Supplementary data

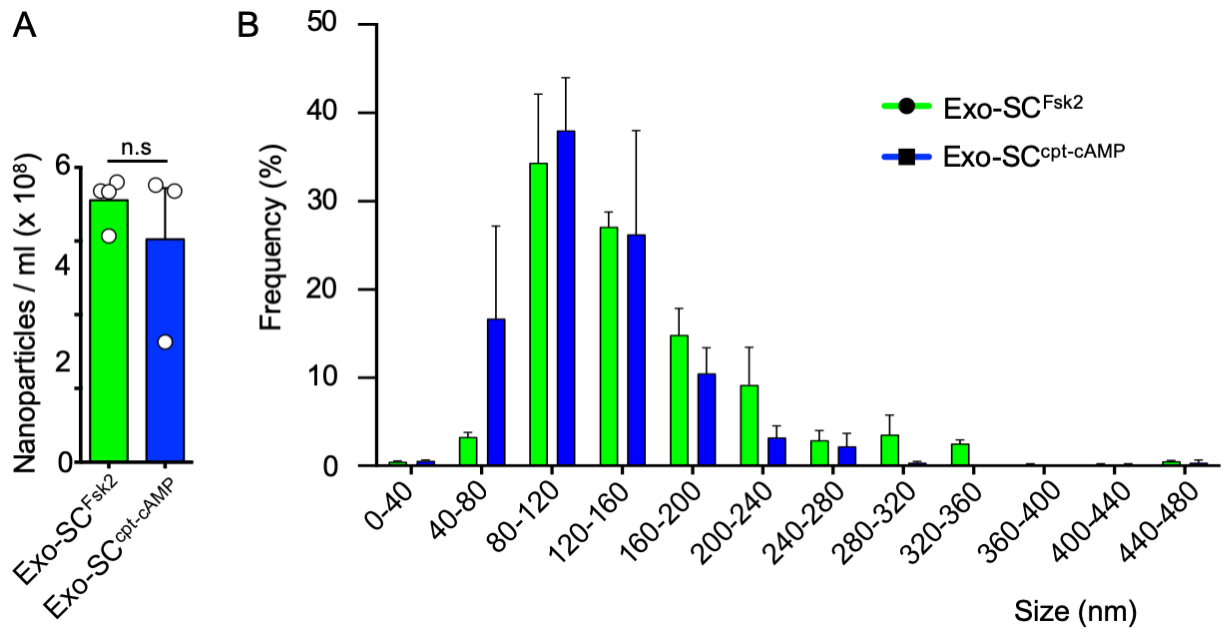

Figure S1. Quantitative comparison of exosomes derived from dSC and rSC. Schwann cell exosomes secreted by an equal number of 2 μM forskolin (Fsk2) or 250 mM cpt-cAMP treated Schwann cells were characterized by nanosigth. **(A)** Density of exosomes derived from dSC and rSC. **(B)** Size profile of exosomes derived from dSC and rSC**.** n.s., non-significant by two tailed t-test.

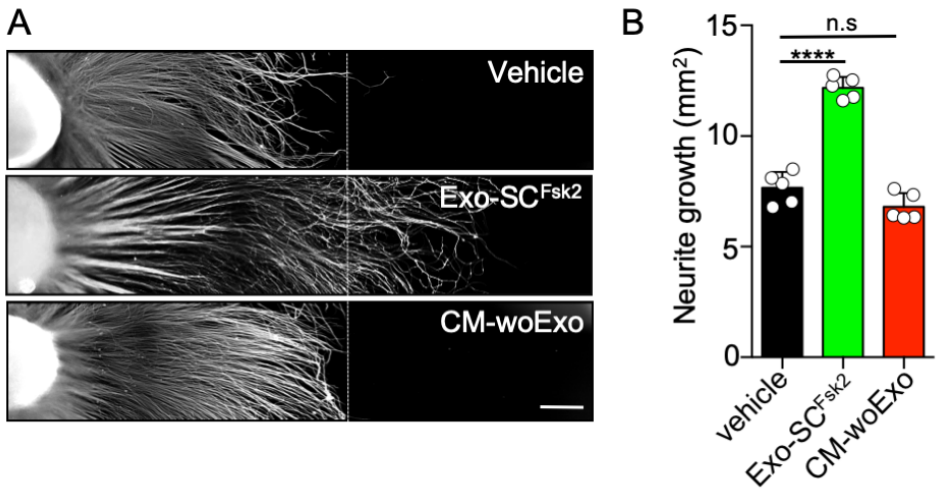

Figure S2. Neurite growth by rSC-exosomes versus rSC-conditioned medium (A) Neurite growth from DRG explants. Different treatments were daily administered per 3 days, including vehicle, exosomes from rSC (Exo-SC^{Fsk2}, 120 ng/ml) and rSC conditioned medium without exosomes (CM-woExo). After 3 days, DRG were visualized by acetylated tubulin immunostaining. Scale bar, 250 µm. **(B)** Neurite growth area was quantified by measuring the neurite growth area minus explant body area. Mean neurite growth of DRG neurons ± SEM, N=5; ****p<0.0001, n.s., non-significant by ANOVA test followed by Bonferroni post-test.

