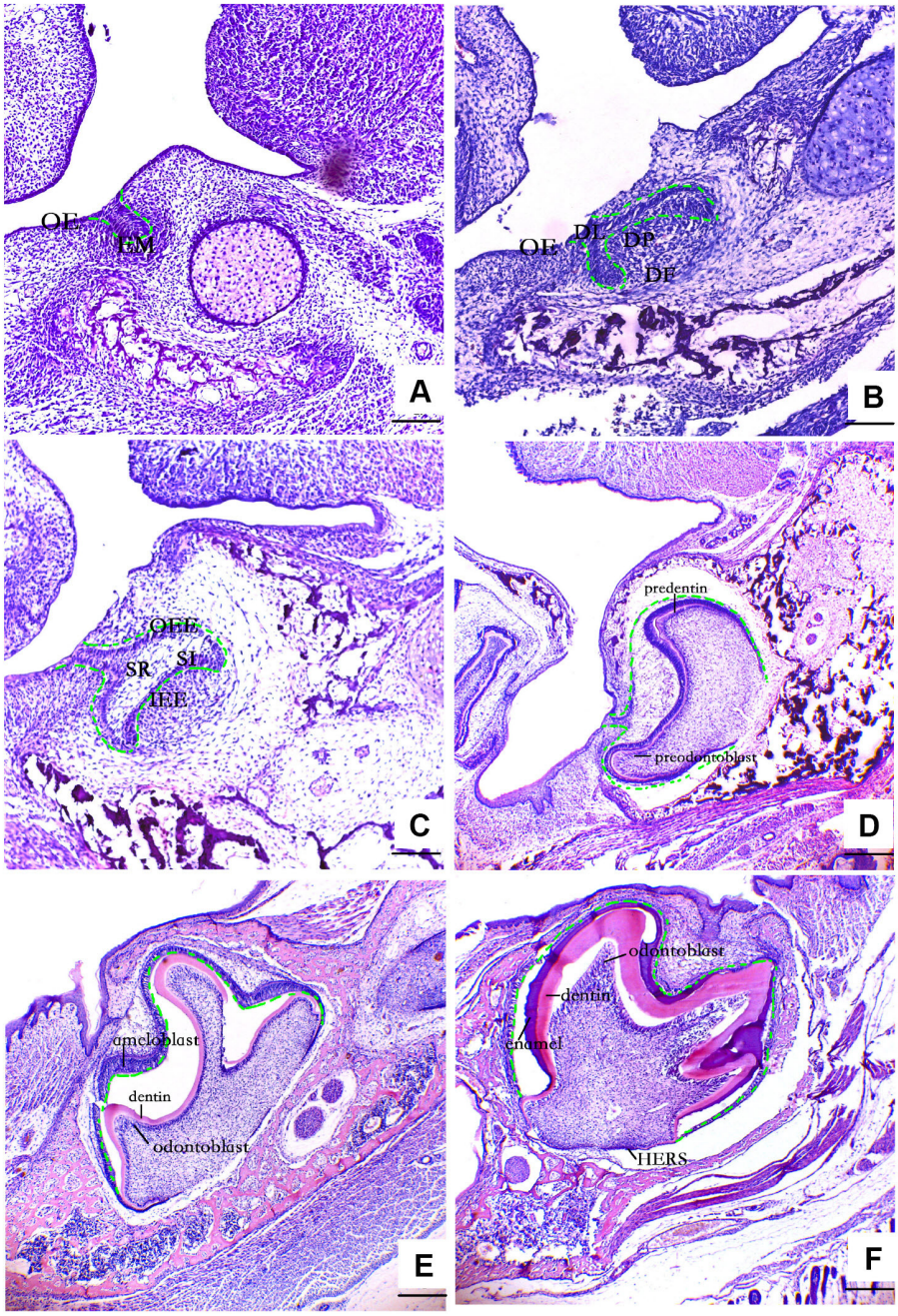
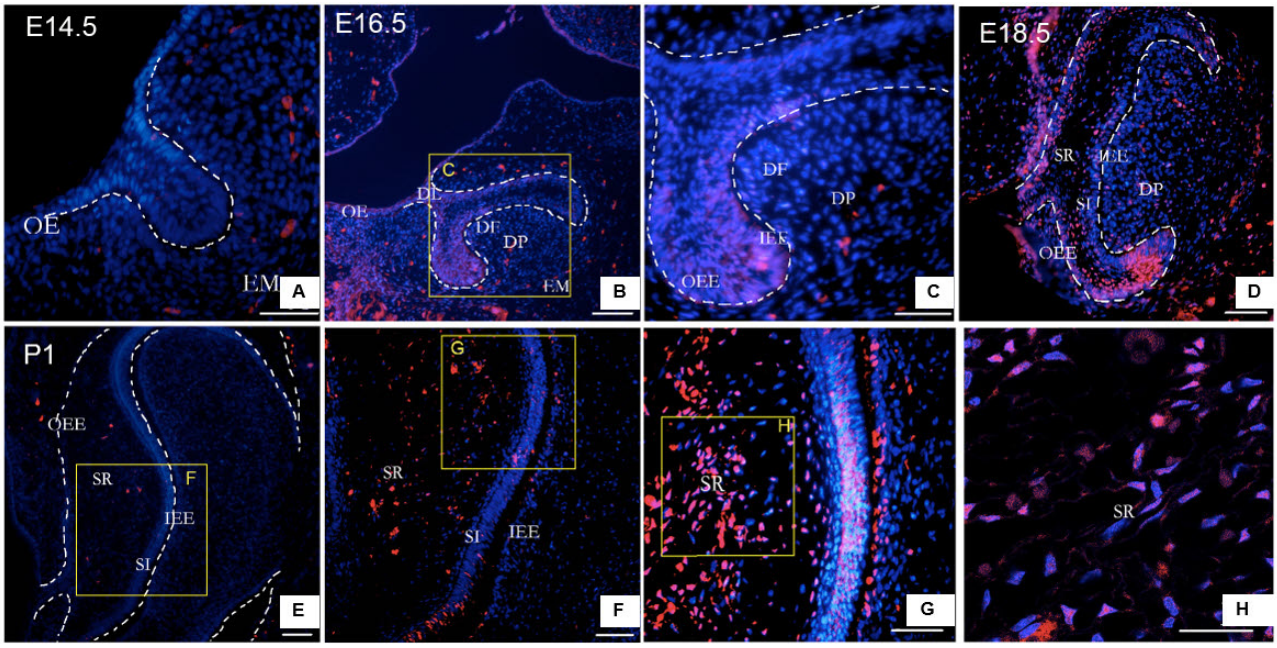
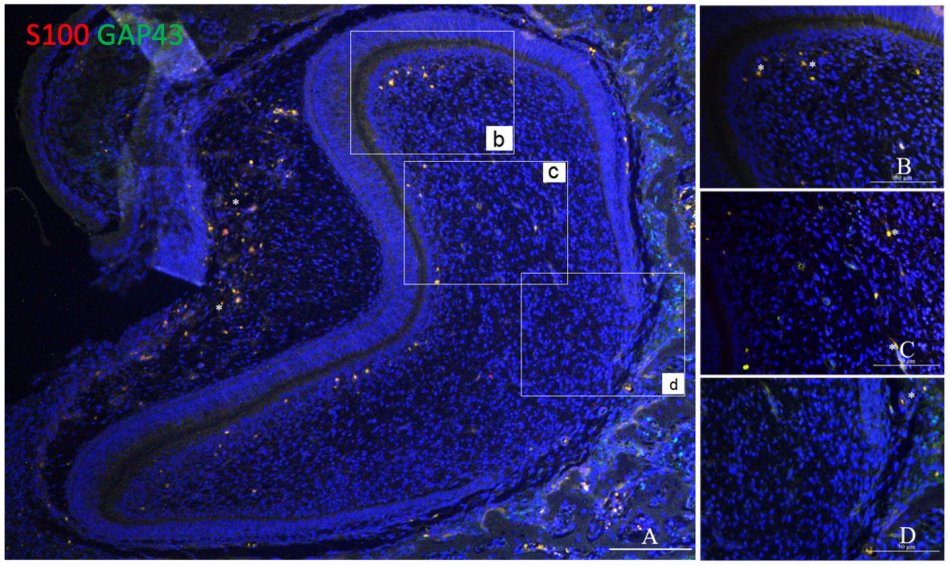


