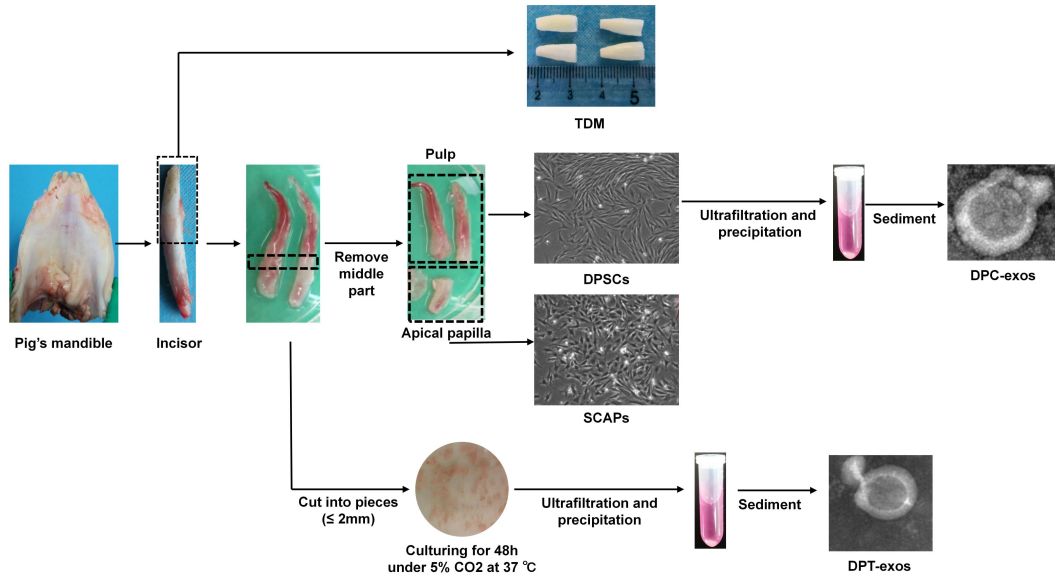
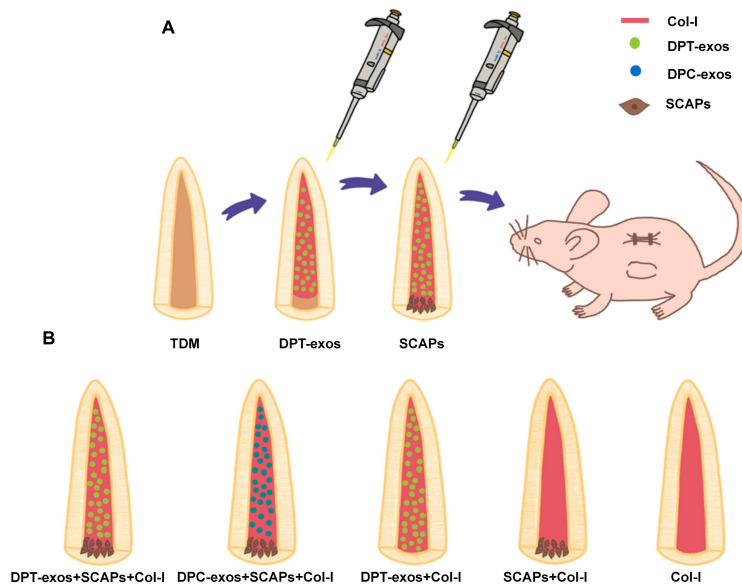


Supplementary materials



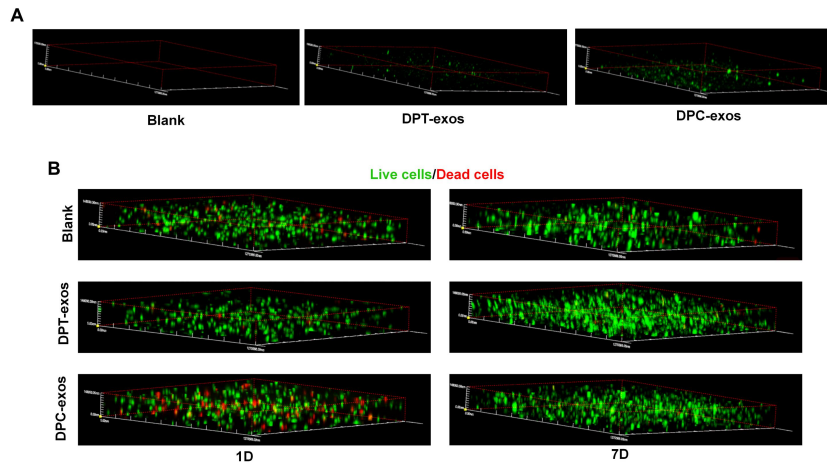
Supplementary Figure 1. Acquisition process for exosomes, cells and treated dentin matrix.

TDM: treated dentin matrix; DPC-exos: exosomes derived from dental pulp cells; DPT-exos: exosomes derived from dental pulp tissue; SCAPs: stem cells from the dental apical papilla.