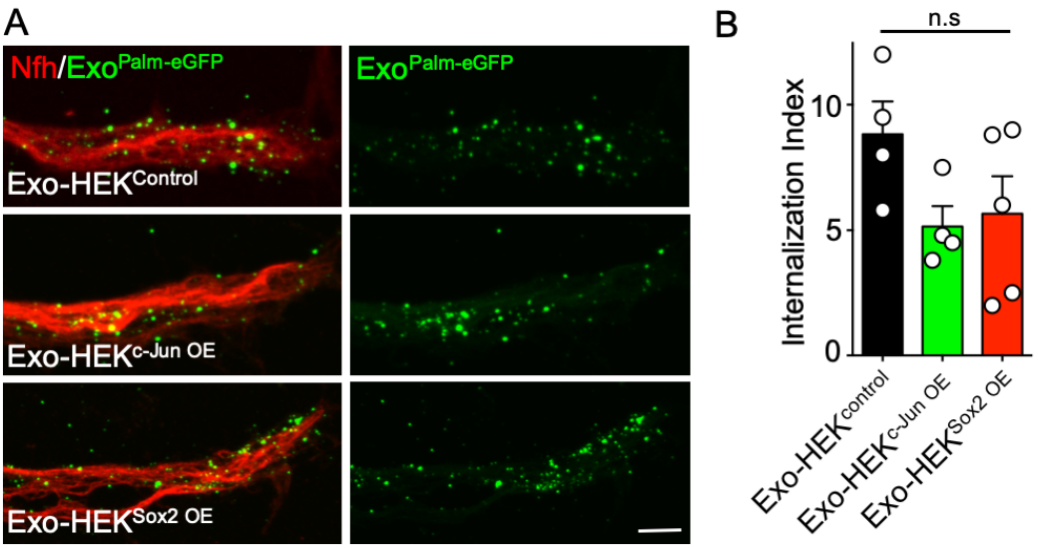

Figure S3. Internalization of HEK-derived exosomes by DRG neurons. (A) Exosomes were isolated from HEK cells transfected with CMV-Palm-eGFP to visualize exosomes and infected with pLenti-CMV-SOX2-P2A-GFP (NM_003106.3), pLenti-CMV-JUN-P2A-GFP (NM_002228) or an empty vector pLenti-CMV-Empty-P2A-GFP. DRG explants were treated with 5 µg of exosome-eGFP for 3 hours, washed and immunostained against neurofilament heavy chain (Nfh, red) and eGFP (green). Scale bar, 2 µm. **(B)** The internalization index was obtained from confocal images and deconvolutioned z-stack images by measuring the eGFP mean staining area colocalized with the Nfh staining. Internalization index from 5 neurites from 4 separate experiments. n.s., non-significant by two tailed t-test.

