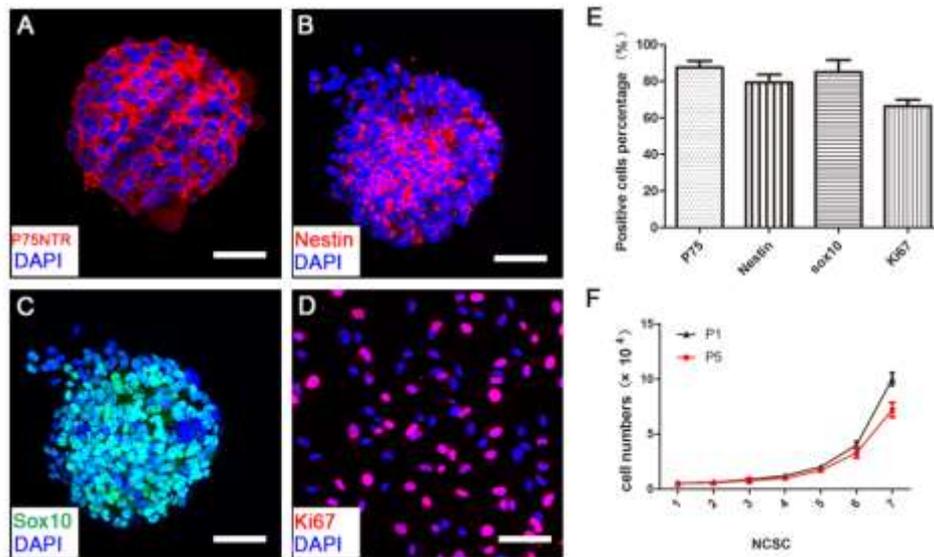
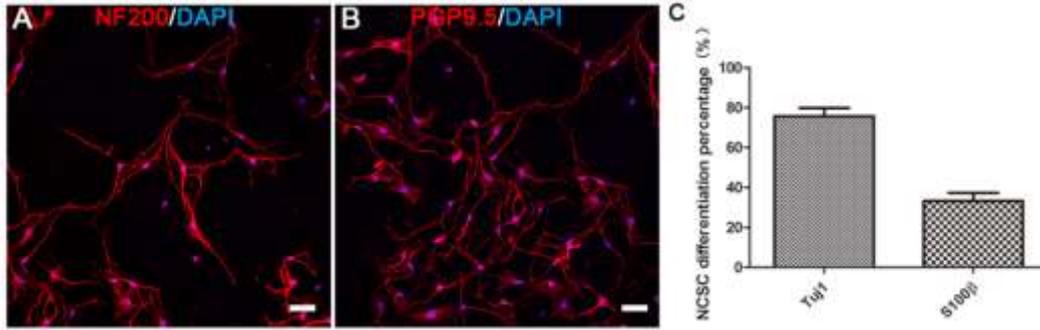