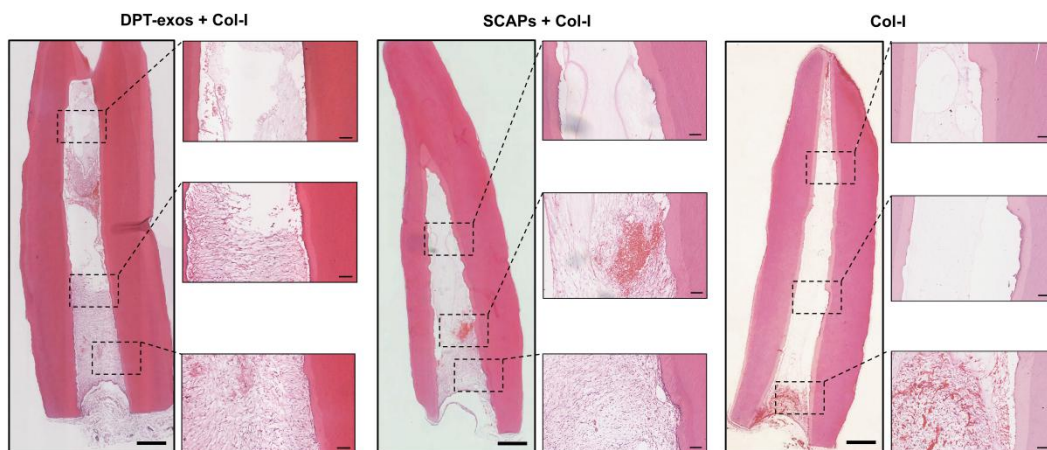


Supplementary Figure 2. Schematic diagram of subcutaneous implantation: (A) DPT-exos, DPC-exos and SCAPs were resuspended with collagen gel respectively and then used to fill TDM in a stratified way. (B) Samples were divided into five groups according to TDM: (DPT-exos+SCAPs+Col-I, test group: pig TDM was filled with collagen gel with DPT-exos and with SCAPs at the root tips; DPC-exos+SCAPs+Col-I, control group: TDM were filled with

collagen gel with DPC-exos and with SCAPs at the root tips; DPT-exos+Col-I, control group: TDM were filled with collagen gel only with DPC-exos; SCAPs+Col-I, control group: TDM were filled with collagen gel without exosomes and with SCAPs at the root tips; Col-I, blank group: TDM were just filled with collagen gel).

