5 µm thick sections were cut. Paraffin sections were deparaffinised and rehydrated, stained with Weigert's hematoxylin (Sigma Aldrich) for 8 minutes, and washed in water. They were subsequently stained in Picro-sirius red (Sigma Aldrich) for one hour, washed in two changes of acidified water, dehydrated, cleared in xylene and mounted in a resinous medium. Bright-field images were acquired using a Leica DM 5500B microscope.

**Cell quantification**

Quantifications of dermal cell populations were performed on whole-mount preparations (embryonic skin) and on cryostat sections (newborn, P9 and P90 skin) of *Nf1*-KO (n=3) mutants and control littermates (n=3). At least two skin biopsies and 4 distant sections of postnatal skin (from the same A-P level) were selected from each individual and subjected to immunolabelling with cell type-relevant antibodies. 40 µm- or 20 µm-thick z-stacks (for whole-mounts and skin sections, respectively) were acquired using a Leica TCS SP5 laser scanning confocal microscope, and the number of cells (containing nuclei) were quantified using 6 to 12 fields from each sample. The scanned surface area corresponds to 0.15 µm2 for E15.5 skin and 0.38 µm2 for other samples. For sectioned samples, upper and lower tissue limits were defined by the epidermis and the panniculus carnosus muscle, respectively. For quantification of the melanocyte lineage, only fields containing a minimum of one traced melanocyte of any kind (follicular or extrafollicular) were included in the analysis due to highly heterogeneous distribution patterns. Cell counting in 6-month-old skin was performed using electron microscopy, based on the ultrastructural characteristics of distinct cell populations. Ultrathin sections were deposited on Copper grid and 15 grid hexagons (0.026 mm2 each) were scanned for each individual (3 *Nf1*-KO and 3 controls). Quantification of TOM+/SOX10+ cell fractions in the adult cervical nerve roots was performed on 20 µm-thick longitudinal sections of *Prss56Cre,R26tdTom* mice (n=3). Cell counts were normalised against the total number of SOX10+ cells. Quantification of traced sensory neurons was performed on whole-mount preparations of cervical dorsal root ganglia isolated from *Nf1*-KO (n=3) and control (n=3) newborn pups and immunolabelled for TOM and TUJ1. Acquired z-stacks were screened for the presence of TOM-positive neuronal perikarya, based on morphological criteria.