

Supplementary Notes

Electrical Stimulation Optimization

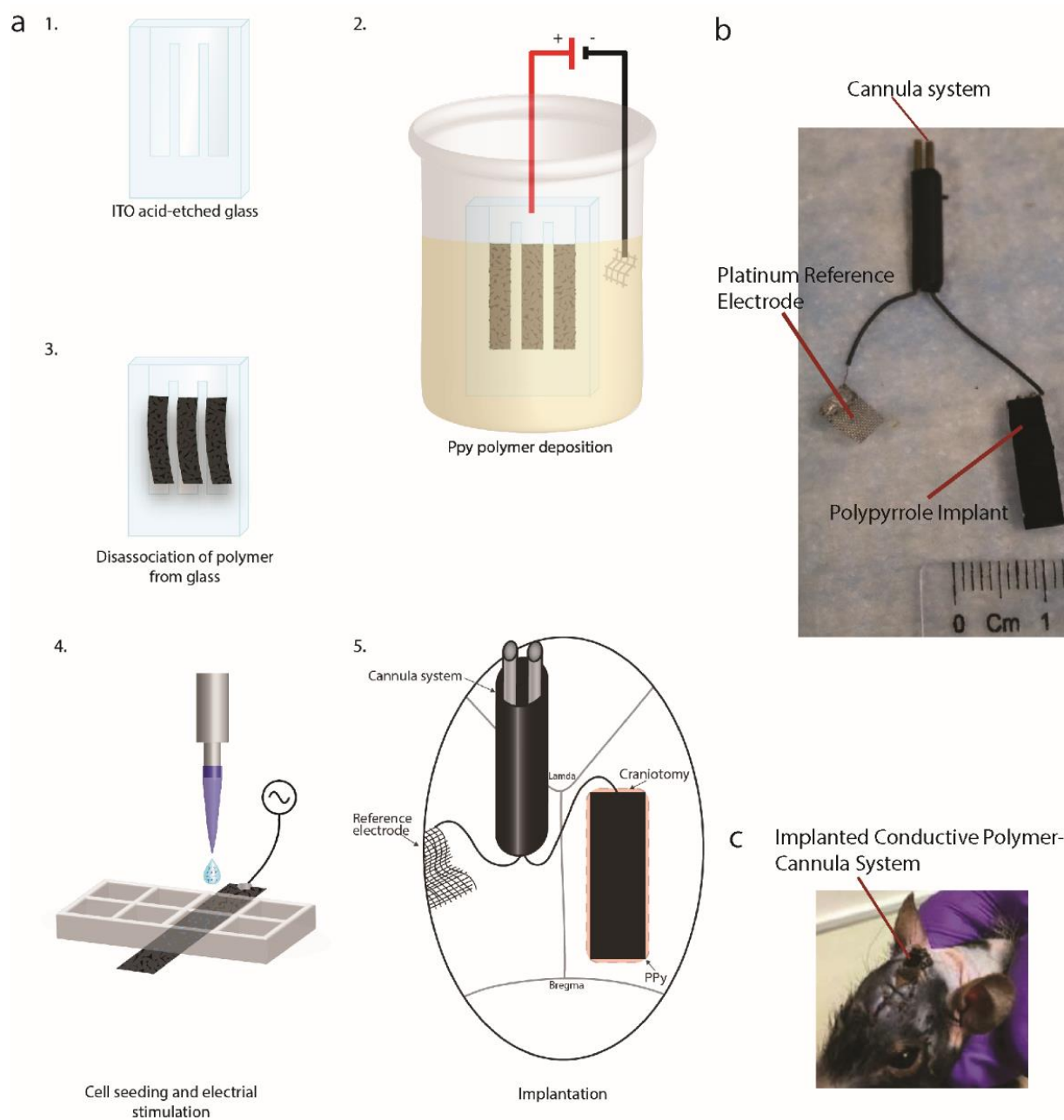
Previous *in vitro* stimulation of NPCs showed changes in VEGFA¹. Using VEGFA as a gene of interest, we electrically stimulated the cells across various voltages ($\pm 200\text{mV}$, 400mV , or 800mV square wave) and frequencies (100 and 200Hz) and monitored the response of VEGFA (Supplementary Fig. 2a). Given that the largest change in VEGFA expression was observed with electrical stimulation of $\pm 800\text{mV}$ at 100Hz, we used these stimulation parameters for our *in vitro* and *in vivo* stimulation paradigms. Under these parameters, cell viability was assessed with Alamar Blue and Live/Dead staining (Supplementary Fig. 2b-d). These viability assays demonstrated that cell viability did not significantly change with electrical stimulation.

Stroke Size Evaluation

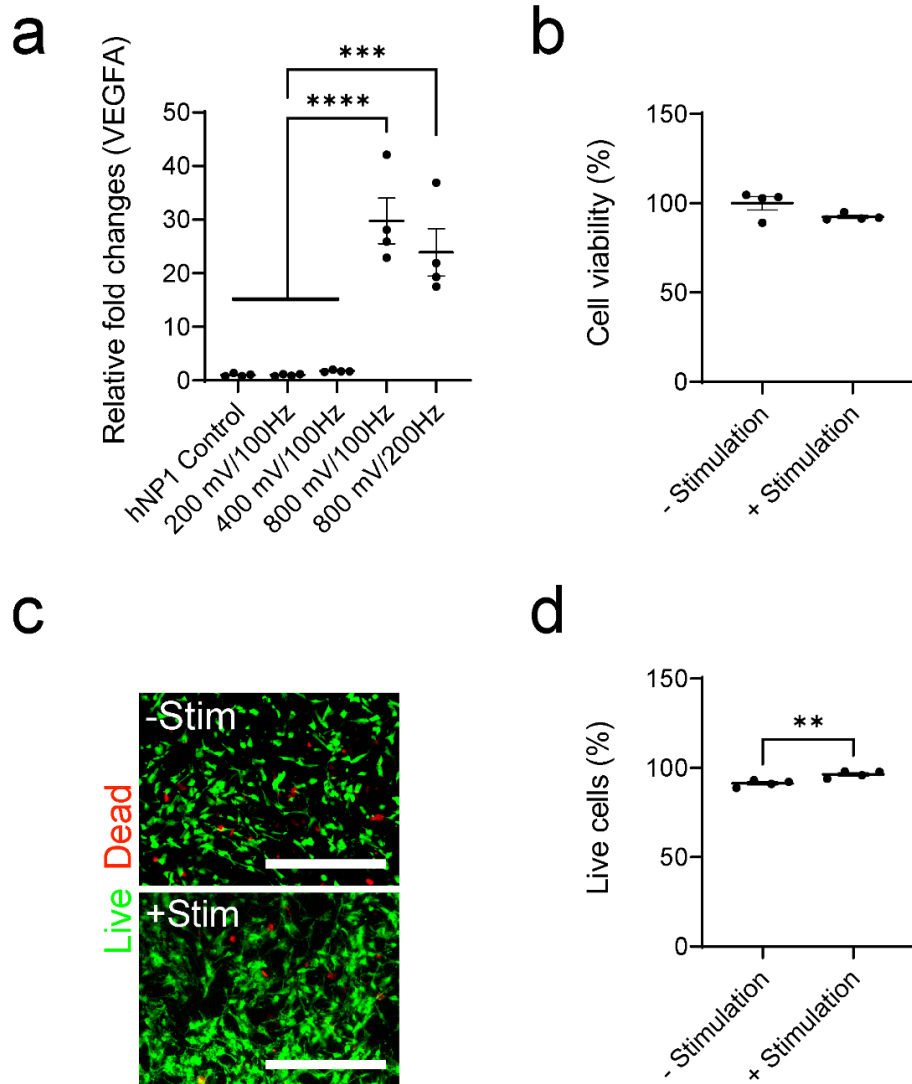
The stroke size was evaluated at 6 weeks post-stroke. Given that interventions were performed 1-week post-stroke, any potential neuroprotective effects that reduce stroke size were highly unlikely. Consistent with this, no significant difference in stroke sizes were observed between any of the groups in our experiments (Supplementary Figs. 6 and 17).

Stroke and Peri-infarct Cell Analysis

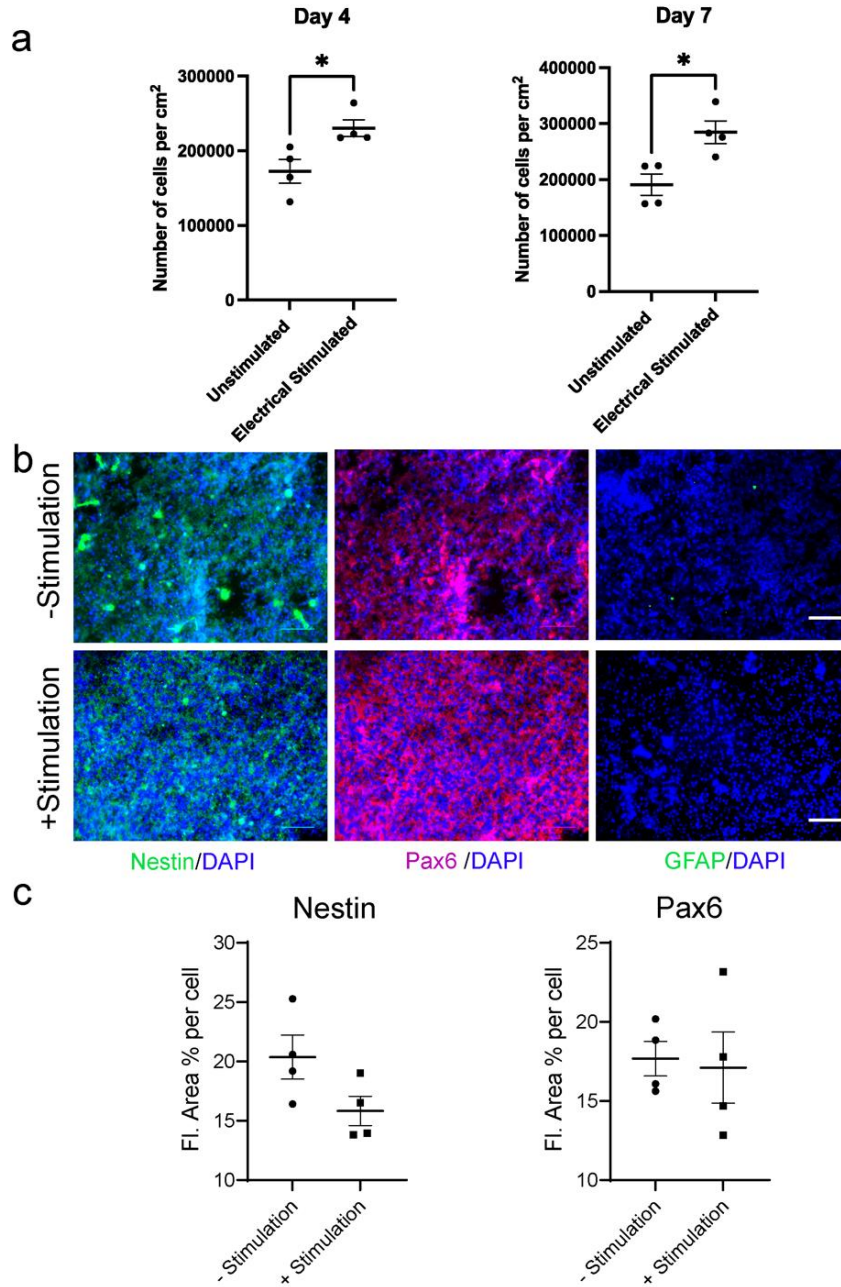
To assess further influences of the combined electrical stimulation and stem cell therapies, we evaluated cell type in the peri-infarct and stroke regions. At the 6-week post-stroke time point, no change in the number of neurons or glia in the stroke or peri-infarct regions were observed (Supplementary Fig. 10).



