

Supplementary Data

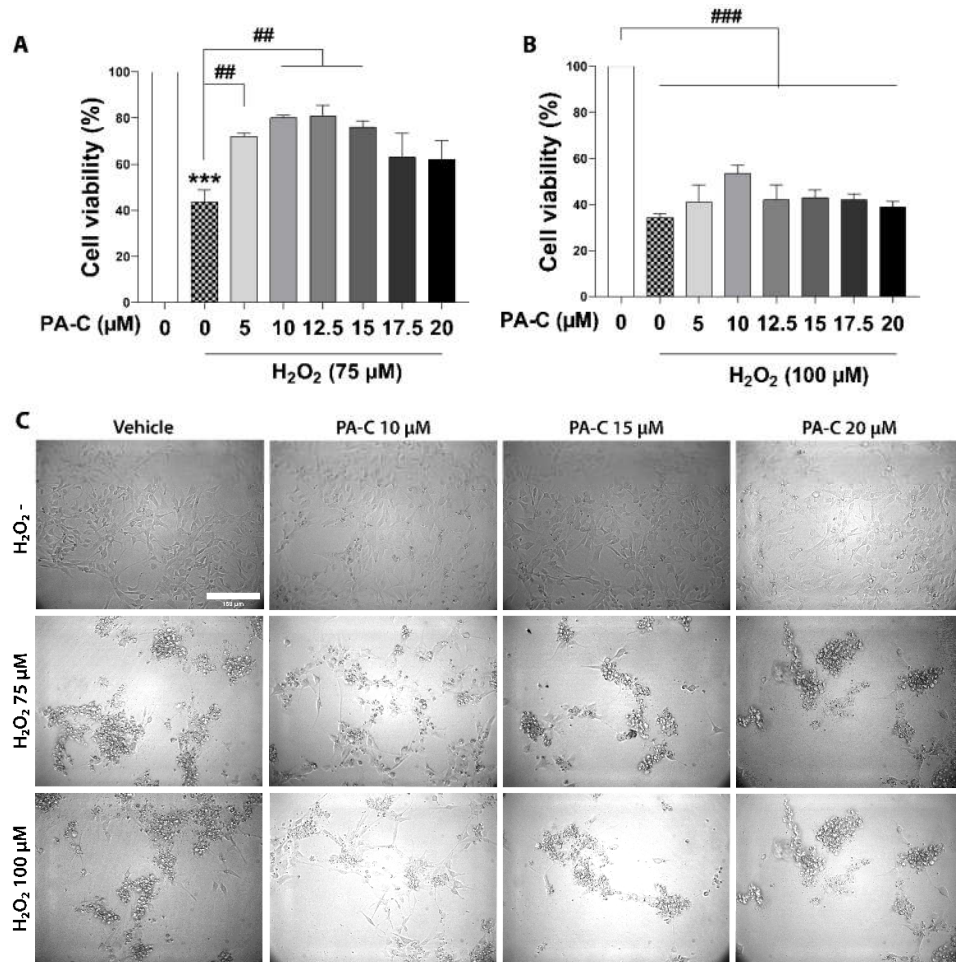


Figure S1. PA-C Protects Against H₂O₂-induced Cytotoxicity in iPSC-NSC. **A** and **B**. MTS viability assay analysis. iPSC-NSC were pre-treated with increasing concentrations of PA-C (5, 10, 12.5, 15, 17.5, and 20 μM) for 30 min and then incubated with 75 μM H₂O₂ (**A**) or 100 μM H₂O₂ (**B**) for 24 h. **C**. Representative bright-field images of the iNSC morphology after pre-treatment and cytotoxicity induction with H₂O₂ (scale bar = 150 μm). Data expressed as mean ± S.E.M. (of three independent experiments) determined by one-way ANOVA with Tukey's multiple comparison test. ***p<0.001 vs control; **p<0.01, ***p<0.001 as indicated.