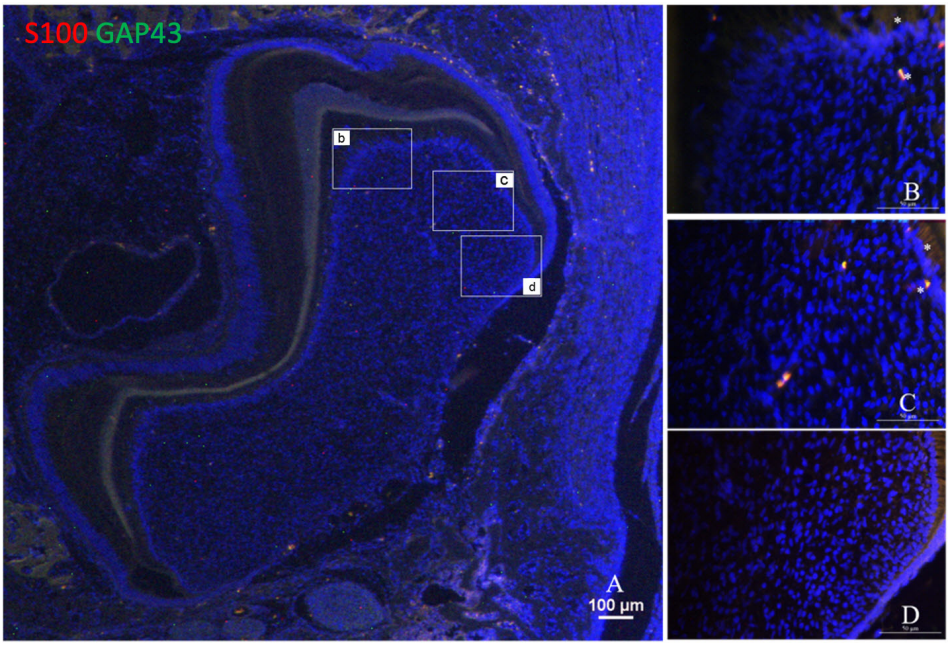
Supplementary Fig. S1. H&E staining results of rat mandibular first molars in different stages. (A) E14.5, tooth germ in bud stage. (B) E16.5, cap stage. (C) E18.5, early bell stage. (D) P1, late bell stage. (E) P7, late bell stage, ameloblasts appeared, and dentin formed. (F) P10, enamel formed, dentin thickened, and Hertwig epithelial root sheath formed. OE: outer enamel, EM: ectodermal mesenchyme, DL: dental lamina, DP: dental papilla, DF: dental follicle, OEE: outer enamel epithelium, SI: stratum intermedium, SR: stellate reticulum, IEE: inner enamel epithelium, HERS: Hertwig's epithelial root sheath.