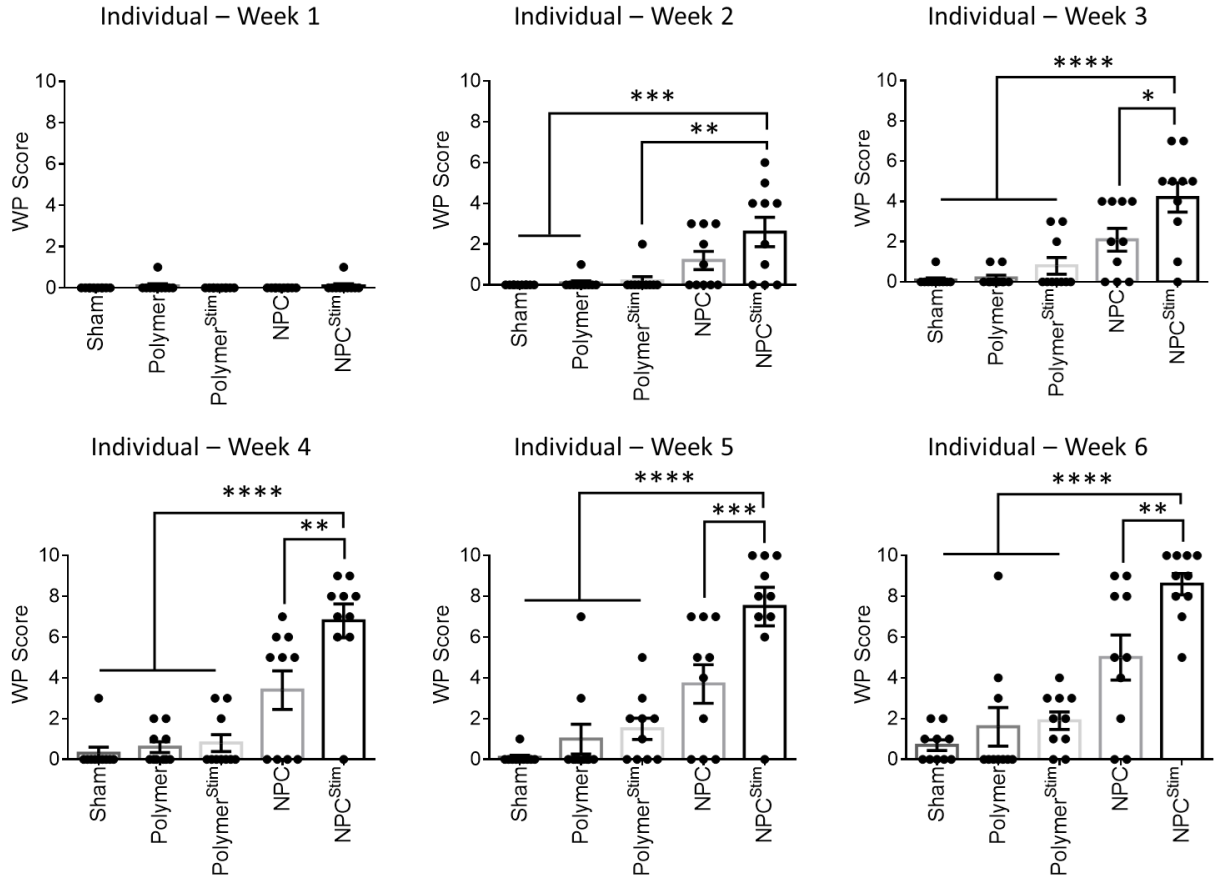
Supplementary Fig. 1 Conductive-Polymer stem cell system. **a**, Schematic fabrication of implantable conductive polymer-stem cell system (PPY – polypyrrole scaffold). **b**, Photograph of cannula system. **c**, Photograph of animal with cannula in place.



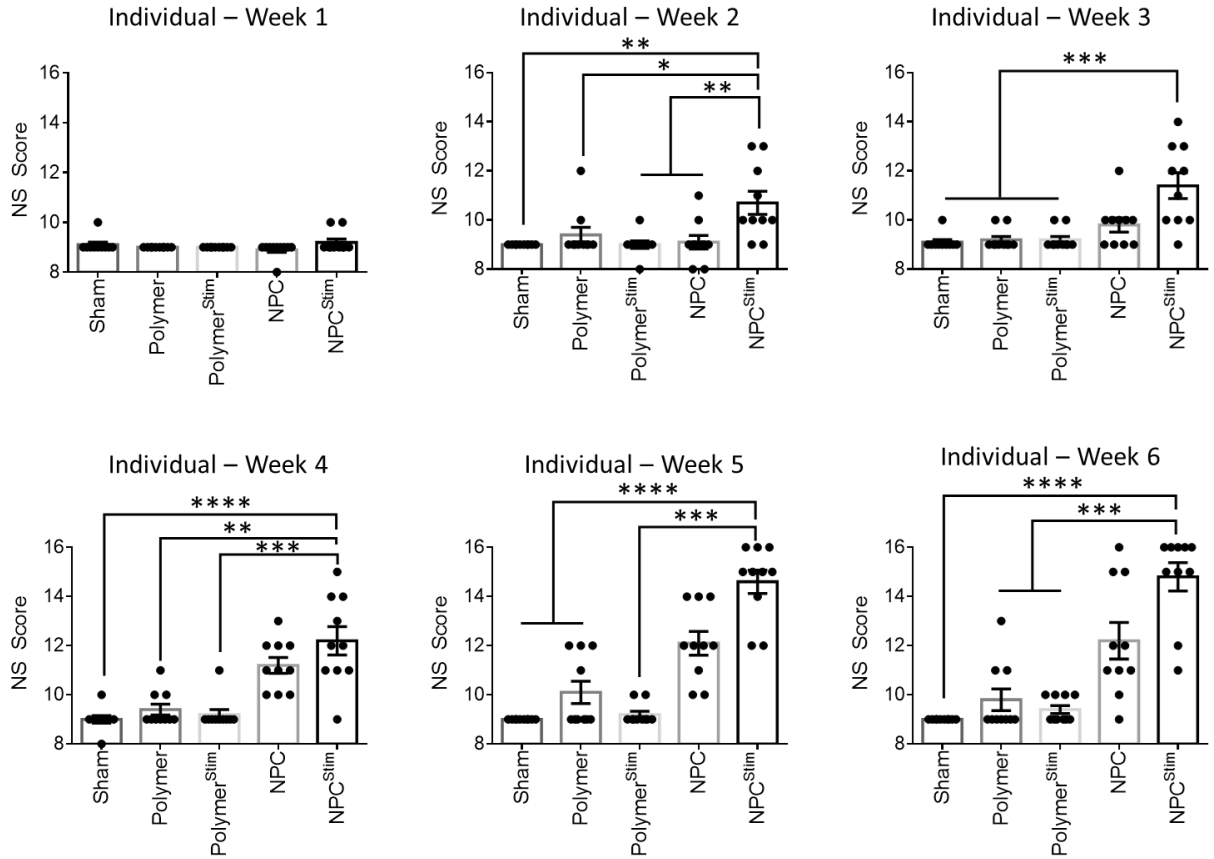
Supplementary Fig. 2 Optimization of electrical stimulation parameters on NPCs. **a**, NPCs expressed significantly higher VEGFA in the 800mV/100Hz and 200Hz stimulations for 1 hr. *** indicates statistical significance compared to control ($P < 0.001$, data shown as mean \pm SEM, $n = 4$). **b**, Cell metabolic viability assay measured via Alamar Blue showing no difference in cell survival between stimulated and unstimulated cells at 800mV with 100 Hz frequency for 1 hr (data shown as mean \pm SEM, $n = 4$). **c**, Representative images of fluorescently-labeled cells stained using a live/dead assay kit. Green (calcein AM) and red (ethidium homodimer-1) indicate viable and dead cells, respectively. Scale bar indicates 100 μ m. **d**, Quantification of the percentage of live cells from live/dead assay (in fig. 2c) showing no significant difference in living cells after electrical stimulation (800mV at 100Hz for 1 hr, data shown as mean \pm SEM ($n = 4$)). **a**, **b**, **d**. Analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test with ** $P < 0.01$, *** $P < 0.001$ and **** $P < 0.0001$.



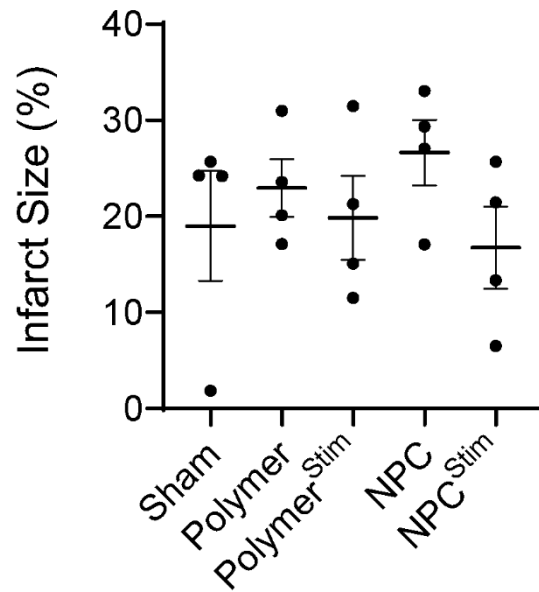
Supplementary Fig. 3 Impact of electrical stimulation on NPC biology. **a**, NPCs proliferated significantly when electrically stimulated compared to un-stimulated groups for at least 7-days. * indicates a statistically significant difference with p -value < 0.05 when analyzed using an unpaired two-tailed t -test. Data shown as $\text{mean} \pm \text{SEM}$, $n=4$. **b**, Representative images of fluorescently-labeled cells stained for mature mitotic markers – Nestin and Pax6, and glial marker – GFAP. Blue represents nucleus. Scale bar indicates $100 \mu\text{m}$. (Data shown as $\text{mean} \pm \text{SEM}$, $n=4$) **c**, Quantification of percentage area under fluorescence per cell from histology (in fig. 2b) showing no significant difference in Nestin and Pax6 after electrical stimulation (800mV at 100Hz for 1hr , data shown as $\text{mean} \pm \text{SEM}$, $n=4$). There were no countable number of cells that stained for GFAP. Analyzed using an unpaired t -test with a two-tailed p -value > 0.05 .