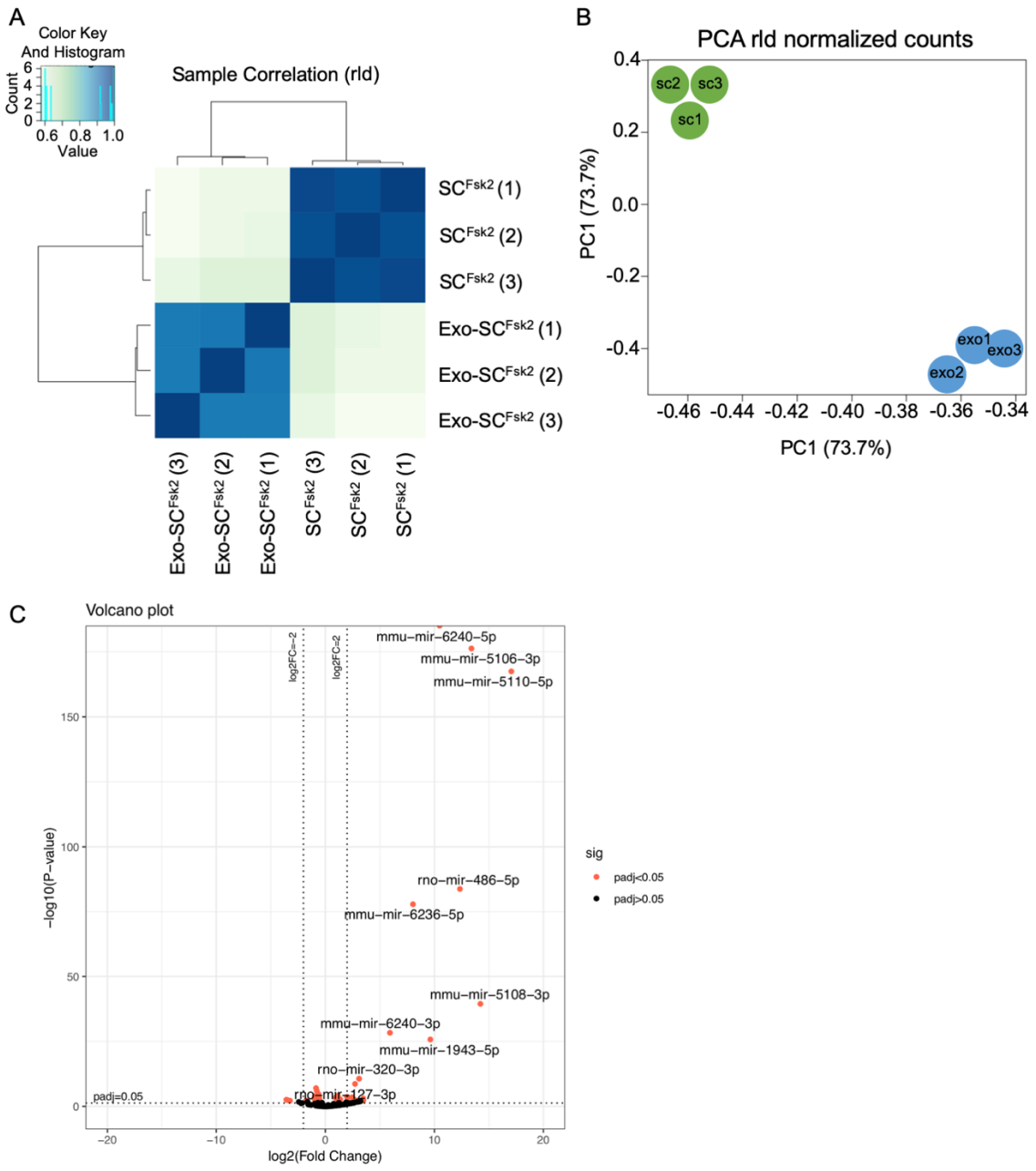

Figure S4. Small RNA-seq analysis of repair Schwann cells and their secreted exosomes. (**A**) Heat map of showing correlation between samples (Pearson's correlation coefficient) using expression levels of miRNAs. Sample labels Exo-SC are for exosomes and SC for Schwann cells. (**B**) Principal Component Analysis (PCA) of analyzed samples (Schwann cell samples in green and exosome samples in blue), indicating that miRNA expression was very different between samples (SC and exosomes). The percentage of variation in the data explained by the first and second principal component is indicated between brackets. **(C)** Volcano plot showing differentially expressed miRNAs from rSC exosomes compared to their cells of origin (rSC). Points are colored by significance. Genes with log2FoldChange < 0 and padj < 0.05 were considered differentially expressed.

Cell type	Condition	Cell count	Conditioned media, CM (ml)	Protein amount in the exosome fraction from 10ml of CM (µg/ml)	Number of exosome particles in 12 ng
Schwann Cells	Fsk 2 µM	2×10^6	10	32.10 ± 7.48	$3.55 \times 10^8 \pm 3.55 \times 10^7$
	cpt-cAMP	2×10^6	10	18.24 ± 5.34	$3.16 \times 10^8 \pm 3.52 \times 10^7$
HEK overexpression	c-Jun	4×10^6	10	95.83 ± 27.11	$5.05 \times 10^8 \pm 3.67 \times 10^7$
	Sox2	4×10^6	10	125.44 ± 24.33	$4.39 \times 10^8 \pm 2.68 \times 10^7$
	Empty	4×10^6	10	131.15 ± 30.40	$6.89 \times 10^8 \pm 2.19 \times 10^7$

Table S1. Relationship between protein content and number of exosome particles per condition. Exosomes isolated from 10 ml of conditioned medium from dSC, rSC, and HEK cells overexpressing c-Jun, Sox2 and empty vector were analyzed measuring protein amounts and the number of particles by nanosigth. After protein quantification by BCA method (described in the materials and methods section), exosomes were normalized to stock concentration of 12 ng/µl. The same preparations were analyzed by nanosigth to determine the particles concentration per volume.