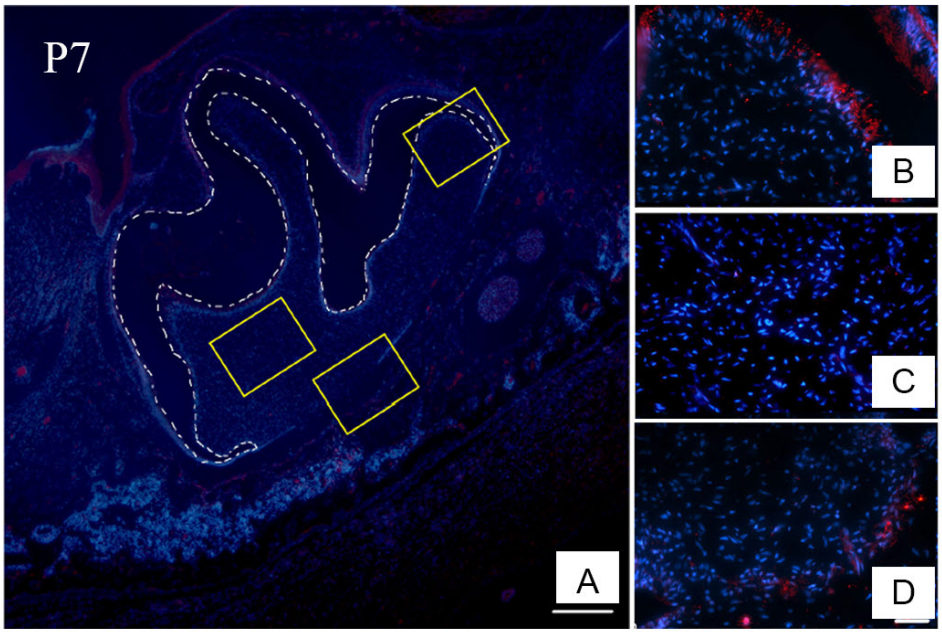
Supplementary Fig. S2. Immunofluorescence staining of Ki67 at different stages of tooth germ development. (A) E14.5, amplification times is 400×. (B) E16.5, amplification times is 200×. (C) Local magnification of (B), amplification times is 400×. (D) E18.5, amplification times is 200×. (E) P1, amplification times is 100×. (F) Local magnification of (E), amplification times is 200×. (G) Local magnification of (F), amplification times is 400×. (H) Local magnification of (G), amplification times is 630×. Ki67 in red. DAPI in blue. OE: outer enamel, EM: ectodermal mesenchyme, DL: dental lamina, DF: dental follicle, DP: dental papilla, OEE: outer enamel epithelium, IEE: inner enamel epithelium, SR: stellate reticulum, SI: stratum intermedium.