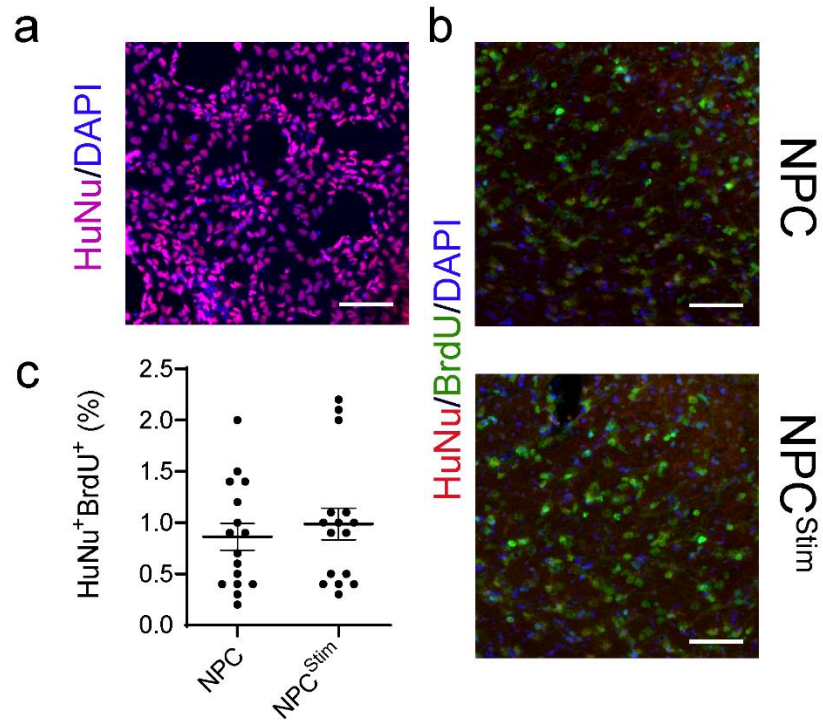
Supplementary Fig. 4 Conductive-Polymer stem cell system improves functional stroke recovery. Vibrissae-forepaw (WP) behavioral testing for individual weeks. NPC^{Stim} group exhibits improved recovery starting at as early as 1-week post stimulation (2-weeks post-stroke) compared to control. Analyzed using log-transform two-way repeated measures ANOVA followed by Dunnett’s multiple comparisons test, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, data shown as mean±SEM, n=10 per group.



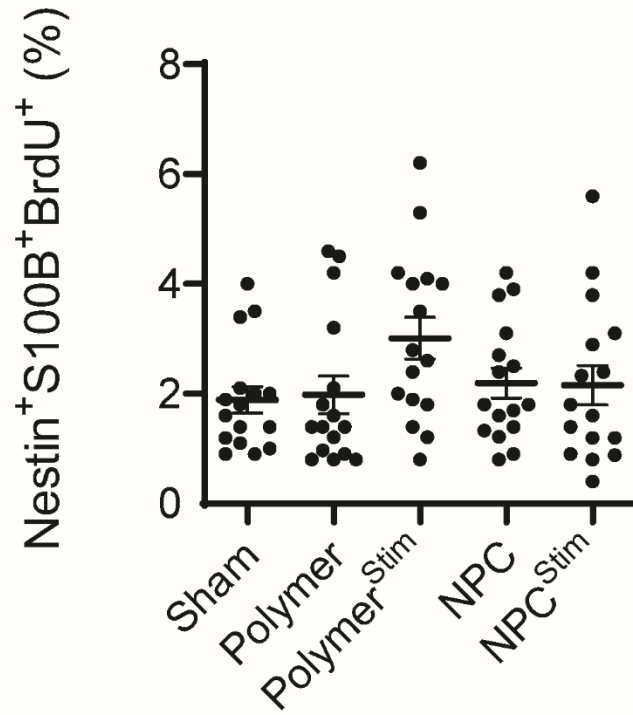
Supplementary Fig. 5 Total neurological score (NS) testing. Neurological score (NS) behavioral testing for individual weeks. NPC^{Stim} group exhibits improved recovery starting as early as 1-week post stimulation (2-weeks post-stroke) compared to control. Analyzed using Kruskal-Wallis followed by Dunn's multiple comparisons test, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, data shown as mean \pm SEM, n=10 per group)



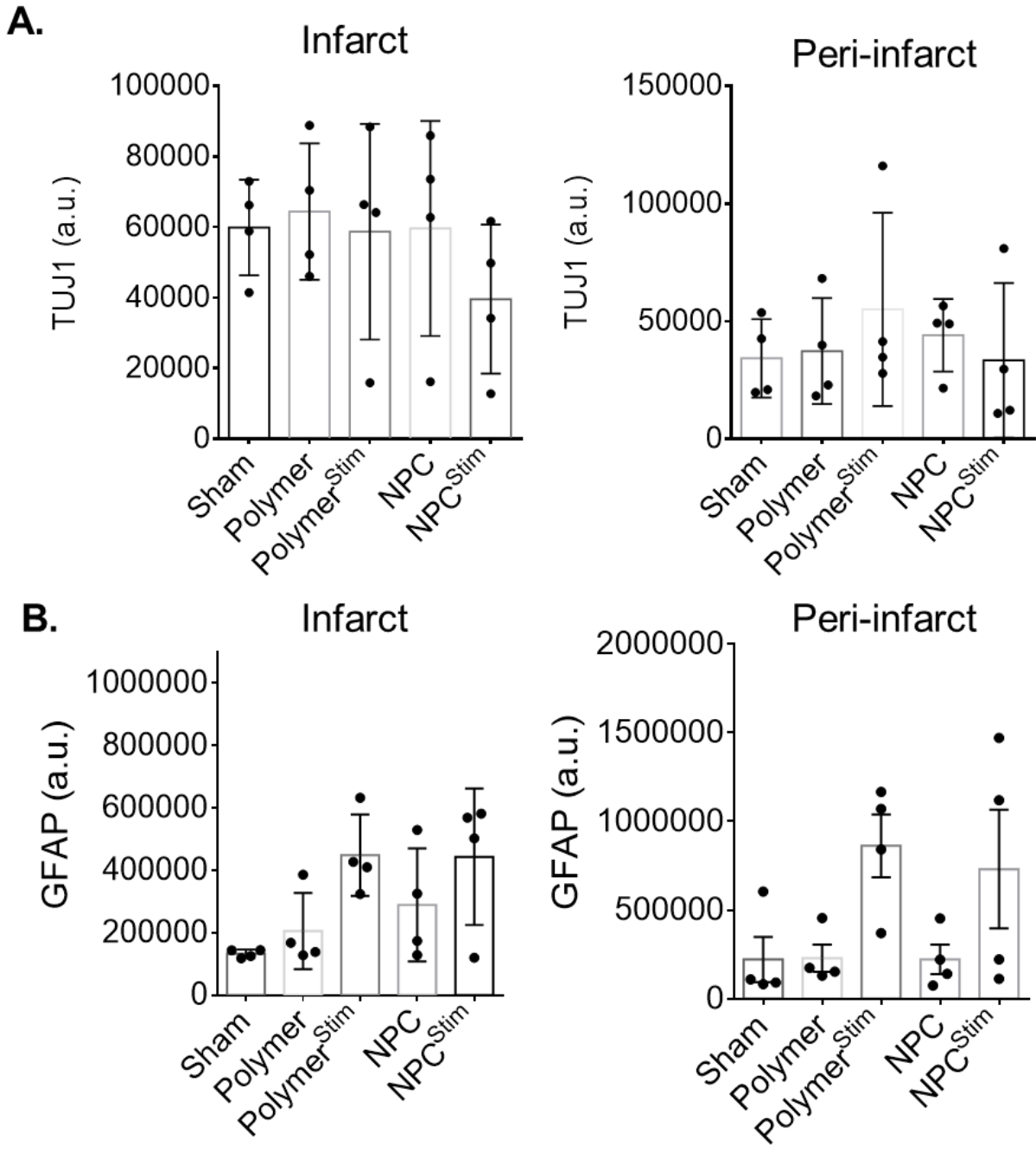
Supplementary Fig. 6 Infarct size. Percentage calculation of infarct size for Sham, Polymer, Polymer^{Stim}, NPC, and NPC^{Stim} animal groups. There were no statistically significant differences between any group. Analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test, data shown as mean±SEM, n=4 per group.



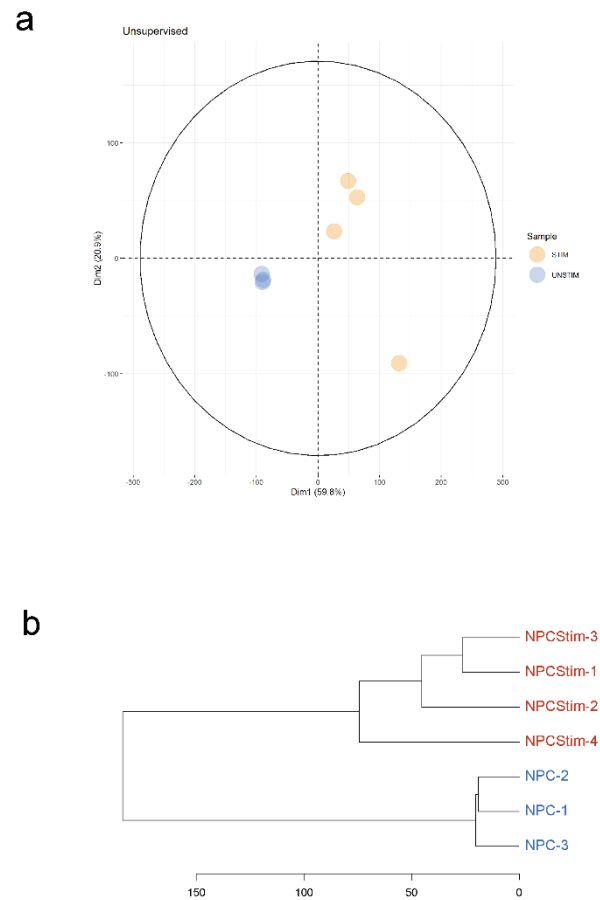
Supplementary Fig. 7 Neural stem cell characterizations. **a**, The human neural stem cells stain well for human nuclear stain (HuNu) *in vitro*. **b**, Representative images of brain slices stained for HuNu (red), BrdU (green) and DAPI (blue). Scale bar indicates 100 μ m. **c**, Cell count analysis for HuNu⁺BrdU⁺ cells in the peri-infarct region of the brain slices showing that around 1% of BrdU⁺ cells stained for HuNu⁺. Analyzed using an unpaired t-test with a two-tailed p-value > 0.05, data shown as average \pm SEM, n=16 images/4 rats.