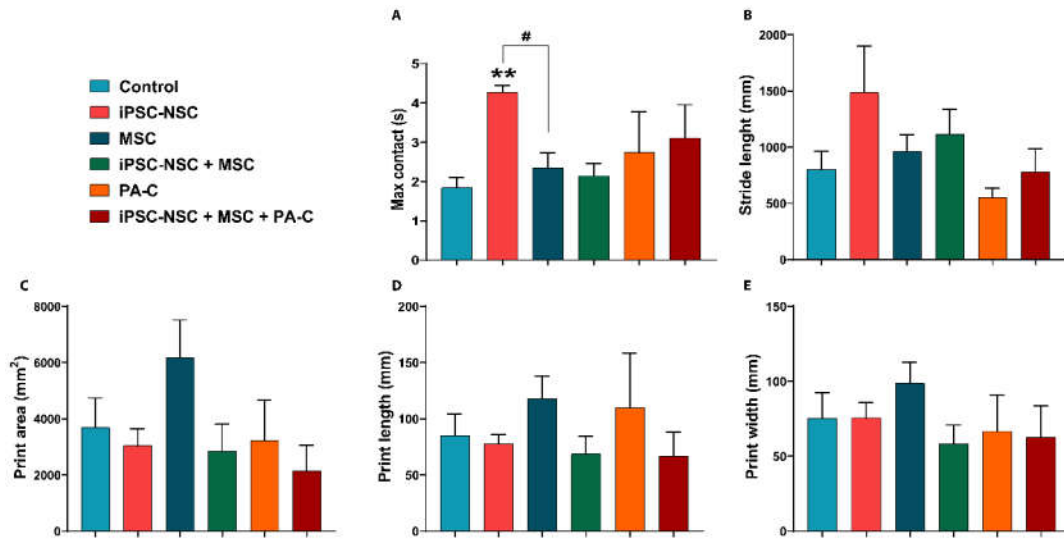


Figure S2. Catwalk Gait Analysis. Quantification of maximum contact (A), stride length (B), print area (C), print length (D), and print width (E) of the hind limbs for each experimental group. Data are expressed as mean \pm S.E.M. determined by one-way ANOVA with Tukey's multiple comparison test (* $p < 0.01$ v control; # $p < 0.05$ as indicated).

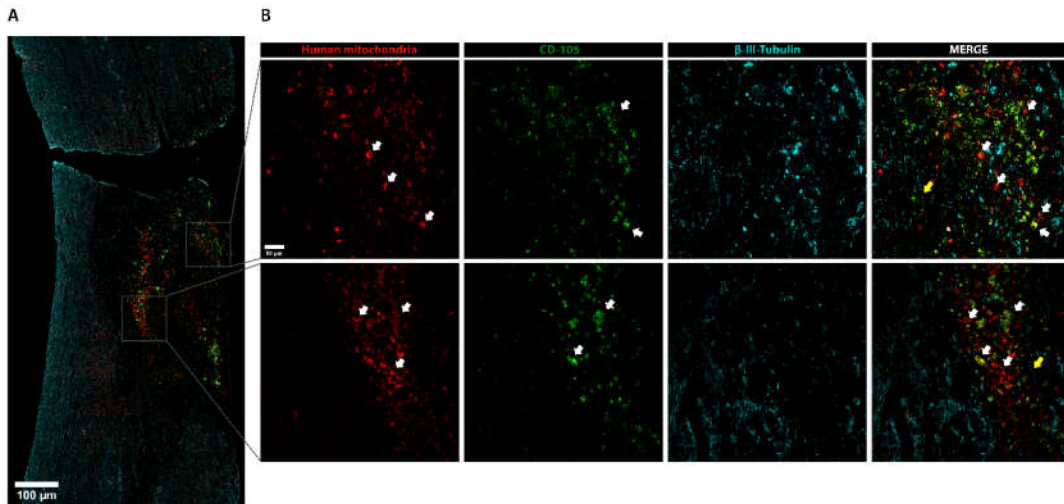


Figure S3. Long Term Survival of Stem Cells Transplants in the Injured Spinal Cord. A. Immunofluorescent longitudinal spinal cord section (including the injury) of ̢-III-Tubulin (blue), human mitochondria (red), and CD-105 (green) at nine weeks post-SCI (scale bar = 150 μ m). B. Enlarged immunofluorescent images for human mitochondria (red), CD-105 (green), ̢-III-Tubulin (blue), and merge showing the cell grafts eight weeks post-transplantation. White arrows identify human transplants - co-localization of staining for human mitochondria (red) and CD-105 (green) identify MSCs while staining for human mitochondria (red) correspond to iNSC. Yellow arrows indicate ̢-III-Tubulin fibers surrounding cell grafts - staining for human mitochondria (red) alone corresponds to iPSC-NSC.