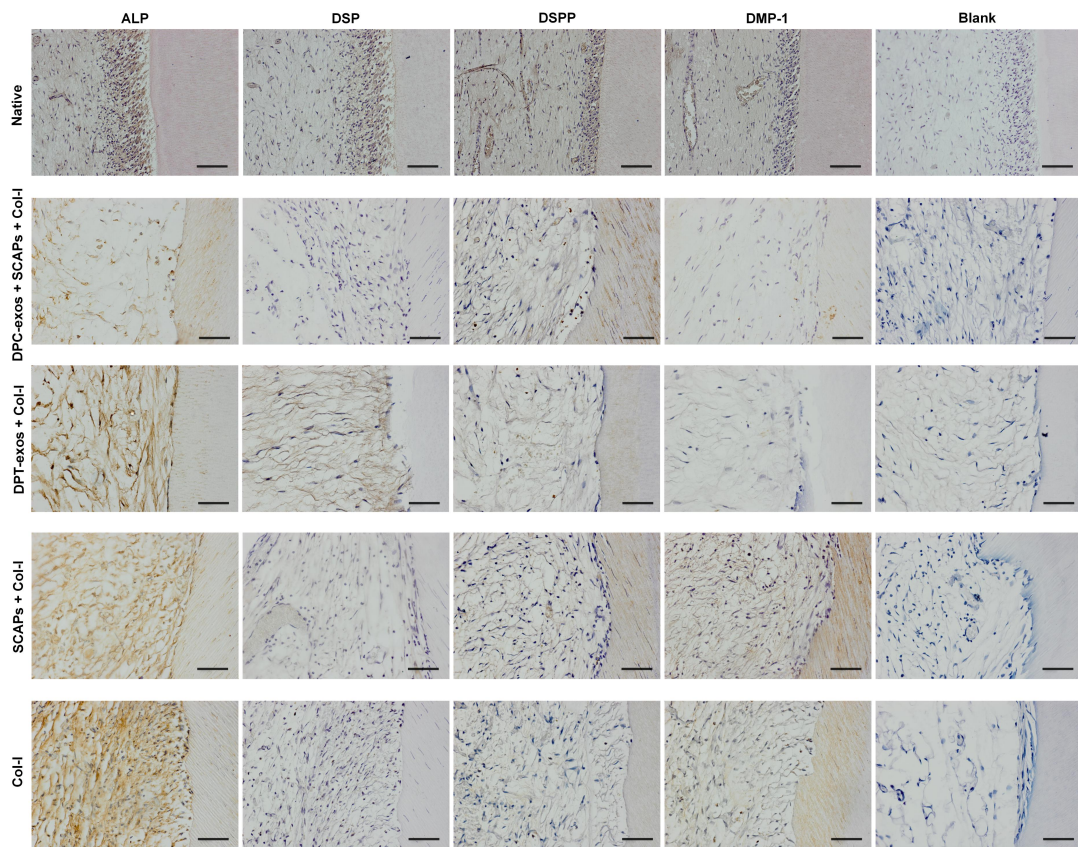


Supplementary Figure 3. Exosomes or SCAPs on collagen gels: (A) The distribution of DPT-exos and DPC-exos on collagen gel.(B) Live/dead staining of cultured SCAPs within collagen gel for 1day and 7days. collagen gel only with DPC-exos; SCAPs+Col-I, control group: TDM were filled with collagen gel without exosomes and with SCAPs at the root tips; Col-I, blank group: TDM were only filled with collagen gel).

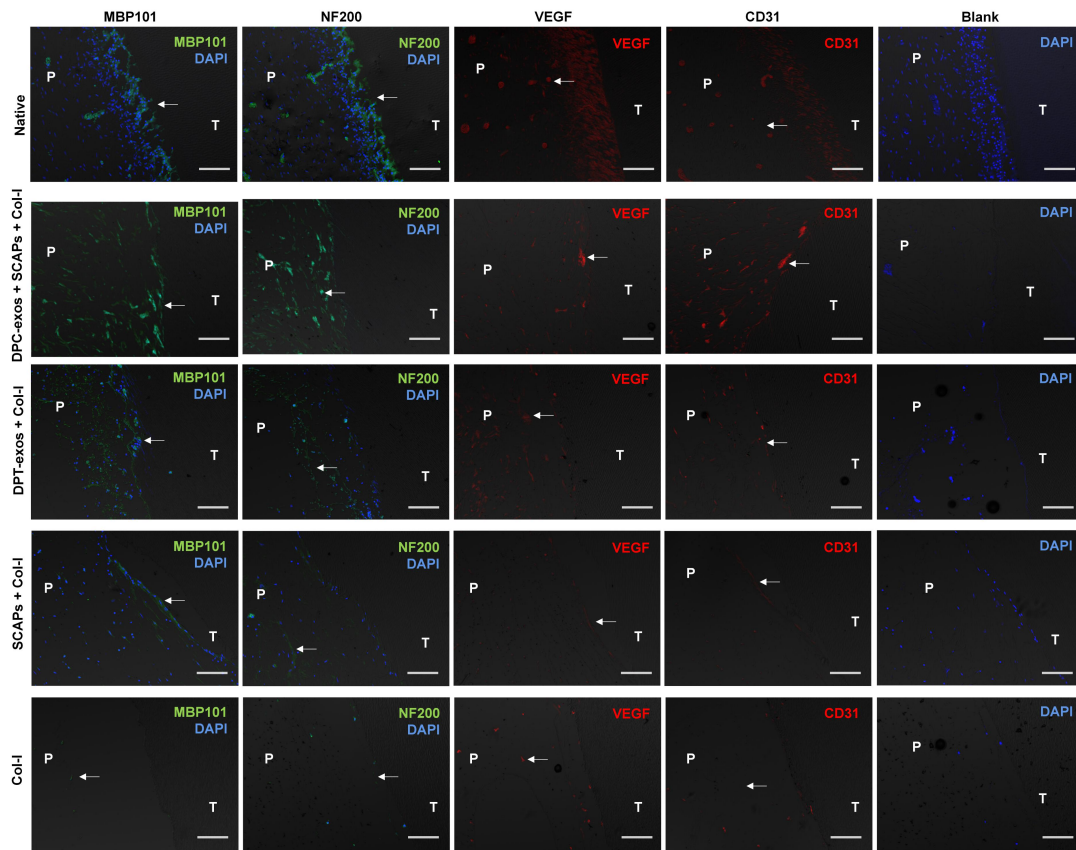


Supplementary Figure 4. Regenerated pulp-like tissue was not observed in other groups: H&E staining showing a small amount of fibrous connective tissue with inflammatory reaction

in DPT-exos+Col-I, SCAPs+Col-I and Col-I groups. Scale bars: 1 mm and 100 μ m.



Supplementary Figure 5. IHC staining of the expression of odontoblastic markers (ALP, DSP, DSPP, DMP1, Blank) in native, DPC-exos+SCAPs+Col-I group, DPT-exos+Col-I, SCAPs+Col-I and Col-I groups. Scale bars: 50 μ m.



Supplementary Figure 6. IF staining showing the expression of angiogenic markers (CD31 and VEGF) and neurogenetic markers (MBP101 and NF200) in native, DPC-exos+SCAPs+Col-I group, DPT-exos+Col-I, SCAPs+Col-I and Col-I groups. Scale bars: 50 μ m.