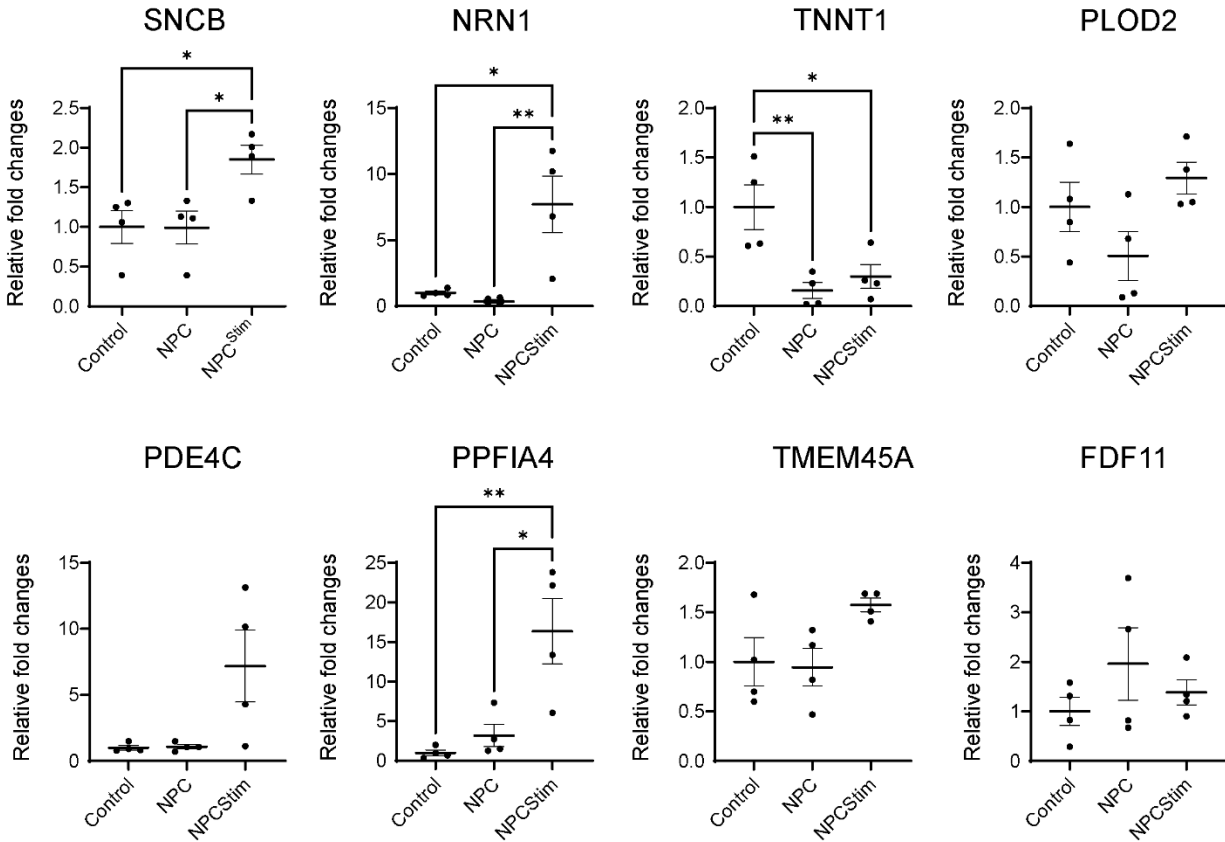
Supplementary Fig. 8 Cell count analysis of co-labeled post-stroke brain slices. Cell counts of Nestin⁺/S100B⁺/BrdU⁺ cells in the peri-infarct (PI) tissue. There were no statistically significant differences between any group. Analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test, data shown as average \pm SEM, n=16 images/4 rats.



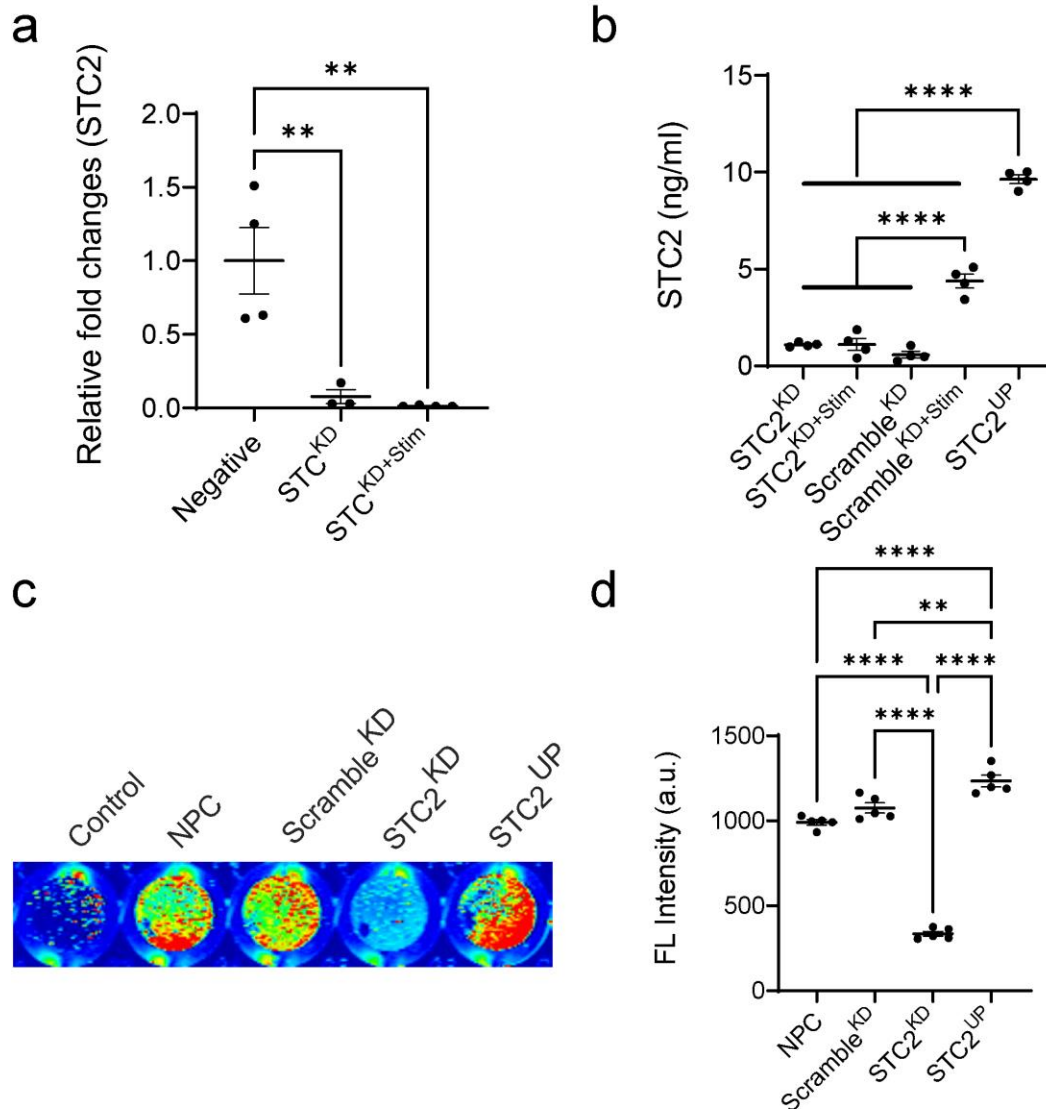
Supplementary Fig. 10 Quantification of neuronal and glial staining at 6 weeks post-stroke. Quantification of area of **a**, TUJ1 and **b**, GFAP staining in brain tissue at the infarct and peri-infarct region at the 6-week time point (a.u. = arbitrary units; data shown as mean±SEM, n=4, analyzed using a one-way ANOVA, followed by Tukey’s HSD post hoc test).



Supplementary Fig. 11 Transcriptome Analysis. a, Unsupervised principal component analysis (PCA) of unstimulated (blue, NPC) and electrically stimulated (red, NPC^{Stim}) neural progenitor cells showing separation of groups. **b**, Unsupervised hierarchical clustering of unstimulated and electrically stimulated NPCs.