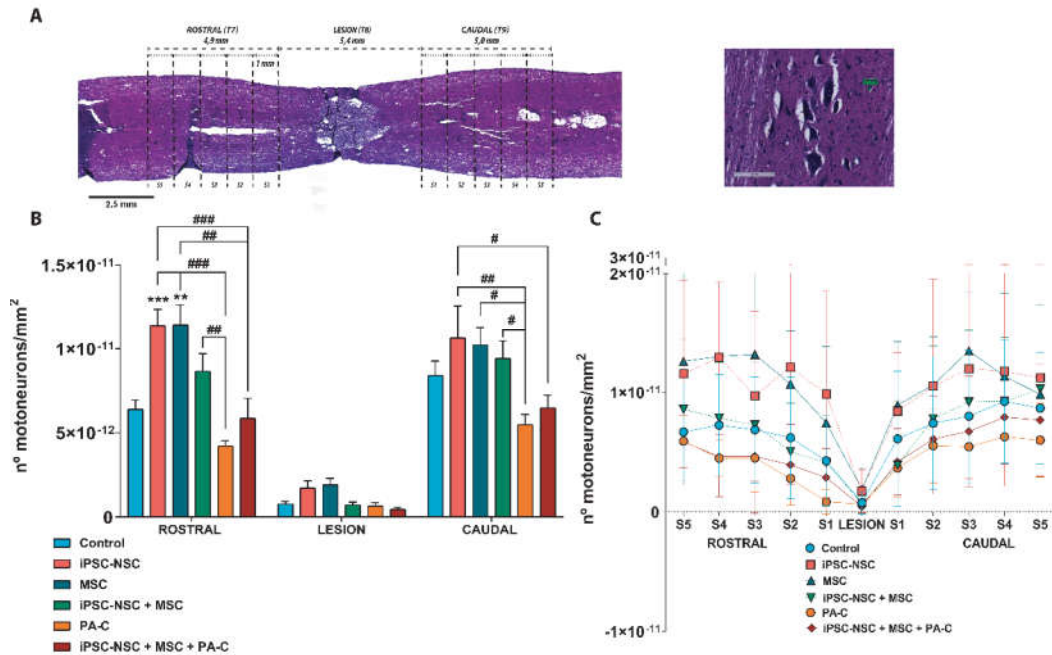


Figure S4. Individual iPSC-NSC and MSC Transplantation Increases Motoneuron Preservation. **A.** (Left Panel) H/E staining of a longitudinal spinal cord section (including the injury) showing a scheme of the thoracic spinal sections (left panel; scale bar = 2.5 mm). We considered T8 as the epicenter of the lesion and the adjacent sections, both rostral and caudal, as T7 and T9, respectively. Moreover, we considered motoneurons as polygonal cells with a diameter of $\geq 20 \mu\text{m}$ (right panel; scale bar = 200 μm). **B.** Quantitative analysis of the motoneuron preservation in the rostral site (T7), lesion (T8), and caudal site (T9). Data (represented as MN/mm²) expressed as mean \pm S.E.M. determined by two-way repeated-measures ANOVA test (Control n=7; iPSC-NSC n=3; MSC n=3; iPSC-NSC+MSC n=7; PA-C n=4; iPSC-NSC+MSC+PA-C n=4). **C.** Overall distribution of motoneurons in the subsections (1 mm) along the spinal cord (represented as MN/mm²). **p<0.01, ***p<0.001 vs. control; #p<0.05, ##p<0.01, ###p<0.001 as indicated.

Table S1. *In vitro* effects of 24 h 10 μM PA-C treatment on genes involved in neurogenesis, cell cycle, or apoptosis in iPSC-NSC (entire data set including non-significant changes). Gene profiling analysis was performed with the RT2 Profiler PCR Array, and statistical analysis was performed with the RT2 Profiler RT-PCR Array Data Analysis program. Between-group (treatment vs. control) gene expression differences were evaluated using Student's t-tests from three independent experiments. *p<0.05 vs. control.

Gene	2 ⁻ ΔCt (PA-C)	2 ⁻ ΔCt (Control)	Fold Change PA-C /Control	Student's t-test p-value
ACHE	0.00192772	0.002428775	0.793700526	0.658533174
ADORA1	0.000409962	0.000911867	0.449585268	0.352218187
ALK	0.023000002	0.018170952	1.265756594	0.579864627
APBB1	0.050922408	0.092854209	0.54841249	0.106907649
APOE	0.068130492	0.076121323	0.895025071	0.688202674