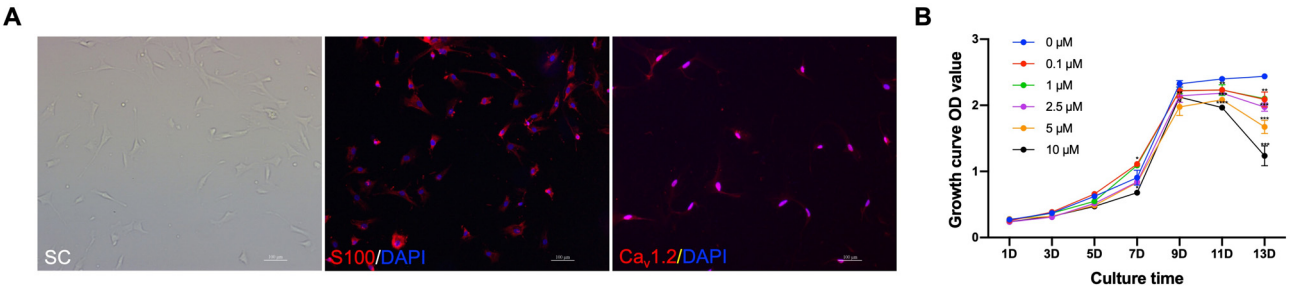
Supplementary Fig. S3. Expression of rat neural development markers (S100β and GAP43) in the tooth germ at P1. (A) P1, amplification times is 200×. (B) Local magnification of b area in (A), amplification times is 400×. (C) Local magnification of c area in (A), amplification times is 400×. (D) Local magnification of d area in (A), amplification times is 400×. S100β in red and GAP43 in green. DAPI in blue. S100: S100β.



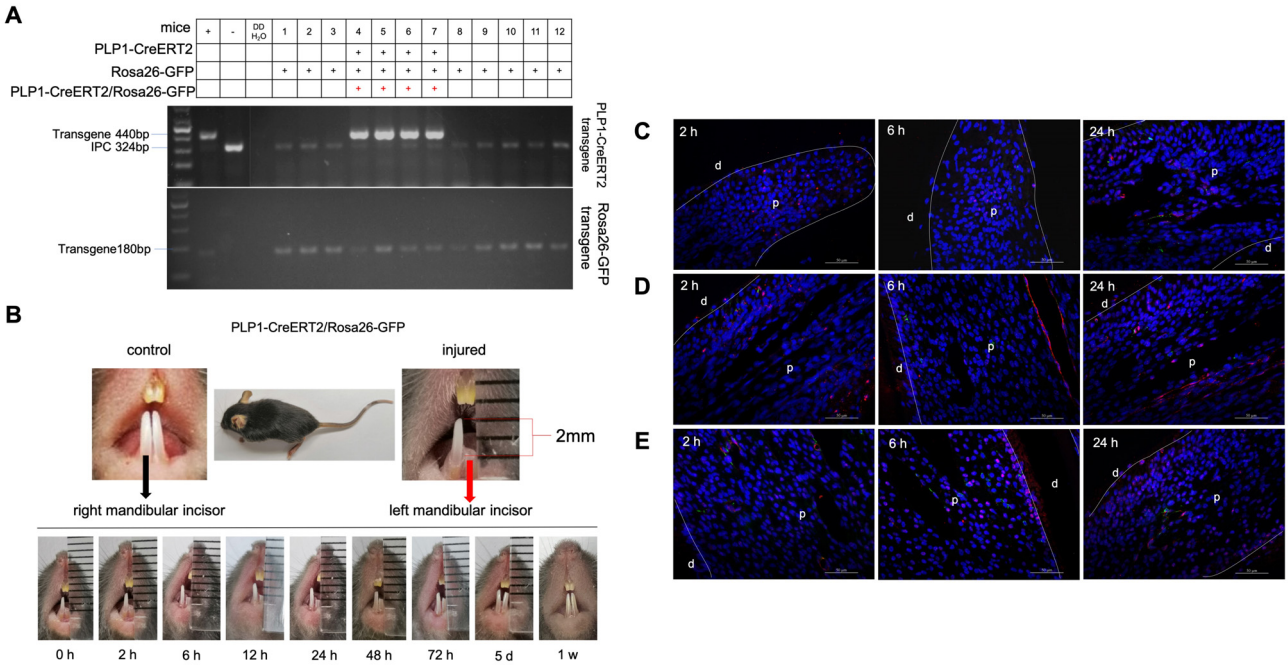
Supplementary Fig. S4. Expression of rat neural development markers (S100β and GAP43) in the tooth germ at P7. (A) P7, amplification times is 200×. (B) Local magnification of b area in (A), amplification times is 400×. (C) Local magnification of c area in (A), amplification times is 400×. (D) Local magnification of d area in (A), amplification times is 400×. S100β in red and GAP43 in green. DAPI in blue. S100: S100β.