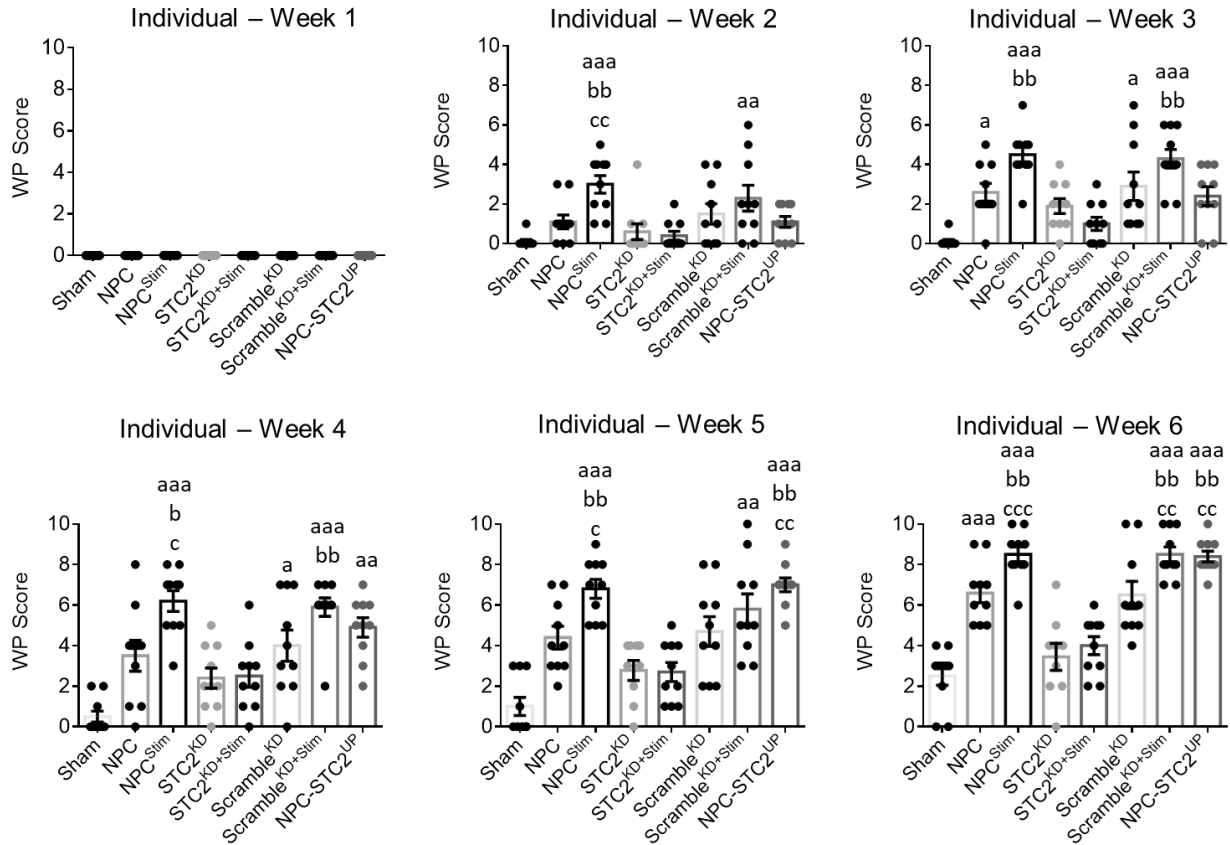


Supplementary Fig. 12 Transcriptome verification with qRT-PCR. qRT-PCR data indicated that electrical stimulation augmented the expression of SNCB, NRN1, TNNT1, PDE4C, PPFIA4, and TMEM45A in NPCs. PLOD2 and FGF11 did not demonstrate augmentation with electrical stimulation. These genes were verified from transcriptome analyses. ** and * indicate statistical significances compared to control and cells with no electrical stimulation (NPC). Analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test with ** $P < 0.01$ and * $P < 0.05$, data shown as mean \pm SEM, $n=4$.

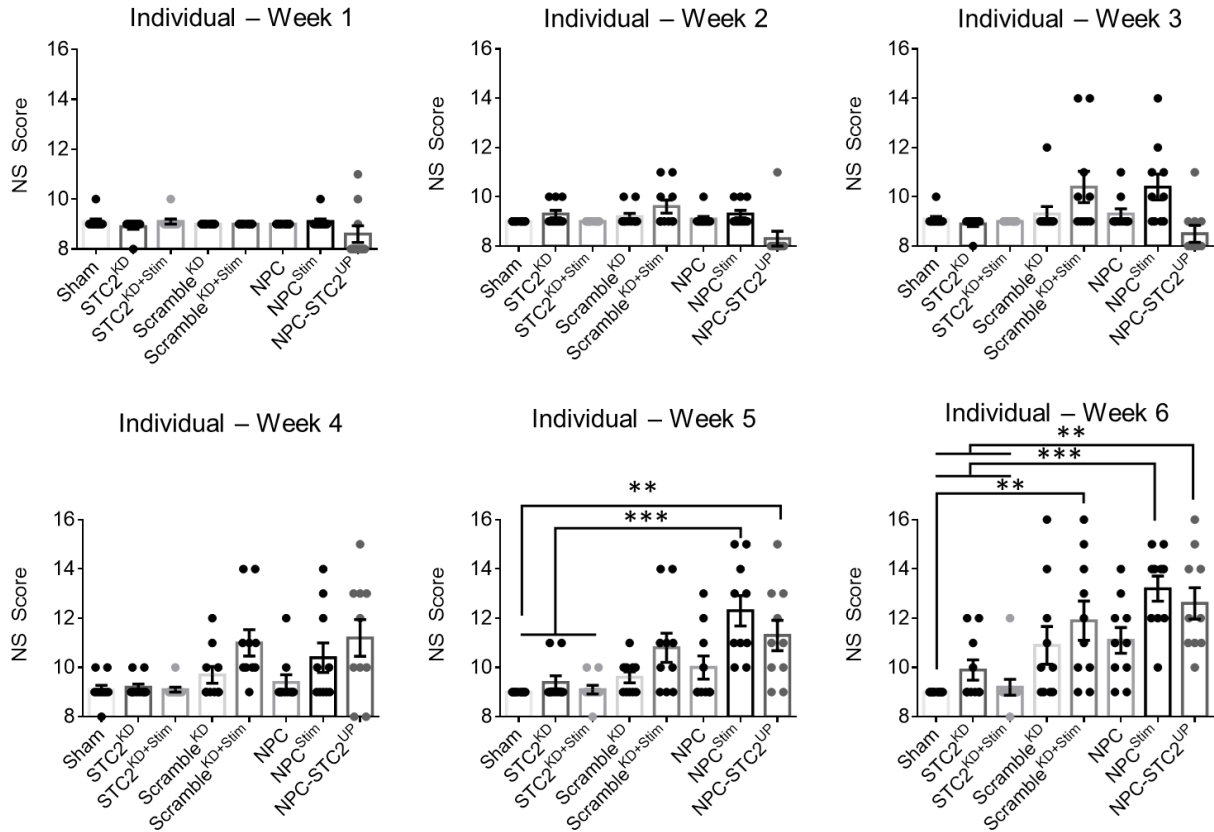


Supplementary Fig. 13 STC2 lentiviral downregulation and upregulation in NPCs *in vitro*.

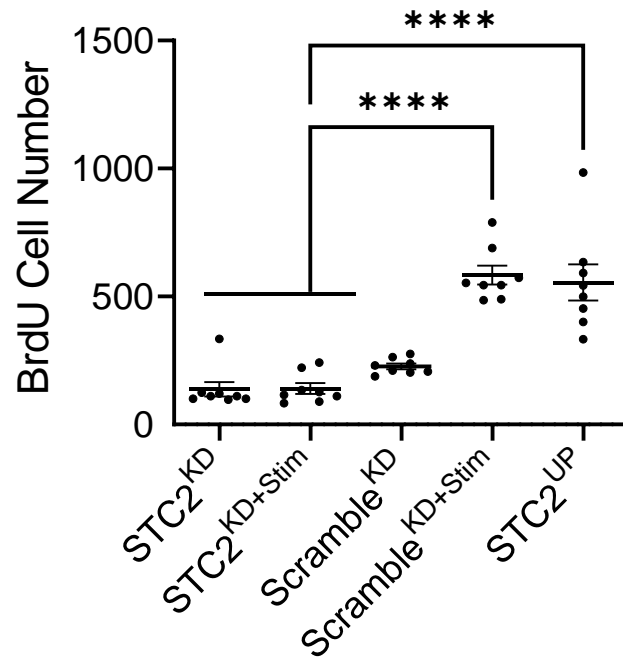
a, qRT-PCR data indicated that STC2 expression after knock-down treatment is minimal and electrical stimulation did not accelerate STC2 expression in NPCs. **b**, ELISA indicated that NPCs after STC2 knock-down did not produce STC2, however, the cells after STC2^{UP}(lentiviral upregulation of STC2) produced significant amount of STC2 compared to other groups. NPCs receiving a scramble lentivirus show that electrical stimulation upregulates STC2 levels. **c**, Representative in-cell western images of human NPCs in different treatment conditions showing increased STC2 expression in Scramble^{KD+Stim} and STC2^{UP} groups. The color from blue to green to red represents increase in intensity of STC2 levels, whose absolute values are quantified in **d**. **d**, Quantification of in-cell western images of each group, demonstrating STC2^{KD} reduces STC2 expression. **a,b,d** ** P<0.01, **** P<0.0001, analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test, data presented as mean ±SEM, n=4 for a, b; n=5 for c, d.



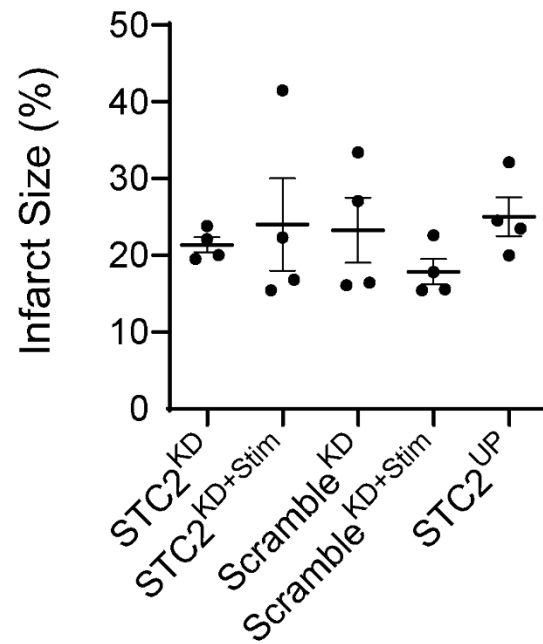
Supplementary Fig. 14 STC2 is an integral component of combined NPC and electrical stimulation functional stroke recovery. Vibrissae-forepaw (WP) behavioral testing for individual weeks. a - indicates statistically significant difference compared to Sham control, b – indicates significant difference compared to STC2^{KD}+Stim, and c – indicates significant difference from STC2^{KD}. Analyzed using Kruskal-Wallis followed by post hoc pairwise Mann-Whitney tests with Benjamini-Hochberg correction to control the false discovery rate at the 0.05 level; a, b, c = P<0.05; aa, bb, cc = P<0.01, and aaa, ccc = P<0.001 respectively, data shown as mean±SEM, n=10 per group.