<i>APP</i>	0.223928663	0.235605389	0.950439478	0.622268867
<i>ARTN</i>	0.001298544	0.001021174	1.271619166	0.865172281
<i>ASCL1</i>	0.019030331	0.010080967	1.887748625	0.533465017
<i>BDNF</i>	0.01641446	0.009919234	1.654811245	0.460038503
<i>BMP8B</i>	0.030701319	0.073189362	0.419477887	0.262706729
<i>CDK5R1</i>	0.003802361	0.004327585	0.878633452	0.488463785
<i>CDK5RAP2</i>	0.020680924	0.018087178	1.143402487	0.533871905
<i>CHRM2</i>	0.040510633	0.035266555	1.148698355	0.665921593
<i>CREB1</i>	0.176097269	0.212339466	0.829319546	0.518084902
<i>DCX</i>	0.00132277	0.006790708	0.194791145	0.348093365
<i>DLG4</i>	0.009340903	0.02006898	0.465439858	0.126582525
<i>DLL1</i>	0.156884832	0.196297147	0.79922115	0.467585629
<i>DRD2</i>	0.016490487	0.068604377	0.240370763	*0.049718167
<i>DVL3</i>	0.003882256	0.005254531	0.73883972	0.653697493
<i>EFNB1</i>	0.001109745	0.00867519	0.127921736	0.348145231
<i>EP300</i>	0.171678083	0.361260421	0.475219739	0.086259627
<i>ERBB2</i>	0.030418886	0.012848803	2.367448977	0.779168253
<i>FGF2</i>	0.681968864	0.473393273	1.440596862	0.965849939
<i>FLNA</i>	0.069884248	0.076650789	0.911722489	0.576845193
<i>GDNF</i>	0.675695169	0.56950396	1.186462635	0.703897519
<i>GPI</i>	0.043619321	0.013518802	3.226567037	0.598364595
<i>GRIN1</i>	0.038860397	0.095024573	0.408951029	0.216262202
<i>HDAC4</i>	1.095136811	1.694795392	0.646176415	0.240166645
<i>HES1</i>	0.003724109	0.003153372	1.180992661	0.476145939
<i>HEY1</i>	0.008019777	0.011367912	0.705474904	0.489747437
<i>HEYL</i>	0.000495479	0.00080677	0.614151575	0.389667921
<i>MAP2</i>	0.125966421	0.178143421	0.707106781	0.077775819
<i>MDK</i>	0.114846419	0.073868911	1.554732811	0.749561769
<i>MEF2C</i>	0.008496657	0.003882256	2.188587403	0.651603344

<i>KMT2A</i>	0.000713785	0.000430344	1.658639092	0.903462276
<i>NEUROD1</i>	0.138163117	0.042133486	3.279175994	0.379843798
<i>NEUROG1</i>	2.101050897	3.274128878	0.641712949	0.401714671
<i>NF1</i>	0.180630211	0.201350056	0.897095409	0.565662024
<i>NOG</i>	0.223411875	0.222381875	1.004631674	0.754971384
<i>NOTCH1</i>	0.239446919	0.301684214	0.793700526	0.519147421
<i>NOTCH2</i>	0.011553265	0.015745803	0.733736182	0.550108561
<i>NR2E3</i>	0.002178843	0.001836419	1.186462635	0.433930202
<i>NRCAM</i>	0.014355802	0.022012159	0.652176035	0.343705044
<i>NRG1</i>	0.215801647	0.106169733	2.032609864	0.536412342
<i>NRP1</i>	0.00051652	0.003793586	0.136156082	0.359897344
<i>NRP2</i>	0.17128188	0.077900574	2.198724227	0.923509888
<i>NTF3</i>	0.091575857	0.137844261	0.664342907	0.439514693
<i>NTN1</i>	0.805400224	0.796149413	1.01161944	0.850833706
<i>TENM1</i>	0.178143421	0.078442416	2.271008858	0.410433009
<i>OLIG2</i>	0.013301915	0.02006898	0.662809721	0.491608264
<i>PARD3</i>	0.704389078	0.618899807	1.138131035	0.822883605
<i>PAX3</i>	0.058224808	0.064903696	0.897095409	0.626583097
<i>PAX5</i>	0.02186011	0.033210374	0.65823136	0.570348282
<i>PAX6</i>	0.214806732	0.039676936	5.413894097	0.716219398
<i>POU4F1</i>	0.013487603	0.008360343	1.613283518	0.711368252
<i>PTN</i>	0.257226487	0.033210374	7.745365568	0.780513573
<i>RAC1</i>	0.00356416	0.002621202	1.359742373	0.474356553
<i>RTN4</i>	0.581470448	0.481111918	1.208597056	0.806057704
<i>S100A6</i>	0.44476375	0.34814924	1.277508892	0.964490187
<i>S100B</i>	3.184597652	3.214166008	0.990800613	0.906197452
<i>SHH</i>	0.002276623	0.008939714	0.254663952	0.399013848
<i>SLIT2</i>	0.904031185	0.206533032	4.377174805	0.712670311
<i>SOD1</i>	0.010655763	0.01800379	0.591862244	0.344690673

<i>SOX2</i>	0.000518912	0.000597452	0.868541486	0.747178997
<i>SOX8</i>	0.68989296	0.470123307	1.467472363	0.621816567
<i>STAT3</i>	0.022165265	0.017310339	1.280463977	0.476661094
<i>TGFB1</i>	0.518031277	0.518031277	1	0.806155891
<i>TH</i>	0.000818032	0.00085672	0.954841604	0.721578193
<i>TNR</i>	0.095464696	0.142047411	0.6720622	0.68573148
<i>VEGFA</i>	0.883383084	0.770808531	1.146047362	0.841497866