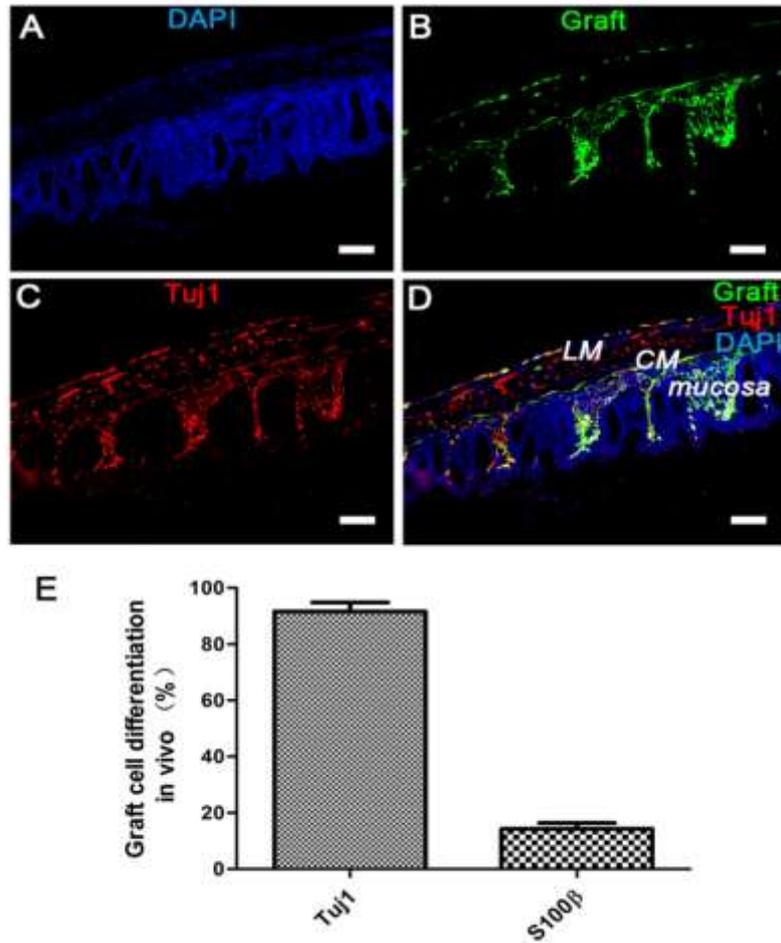
## Supplementary material



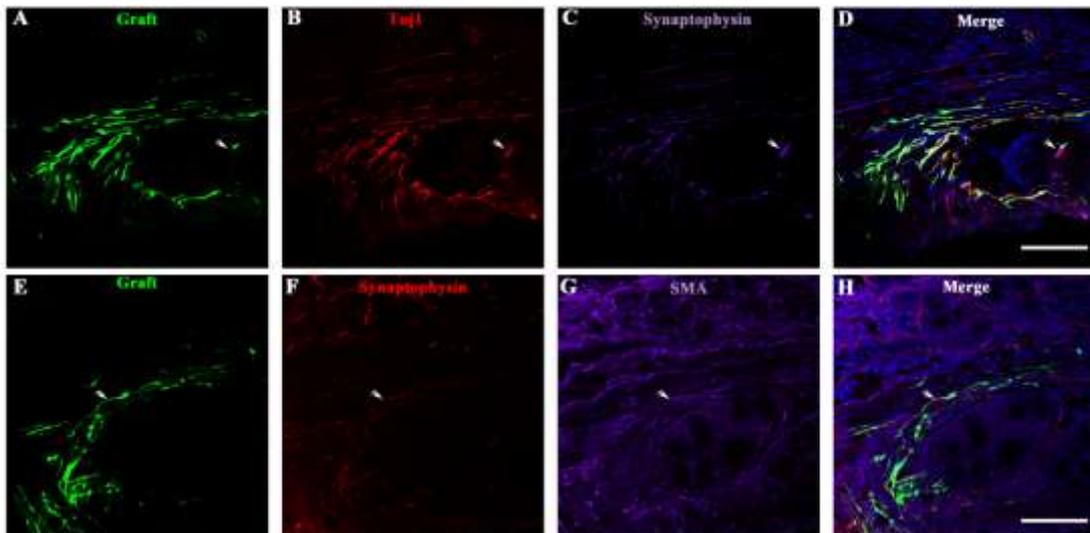
**Figure S1. DRG-derived neural crest stem cells identification in spheres and demonstration of proliferation ability *in vitro*.** (A-C) DRG-NCSCs cultured as spheres in low-attachment plates after two passages were counter-stained with DAPI and immunostained with the NCSC markers P75 (A) and Sox10 (C), the NSC marker Nestin (B). Scale bars, 50  $\mu\text{m}$ . (D) DRG-NCSCs cultured as monolayer after five passages were counter-stained with the proliferation marker Ki67. Scale bar, 50  $\mu\text{m}$ . (E) Most cells had immunoreactivity to the NSC marker Nestin and the NCSC markers P75 and Sox10. (F) The proliferative ability of DRG-NCSCs at passage 1 and passage 5 over the course of 1-7 days. The proliferative ability was slightly decreased after four passages.



**Figure S2. Immunocytochemical analyses of the differentiation ability of DRG-derived NCSCs.** (A-B) Immunostaining of DRG-derived NSCs after exposure to neural differentiation medium for 12 days, with terminal differentiation into neurons and glial cells as recognized by antibodies of neuron markers NF200 and PGP9.5, respectively. Nuclei were counter-stained with DAPI. Scale bars, 100  $\mu$ m. (C) The proportions of Tuj1 and S100 $\beta$  cells showed that most cells had immunoreactivity to the neuron marker Tuj1.



**Figure S3.** The section staining showed that graft-derived EGFP<sup>+</sup> cells had immunoreactivity to pan neural marker Tuj1 at 2 weeks after implantation into the distal colon. Transverse sections of mouse colon were counterstained in blue with DAPI to identify cell nuclei. (A-D) The transverse section staining showed that most of EGFP<sup>+</sup> cells were Tuj1<sup>+</sup>. Scale bars, 100μm. (E) Most EGFP<sup>+</sup> cells were Tuj1<sup>+</sup> and fewer than 10% were S100β<sup>+</sup>.



**Figure S4. Exogenous DRG-NPs established synaptophysin with endogenous neurons and smooth muscle.** (A-D) Transplanted cells engrafted within the gut differentiated into Tuj1<sup>+</sup> neurons. Tuj1 labeled and EGFP<sup>-</sup> cells represented autologous enteric neural cells. Synaptophysin (SYP)-expressing vesicles are identified widely in the visual field and also overlapped with GFP and Tuj1-labeled cells. Some synaptophysin was expressed between GFP and Tuj1 double-labeled cells and Tuj1-only positive cells (D, arrow). This suggested that synaptophysin had been produced between exotic and endogenous neurons. Scale bars, 100 $\mu$ m. (E-H) The longitudinal section showed that exogenous DRG-NPs establish synaptophysin with smooth muscles in the intestine 3 weeks after transplantation. Transplanted EGFP<sup>+</sup> cells engrafted within the gut and smooth muscles were immuno-stained as SMA<sup>+</sup>. Synaptophysin-expressing vesicles are identified between exogenous EGFP<sup>+</sup> cells and SMA-labeled cells (H, arrow shows). Scale bars, 100 $\mu$ m. (H) The merged image from (E, F, and G) shows synaptophysin between the smooth muscles and exogenous EGFP<sup>+</sup> cells.