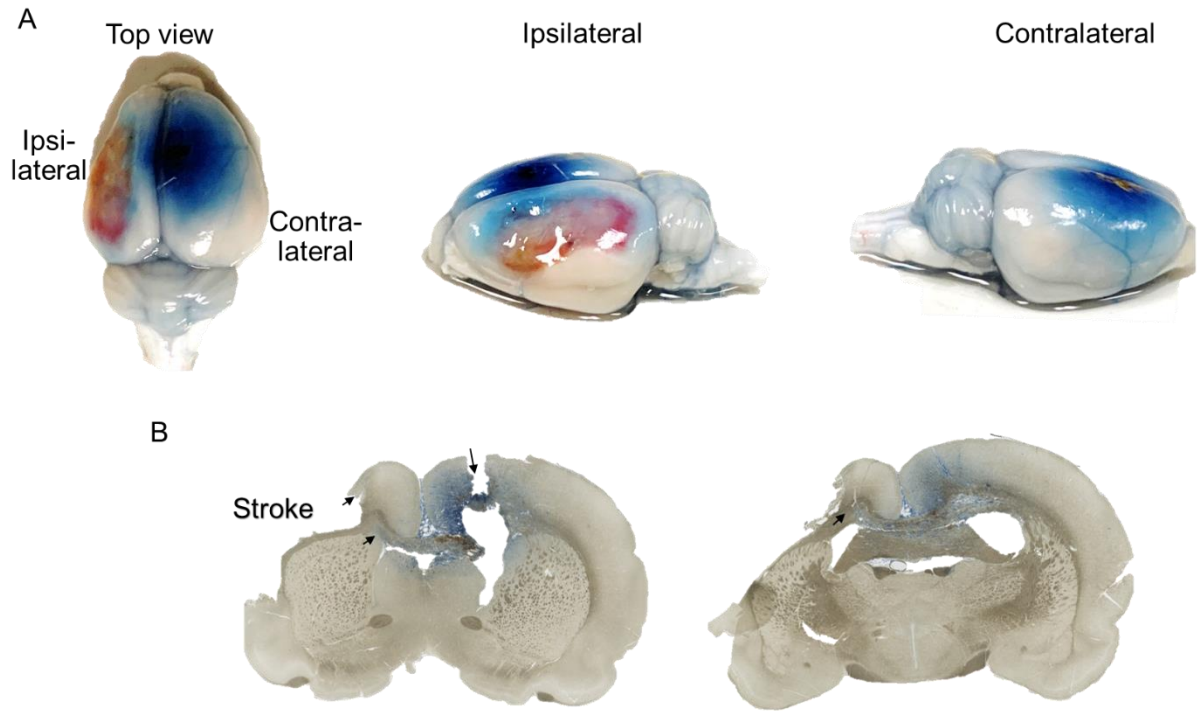
Supplementary Fig. 15 Total neurological score (NS) testing. Neurological score (NS) behavioral testing for individual weeks. Scramble^{KD+Stim}, NPC^{Stim} and STC2^{UP} exhibited greater recovery beginning at 4 weeks post-stroke compared to other groups. Analyzed using Kruskal-Wallis followed by post hoc pairwise Mann-Whitney tests with Benjamini-Hochberg correction to control the false discovery rate at the 0.05 level; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, data shown as mean \pm SEM, $n=10$ per group.



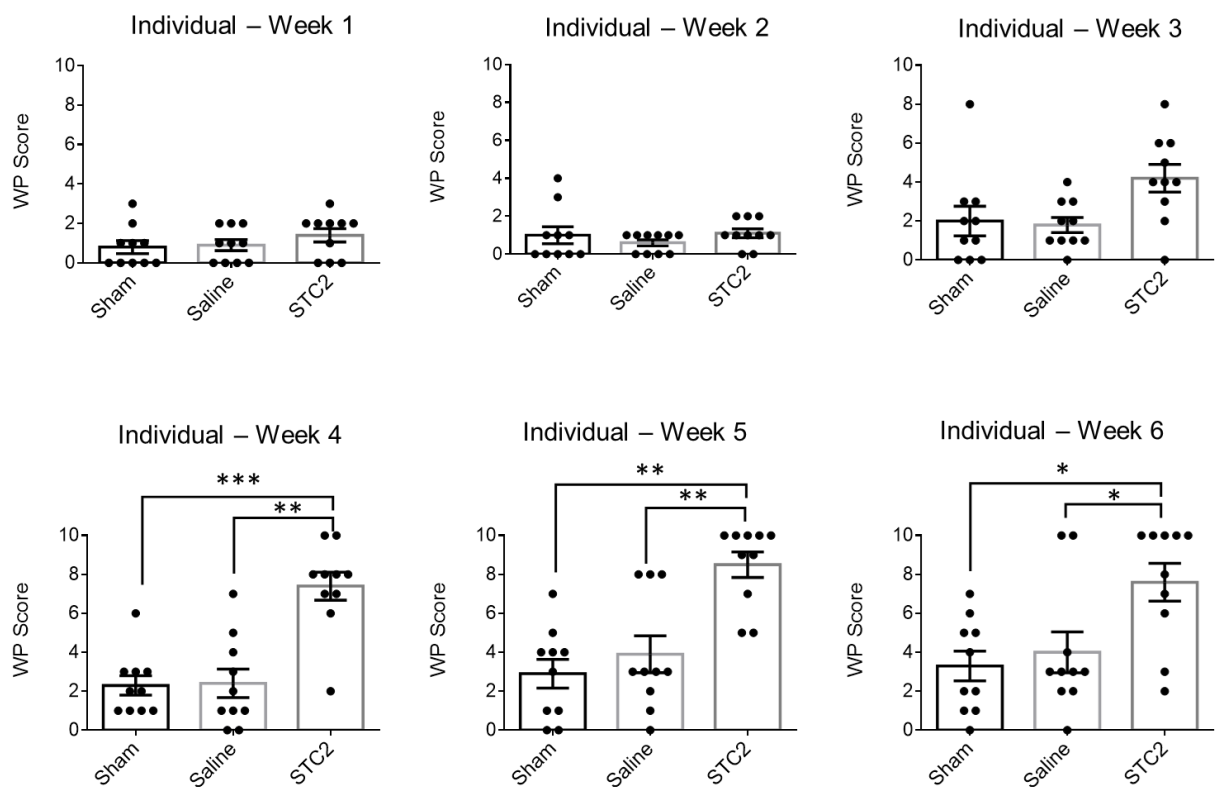
Supplementary Fig. 16 Cell count analysis of post-stroke brain slices. BrdU⁺ cells in the MD region (between subventricular zone and peri-infarct) for various experimental groups. Analyzed using one-way ANOVA followed by Tukey's HSD post hoc test for multiple comparisons, **** indicates $p < 0.0001$, data shown as mean \pm SEM, $n = 8$ images/4 rats.



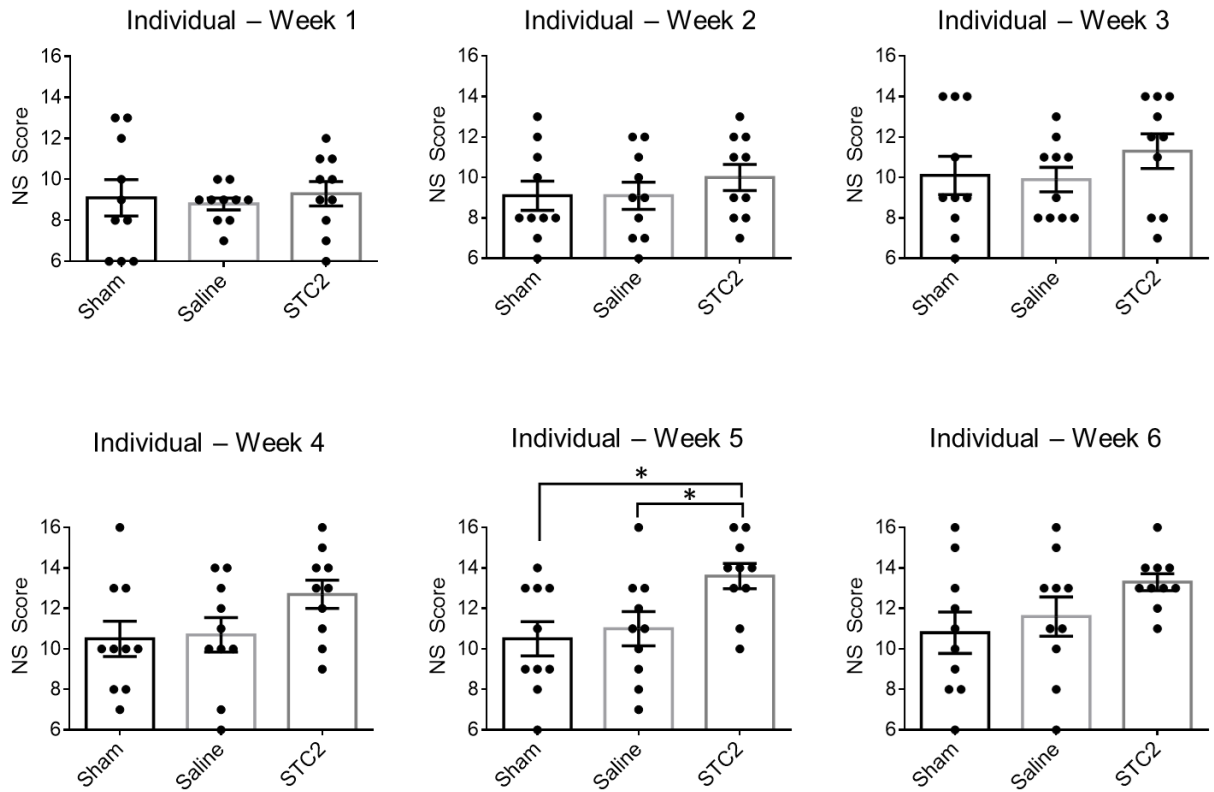
Supplementary Fig. 17 Final infarct size. Percentage calculation of infarct size for STC2^{KD}, STC2^{KD+Stim}, Scramble^{KD}, Scramble^{KD+Stim}, and STC2^{UP}. There were no statistically significant differences between any group. Analyzed using one-way ANOVA followed by Tukey's HSD post hoc test for multiple comparisons, data shown as mean±SEM, n=4.



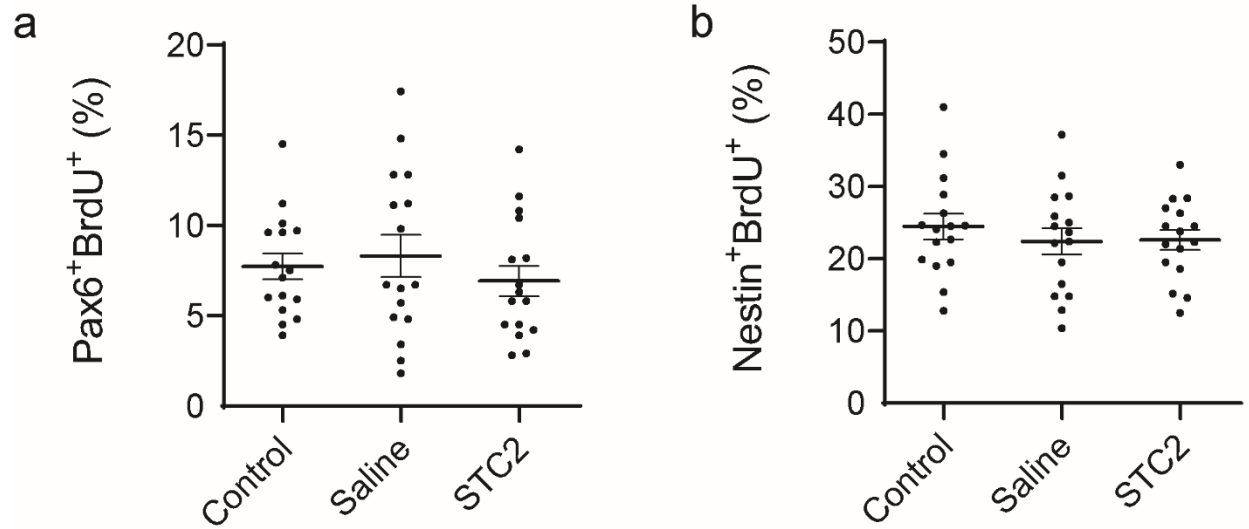
Supplementary Fig. 18 Intra-ventricular delivery of trypan blue solution via mini-osmotic pump. a, Top and side view of rat brain administered with trypan blue solution after stroke. **b,** Bright field images of brain slices with arrows showing the tear due to needle injected from mini-osmotic pump and trypan blue (blue) distributed from the contra-lateral ventricles towards the subventricular and peri-infarct region.