Supplementary Fig. S5. Immunofluorescence staining of Ki67 at P7 of tooth germ development. (A) P7, amplification times is 40×. (B-D) The local magnification of the pulp horn, central pulp and apex square in (A) and amplification times are 400×. Ki67 in red. DAPI in blue.



Supplementary Fig. S6. The expression of S100 and Cav1.2 in Schwann cells (SCs) and the proliferation of SCs with various concentrations of nimodipine. (A) Cells showed typical fusiform-shaped morphology and were positively stained with SCs marker S100 and Cav1.2. Scale bar=100 μm. (B) Proliferation of SCs treated with different concentrations of nimodipine. The black asterisk represents statistics for all the groups (n=5). *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 SCs with nimodipine versus control.



Supplementary Fig. S7. The incisor injury established and the expression of Schwann cells (SCs)-derived cells and $Ca_v1.2$ in PLP1-CreERT2/Rosa26-GFP tracing mice. (A) Identification of Cre and GFP genotypes of F2 generation mice from model mice. (B) Incisor injury was constructed in the PLP1-CreERT2/Rosa26-GFP tracing mice model. As the left mandibular incisor was the experimental group and the right was the self-control group, we ground mandibular incisors for 2 mm. The mandible was taken as the sample. Then, it was found that the injured incisors were basically recovered at 1 week after injury. (C-E) represent the expression of GFP^+ cells (green) and $Ca_v1.2$ (red) at the dental cusp, middle teeth, apical area of control, and injured incisors with recovery for 2, 6, and 24 hours, respectively. Scale bar = 50 μm. d: dentin, p: dental pulp.

Supplementary Table S1. List of primers used in the present study

Gene	Forward primer (5′-3′)	Reverse primer (5′-3′)
GADPH	5′-CCAGAACATCATCCCTGCCTCT-3′	5′-GACGCCTGCTTCACCACCTT-3′
Runx2	5′-TCCAGACCAGCAGCACTCCATA-3′	5′-TCCATCAGCGTCAACACCATCA-3′
DSPP	5′-GGAGCCACAAACAGAAGCAACA-3′	5′-TGGACAACAGCGACATCCTCAT-3′
DMP-1	5′-CAGGAAGAGGTGGTGAGTGAGT-3′	5′-TGGATTCGCTGTCTGCTTGCT-3′
GFP	5′-TCCTTGAAGAAGTGGGTGCG-3′	5′-AAGTTCATCTGCACCACCG-3′
oIMR3798/8346	5′-AGGTGG ACCTGATCATGGAG-3′	5′-ATACCGGAGATCATGCAAGC-3′
oIMR7338/7339	5′-CTAGGCCACAGAATTGAAAGATCT-3′	5′-GTAGGTGGAAATTCTAGCATCATCC-3′

Supplementary Table S2. Schwann cell molecular markers in different phenotypes

Schwann cell phenotype	Molecular marker
Neural crest cell	ErbB3, L1, $P75^{NTR}$, Sox10, Oct6, AP2α
Schwann cell precursor	ErbB3, L1, $P75^{NTR}$, Sox10, Oct6, AP2α, Cad19, BFABP, P0, GAP43, PLP, Dhh, MPZ, Serpin2
Immature Schwan cell	ErbB3, L1, $P75^{NTR}$, Sox10, Oct6, BFABP, GAP43, S100, GFAP, MAL, Galectin, NCAM, MPZ
Myelinating Schwann cell	Sox10, Oct6, S100, Krox20, MBP, MPZ, P0
Non-myelinating Schwann cell	Sox10, Oct6, $P75^{NTR}$, S100, NCAM, GAP43, L1