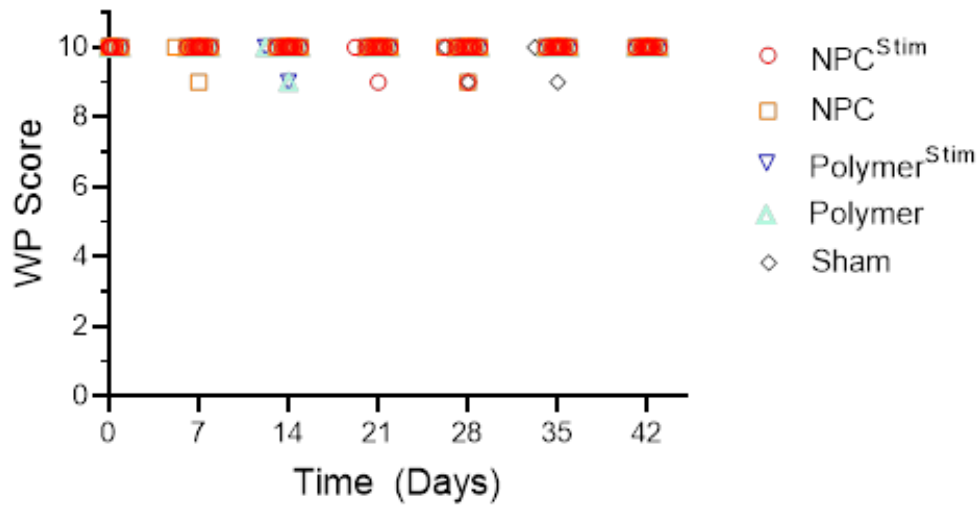
Supplementary Fig. 19 Intraventricular STC2 delivery improves functional stroke recovery. Vibrissae-forepaw (WP) behavioral testing for individual weeks. There was a statistically significant difference between WP Scores of the STC2 group versus both the Sham and Saline group starting at week 4 post-stroke. Analyzed using log-transform two-way repeated measures ANOVA followed by Dunnett's multiple comparisons test, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, data shown as mean \pm SEM, $n=10$ per group.



Supplementary Fig. 20 Total neurological score (NS) testing. Neurological score (NS) behavioral testing for individual weeks. There was a statistically significant difference in NS Scores between the STC2 group versus both the Sham and Saline group at 5-weeks post-stroke. Analyzed using Kruskal-Wallis followed by Dunn's multiple comparisons test, * $p < 0.05$, data shown as mean \pm SEM, $n=10$ per group.



Supplementary Fig. 21 Cell count analysis of co-labeled post-stroke brain slices. a, Cell counts of Pax6⁺Brdu⁺; **b**, Nestin⁺Brdu⁺ cells in the peri-infarct (PI) tissue. There were no statistically significant differences between any group. Analyzed using a one-way ANOVA, followed by Tukey's HSD post hoc test, data shown as mean±SEM, n=16 images/4 rats.



Supplementary Fig. 22 Behavioral assessment scores of the ipsilateral limb (non-effected limb). The vibrissae-forepaw behavioral assay was evaluated for the potential confound of testing effect via longitudinal assessments of the limb ipsilateral to the stroke as a non-effected control. There was no significant difference between WP Scores in any group at any timepoint. Analyzed using Kruskal-Wallis with Dunn's multiple comparisons test, data shown as mean \pm SEM, n=10 for each group respectively.

Supplementary Table 1. Ingenuity pathway analysis molecules

Top Analysis-Ready Molecules		Expression Value (LogFC)	
Upregulated	CA9	9.661	
	PDE4C	8.106	
	PPFIA4	7.997	
	AHNAK2	7.728	
	SNCB	7.577	
	ARFGEF3	7.539	
	HSF4	7.391	
	NRN1	7.178	
	SMIM24	7.070	
	STC2	6.905	
	Downregulated	TM4SF18	-3.484
F13A1		-3.297	
KCNJ6		-2.983	
HES5		-2.706	
SFXN2		-2.564	
ACAT2		-2.529	
SLITRK1		-2.450	
KLF15		-2.425	
MYB		-2.403	
RRM2		-2.305	

Supplementary Table 2. Top 15 hallmark pathways (blue highlight indicates STC2 is leading edge)

pathway	prval	padj	ES	NES	nMoreExtreme	size	leadingEdge
HALLMARK_HYPOXIA	0.0002155	0.0021614	0.7938585	2.747115		0	157 PPIFA4, STC2, P4HA2, IINH4, NDRG3, BHLHE40, ALDOC, AK4, THEM54, DDIT4, ANGSTL4, PYGM, FAM162A, ROBA, VEGFA, STC1, PPP1R3C, LOX, EPN1, HMOX1, PKPFR3, PIM4L1, CCR4, PDK1, HK2, ADORA2B, ENO2, PIK1, GBE1, ADAM, AMPD3, FEN1, ALDOA, DDIT3, PIRF, ATR, KMOA, PFKFB, AMKZF1, ENO1, MGI1, WDR1, SLCO3, EPHE2, DHM, HPI3, VPS1, ANXA2, PWRK1, CAL2, PGM1, HPSA, PLIN2, PPP1R15A, ATP7A, EMPD1, CD, HX1, GADD45, KLHL24, NR3C1, PRKAG3, ZFP16, DINA, FOS, GALK1, IRS2, JUN, MYF, PPARC3A, PRK3, CAV1, THL1, MAL2, TNFAIP3, SCARB1, HAFF, BTG1, KOLER2, SERPINE1, SH2D3, TIPARP, IDS, CDKN1C, PDGFB, ENO3, HEMA, CCG2, VLDLR, FOXO3, DUSP1, G1R9, CITED2, GAA, PGG2, SLCO3A, CDKN1A, CHST3, GDI, NEDD4L, SLCO6A, TPST2
HALLMARK_E2F_TARGETS	0.0005714	0.0199375	-0.713125	-3.723593		0	196 RRM2, TRIP13, RPL3, LMNB1, SPC25, DLGAP5, UCM4, CENPE, PLK4, GINS1, HMO5, KIF4, TMPO, DSCC1, BUB1B, SMC4, CDC25A, H2AF, SESEF, GINS4, SRSF1, MCM6, WRB2, POLA2, DNAP3, CENPM, GINS3, AURKB, RAD51AP1, HELLS, MCM5, RANBP1, SUV39H1, MADL1, LUBEZ1, NME1, KIF38B, BIRC5, DEFOC1, CDC20, ASF1B, CSE1L, SPAG5, PRIM2, CHEK1, TACC3, ATAD2, MCM2, AURKA, MELK, BRCA1, COKI, MCM7, CKS1B, MCM3, CENBF, MMS2L1, PLK1, BARD1, KIF2, CDC48, NASP, CCNE1, LIG1, RACGAP1, TOP2A, CDCA3, DEK, MSH2, MMS1, HNRNP0, RNASEH2A, HMHR, KPN2A, USP1, PSMC3BP, H2AFZ, TCF19, TIMELES, RPA3, KIF2C, TRAF2, ORC6, PCNA, ESPL1, NUP107, DCTPP1, TIPIN, CDKN2C, NBN, TK1, DNMT1, UNG, EZH2, ING3, POLD1, BRCA2, CBX5, ANP32, STAG1, POLD2, DUT, UBR1, CDKN3, CIT, SPC24, SMC1A, LBR, LYAR, PHF5A, STMN1, RPA2, SNRPB, RAD1, RHO2, DMOSS2, RFX2, UBE2S, TUBB, TUBG1, PRKDC, SMC6, MLI1, NOP56, ZW10, NUFP25, SHMT4, CHEK2, CTCF, CDC25B, BOKNA, PIP51, POSS5, POLE, PTTG1, DONSOM, PBP1, E2F8, POF7, HMG2, RAD51C, ORC2, RAD21, PADS4, RPA2, RBBP7, NAOS1, POLD2, CKS2, EED, NDR9A, IJF5, SRSF1, DCK, NUDT2
HALLMARK_G2M_CHECKPOINT	0.0005536	0.0199375	-0.712688	-3.443899		0	195 CDCT, CDCA5, LMNB1, RAD51, CDG, CENPE, PLK4, HMO5, CCHN2, GFAA, TMPO, HPS, SMC4, CDC25A, H2AF, SRSF2, SRSF1, MCM6, EXO1, MYBL2, POLA2, HSPAB, TTK, P8K, AURKB, H2AF5, GINS2, PRCL1, BUB1, SUV39H1, MAD2L1, NDC80, RFX2, BIRC5, STIL, KIF11, ZFP1, CDC20, TPX2, CHAF1A, PRKAD, CNF, CHEK1, TACC3, UBE2C, MCM2, NUSP1, AURKA, CENPA, SPO, SMC1, CDK1, CKS1B, EDP2, MCM3, CENBF, PLK1, BARD1, KIF2C, CENPF, NASP, RACGAP1, INCENP, TOP2A, MMS1, HNRNP0, HISTH2BK, FEN3, HMAR, DEFA, KPN2A, RB1, POL1, KIF20B, H2AFZ, HMGN2, SOLE, SNR0D1, AHD1, KIF3C, DTMUK, TRAF2, ORC6, ESR1, TRAP, CDKN2C, TDP1, TRAP, DKC1, EZH2, H2AF, BRCA2, STAG1, BUB3, CDKN3, SMC1A, LBR, STMN1, RPA2, WRN, LIG3, CCND1, CASPAP2, E2F3, UBE2E, NARCKS, FANCC, SRSF10, NRK2, CDC27, RBM14, UCK2, CTCF, CDC25B, DDX39B, POSS5, POLE, EW581, PTTG1, NUSP6, E2F4
HALLMARK_ANGIOGENESIS	0.001598	0.024985	0.6392163	1.715500		31	22 VEGFA, STC1, ANG2, MSX4, JAG1
HALLMARK_MYC_TARGETS_V2	0.0010267	0.055989	-0.6967494	-1.977404		0	56 MCH4, PLK4, MCM5, UTP20, P115, SPA, TMEM97, DCTPP1, GRW1, RRP5, UNG, NIRT04, PUS1, PRMT3, PPRC1, LAS1L, BYSL, NOP56, HSP1, KIP1, CBX3, MYBBP1A, NDUFA4, TCOF1, NOP56, GNL3, RRP12, PAZ2A, NOP2, RABEP3, SORD, CDK4, WDR45, SLC19A1, DDX3B, HSPD1, NOLC1, NOLA4, TRF2D4, AIMP2
HALLMARK_TNFA_SIGNALING_VIA_NFKB	0.0002173	0.021624	0.6055740	2.070813		0	140 BHLHE40, VEGFA, EFNA1, PRKTE1, KLF10, FOSL2, ATF3, TP53, SLC3A3, SOSTM1, TNIP1, CEBPB, NAMPT, NFIL3, NFKB1, PPP1R15A, NR4A3, KDM6B, ZFP36, FOS, BCL2, GADD45B, IRF2, JUN, MDM1, GADD45A, HSEGF, GEM, FERL1, E1F1, TNFAIP3, JAG1, MAFK, E1G1, SAT1, TAP1, SERPINE1, SLC15A6, CEBP, DUSP5, TIPARP, LIF, F2RL1, NFKB2, MAP3K4, DUSP1, ICAM1, NFAT5, RELB, REL, JUNB, TRIS1, BAGML1, RHOE, CDKN1A, TRIP10, SDCA, PLK2, PHLDA2, NR4A1, KLF2, RNF298, MYC
HALLMARK_GLYCOLYSIS	0.0002145	0.0021614	0.5948552	2.084232		0	107 PPIFA4, STC2, EGFR3, SLC6A3, P4HA2, AK4, PLOD2, DDIT4, ANGSTL4, PYGM, FAM162A, VEGFA, STC1, PIM4L1, CKCFH, HK2, NOL3, ADORA2B, ENO2, PKG1, ANG, ALDOA, PLOD1, PFKFB, AMKZF1, LNO, MGI1, EFNA3, LDHA, GYS1, LHP1, RRM2, GALK1, IRS2, MYF, MFI, OSC4, PDK1, TPI1
HALLMARK_MYOGENESIS	0.0002206	0.0021614	0.5945788	2.024074		0	128 PPIFA4, STC2, P4HA2, PYGM, PDP1R2, TNNT1, TNNC3, KLF5, ERBB3, AHC, COL1A1, RYR1, HBC, SH3BPGR, MEFC2, GSN, ATP2A1, COLEA2, NCM1, FOXO4, DINA, GADD45B, HBEF, MAP3K3, SPEG, CD35, EPHE2, HDAC5, OCL1, TCAP, PIGIS, CHIRN1, CTF1, MEL2D, COL4A2, SIRT2, AK1, ENO3, B1T1, ADCY9, CACNA1H, FKBP1B, KCNB1, TPM2, NQO1, GAA, CDKN1A, KCNIB2, KIF3C, PTPN22
HALLMARK_P53_PATHWAY	0.0002157	0.0021624	0.5839886	2.022314		0	155 NDRG1, EPRS1, DNMT3, FAM125A, S100A8, HMOX1, RHBDP2, OSOIN1, DDIT3, ATF3, TP53, PTPRE, TRB3, STOM, TXNIP, JAG2, PPP1R15A, SLC2A2, FOS, JUN, MDM1, GADD45A, SLC7A11, HBEF, UPP1, BTG1, ABHD4, SAT1, TAP1, VIMAS, BLCAP, VAMP9, ANKRA2, CEBPA, AK1, LIF, CTSD, SERTAD3, TSPY2, GNA2, FOXO3, HIST3H2A, H2AF1, CDKN1A, HMK2, MAPK3K4, PLK2, PLK3, ZFP36L1, RALGDS, RNF198, ACVR1B, HESX1, ZMAT3, TOB1, PMM1, HSP90A
HALLMARK_KRAS_SIGNALING_DN	0.0004813	0.0033694	0.5707559	1.805565		1	69 SNCB, SLC6A3, MYO15A, ARHGAP10, GFBP2, KCNN1, PRKX, RGS11, SLC38A3, KCND1, TNIN3, RYR1, VEGK2, DLK2, CLTN3, COP2, SLC29A3
HALLMARK_MYC_TARGETS_V1	0.0005714	0.0199375	-0.567247	-1.710288		0	196 CDCA4, MCM4, CCHN2, SRSF7, RRM1, SRSF2, SRSF1, MCM6, MCM5, RANBP1, MADL1, NME1, HNRNP2B1, CDC20, PCH2, MCM1, DEK, HNRNP0, TMS, KPN2A, RFC4, USP1, SRSF3, SRA, H2AFZ, SNRPO1, NCBP1, CTC1, TRAF2, PCNA, ABCL1, HNRNP0, TDP1, RRP5, FAM122A, CSTF2, SPMO1, DUT, BUB3, PRDX3, SRPK1, PRK32, SNRPB, HNRNP0, SNRPB, PSM2, PSM14, TARDBP, ILF2, C10BP, CDK2, NOP56, HSP1, CBX3, GLO1, SNRPA, ERF3, ERF4, ERH, MRPL23, PPIA, NHP2, VBP1, G0T2, NOP16, GNL3, PSMB5, DHX15, ORC2, DDX21, HNRNP0, PAZG4, SNRPD, POLD2, POLE3, HNH2Q, MRPS, PSM4, UBA2, ERF3, YWHAE, SSBP1, CCT2, KPNB1, RAN, STARD7, CDK4, SERBP1, PPM1G, SET, EIF3AX, SMARCC1, XPO5, DDX38, EIF2S1, GBBP1, CULL1, ACPI, CCT7, HSPD1, NOLC1, HDGF, HDG2, LSM7, E1F1, CTC3, PSM4, AIMP2, PRPF3, SYNERGIP, HDCC2, NCBP2, FHB, SF3B3, HNRNFC, SSB, EEF1B2, PSMO3, SNRPB2
HALLMARK_COAGULATION	0.0110710	0.058323	0.5028667	1.582797		45	69 ANG, CD9, F12, ITGA2, GSN, CTSK, LRPL1, C1R, F10, MST1, MAF, SERPIN E1, SIRT2, CTSS, PDGFB, LTAH, F8, MMP11, LGMN, ANXA1, KLF7, LAMP2, CTSH, CIS, SH2B2, FURIN, F2RL2
HALLMARK_HEME_METABOLISM	0.0004902	0.0033694	0.4805425	1.694929		1	146 P4HA2, TNF1, OPTN, BLVRB, MGI1, PPP2R5B, ASNS, RAP1GAP, HTATIP2, SNIP1, NR3C1, RIKK3, SLC7A11, EPOR, SIRT2, ISCA1, SMOX, TTRC, ELL2, DCAM, CTSS, SLC6A3, ENDOU1, ATP6V0A1, YPEL5, FYO9, FOXO3, NFE2L1, ATGA, LRFD1, NARF, SLC2A1, SYCA, HFD, MARCH8, EZH1, CLDN5, LAMP2, KHN1Y, SLC10A3, MGRN1, HEBP1, SDCBP, OIPC, CAST, ALAD, CTNS, PGLS, BTG2, RBM38, MARCH2, TSPN15, NEK7, SYNL1, SLCAA, IGFBP3, AGPAT4, PRK39A, TM6C2, CCR29A, MEX3A, RNF179A, GGI3
HALLMARK_ESTROGEN_RESPONSE_EARLY	0.0008770	0.0053716	0.4743353	1.625348		3	137 STC2, BHLHE40, OHR53, MAP1, KLF10, TFC39A, SEMA3B, BLVRB, SEC14L2, PAPP52, CAL2, DHR52, SLC7A5, KR19, FOS, PLA2G1B, RARA, KDM4B, SH3BP5, TBC1D30, ALDH3B1, SCARB1, PEX11A, ZNF135, MAP6E1L1, SH2D3, SYNERG1, ENDOD1, TIPARP, ADCY3, UNC119, FLNB, B6GAL1, SLC2A1, TSKJ, AEF1, IGF1R, MYC, CALCB, TGF1, E1F1, NRP1, FAM63A, CELSR1
HALLMARK_APOPTOSIS	0.0017746	0.0088967	0.4681021	1.588828		7	124 HMOX1, ENO2, DDIT3, ATF3, SMTAD7, ERK8, TXNIP, PPP2R5B, SOSTM1, TSP0, GSN, KNP1S, HSP1, RARA, GADD45B, JUN, GADD45A, RIF, CAU1, SAT1, TAP1, LMNA, SATR1, RHA, MAD, KCF3, NEMO, RHOE, CDKN1A, ANXA1, HIF1, PDGFRB

Supplementary Table 3. Upregulated genes due to electrical stimulation

Gene	RNA Seq			qRT-PCR		
	Log FC	Adjusted p-value	Significance	Mean Diff. between fold change ($\Delta\Delta C_T$) NPC ^{stim} and NPC	Adjusted p-value	Significance
STC2	6.9	0.00001	****	12.5	0.003	**
SNCB	7.6	0.00003	****	0.9	0.034	*
NRN1	7.2	0.00034	***	7.3	0.006	**
TNNT1	4.0	0.00004	****	0.1	0.797	ns
PLOD2	5.7	0.00000	****	0.8	0.081	ns
PDE4C	8.1	0.00005	****	6.1	0.055	ns
PPFIA4	8.0	0.00013	***	13.1	0.013	*
TMEM45A	5.0	0.00011	***	0.6	0.087	ns
FGF11	4.7	0.00033	***	0.6	0.681	ns

Supplementary Table 4.

Modified Neurological Severity Score	Points
Motor	
Postural Reflex 2 symmetric touchdown (normal) 1 asymmetric touchdown + resistant to pushing 0 asymmetric touchdown + no resistance to pushing	2
Raising rat from the base of tail 3 Both paws touching surface simultaneously 2 One paw touches the surface before the other 1 Flexion of forelimb but unable to touch 0 Unable to touch any limb (forelimb or hindlimb)	3
Walking	
3 Normal 2 Difficulty walk straight 1 Circling in the direction of the paretic side 0 Falling to paretic side	2
Sensory	
2 Proprioceptive test (pressing paw against table edge to stimulate muscles) 1 Placing test (responds to visual and tactile stimuli)	2
Beam Test	
6 Balances with steady posture and crosses beam without any paw slip 5 Grasps side of beam without slipping 4 Hugs the beam and one limb slips from the beam 3 Hugs the beam and two limbs fall down from the beam 2 Attempts to balance on the beam but falls off (>40s) 1 Attempts to balance on the beam but falls off (>60s)	6

0 Falls off without attempt to stay on (<20s)	
Maximum Points	16

Supplementary References

- 1 George, P. M. *et al.* Electrical preconditioning of stem cells with a conductive polymer scaffold enhances stroke recovery. *Biomaterials* **142**, 31-40, doi:10.1016/j.biomaterials.2017.07.020 (2017).