Supplementary Table S3. The expressions of Schwan cells specific markers in different stages of the rat tooth germ

Gene	E14.5 (log2FoldChange)	P7 (log2FoldChange)
Erbb3	4.92723	2.74858
S100b	8.59501	1.03634
S100a1	74.0986	49.0792
S100a4	54.9962	21.6119
Pou3f1	0.598325	0.050313
Pou3f3	1.52571	0.298334
Pou3f4	0.064404	0
Tfap2a	10.6013	0.797158
Tbx22	0.887903	0.206156
L1cam	0.59476	0.455415
Cd274	0.823693	1.77323
Ngfr	26.9399	17.1637
Ngf	1.30314	4.72933
Sox10	0.692524	0
Mitf	1.18546	0.785004
Cdh19	0.047765	0.016064
Phox2b	0.01245	0.012561
Fabp7	0.865749	0
Rplp0	1943.33	1115.54
Gap43	21.0445	3.82284
Plp1	2.43175	0
Pnpo	3.75238	7.65161
Dhh	0.30437	0.274908
Mpz	9.11272	5.70247
Epcam	99.5179	18.2318
Sfn	98.2114	42.4497
Gfap	1.67122	0.028132
Mal	0.468726	0.202729
Lgals3	31.7673	47.9414
Lgals1	642.553	116.021
Ncam1	17.0857	6.74079
Mpz	9.11272	5.70247
Egr2	0	0.07339
Mbp	4.74517	1.28397
Ache	3.78231	0
Mki67	30.6863	3.60257

Supplementary Methods

Culture and identification of Schwan cells

The human cell line of Schwan cells (SCs) was purchased from ScienCell Research Laboratories (No. 15638; ScienCell) and cultured in Schwann cell medium (SCM; ScienCell) as used in the previous study (1). After cell adherence, SCM was removed, and cells were washed with PBS. And then, S100 immunofluorescence staining was performed to identify the cells.

Cell viability with various nimodipine concentrations

SCs were seeded in 96-well plates (3,000 cells/well) and cultured with SCM with 0, 0.1, 1, 2.5, 5 and 10 μmol/L nimodipine (Bayer). At certain time points, the Cell Counting Kit-8 (CCK-8) assays were performed to test the cell viability. Cells in each well were incubated with 10 μL CCK-8 solutions (Beyotime) for 2 hours after adding nimodipine to SCM for 1, 3, 5, 7, 9, 11, and 13 days. Subsequently, OD values at 450 nm were measured using a microplate reader.

The establishment of PLP1-CreERT2/Rosa26-GFP genotype lineage tracing model mice

The PLP1-CreERT2 transgenic C57 mice (Jackson Laboratory) were mated with 8-week-old wild type C57 mice, and we got filial generation C57 mice to be detected. At the same time, the Rosa-26-GFP C57 mice were mated and got filial generation to be detected. Then we extracted DNA from the tail of the mice to be detected, took polymerase chain reaction, carried out agarose gel electrophoresis, observed imaging and obtained identification results. Positive Cre F1 generation C57 mice were chosen to mate with positive Rosa-26-GFP F1 generation C57 mice and got filial generation F2 to be detected. Then we chose positive PLP1-CreERT2/Rosa26-GFP F2 generation for mating and obtained F3 generation (Supplementary Fig. S7A). Primers used for detecting the positive Cre and positive Rosa-26-GFP generation are shown in Supplementary Table S1. From this, we establish a mice lineage table.

Tamoxifen-induced expression of GFP in model mice

4-week-old PLP1-CreERT2/Rosa26-GFP mice were given by gavage once a day for continuous 3 days with Tamoxifen (80 μg/g, 3～4 mg/per) and induced GFP expression. 24 hours after gavage, mice were fixed by cardiac perfusion with 4% PFA. Then we removed the mice's sciatic nerves, fixed them in PFA, and embedded them in paraffin. After that, we identified whether Tamoxifen was induced successfully.

References

1. Li J, Ju Y, Liu S, Fu Y, Zhao S. Exosomes derived from lipopolysaccharide-preconditioned human dental pulp stem cells regulate Schwann cell migration and differentiation. Connect Tissue Res 2021;62:277-286