

## Supplemental Information

**Supplemental Table 1.** List of primers used for single-cell RT-PCR

<b>Gene/primer</b>	<b>Forward</b>	<b>Reverse</b>
<i>Gapdh</i> inner	CCAGCCTCGTCCCGTAGACA	CGCTCCTGGAAGATGGTGAT
<i>Gapdh</i> outer	GAGAGGGAGGAGGGGAAATG	CTCGTGGTTCACACCCATCA
<i>Rest</i> inner	ACCACTACATGGCACACCTG	TTCTCACCTGAATGAGTCCGC
<i>Rest</i> outer	GAACCCCAGCCCGTATTTGA	TCTCACCTGAATGAGTCCGC
<i>Kcnq2</i> inner	AGGAAGCCGTTCTGTGTGAT	GCAGAGGAAGCCAATGTAC
<i>Kcnq2</i> outer	TCTCCTGCCTTGTGCTTTCT	GCATCTGCGTAGGTGTCAAA
<i>Kcnd3</i> inner	GAGGGGGTAGTGGGGAGTAA	CCCCTAATGCCAATCCCCT
<i>Kcnd3</i> outer	CACCAGTCGCTCCAGCCTTAAT	GGGCAGCTCTTGGTCTTGTG
<i>Oprm1</i> inner	ACTTCTGCATTGCCTTGGGT	AGAAAGCACATACCTGGTGGTT
<i>Oprm1</i> outer	TACAGGCAGGGGTCCATAGAT	TTCTCCAGTAACCGACCTCCT
<i>Scn10a</i> inner	ACCGACAATCAGAGCGAGGAG	ACAGACTAGAAATGGACAGAATCACC
<i>Scn10a</i> outer	TTGAAGAAGACACCGACGCA	TGTAAAACAGGCTTCGGGCT

**Supplemental Table 2.** Incidence of detection of *Rest* and four of its target genes in DRG neurons as detected by single-cell RT-PCR in tamoxifen-injected *Rest*<sup>loxP/loxP</sup>/WT mice in control conditions, four weeks after the SNI injury and in the tamoxifen-injected *Rest*<sup>loxP/loxP</sup>/AvCreER-T2 mice after the SNI injury.

Gene name		<i>Rest</i> <sup>loxP/loxP</sup> /WT (control)	<i>Rest</i> <sup>loxP/loxP</sup> /WT+SNI	<i>Rest</i> <sup>loxP/loxP</sup> /AvCreER-T2+SNI
Total number of neurons analysed		79	89	79
Number of positive cells (%)	<i>Gapdh</i>	79 (100)	57 (64)***	79 (100)###
	<i>Rest</i>	15 (19)	48 (54)***	4 (5)###
	<i>Kcnq2</i>	46 (58)	19 (21)***	30 (38) <sup>#</sup>
	<i>Kcnd3</i>	48 (61)	29 (33)***	52 (66)###
	<i>Oprm1</i>	32 (41)	24 (27)	25 (32)
	<i>Scn10a</i>	18 (23)	14 (16)	18 (23)

\*\*\* Significantly different from control; Fisher's exact test, p<0.001

<sup>#</sup>, ### Significantly different from tamoxifen-injected *Rest*<sup>loxP/loxP</sup>/WT mice after the SNI injury; Fisher's exact test, p<0.05 or p<0.001

**Supplemental Table 3.** RE1-containing K<sup>+</sup> channel genes, their expression in sensory afferents and chronic pain associated downregulation.

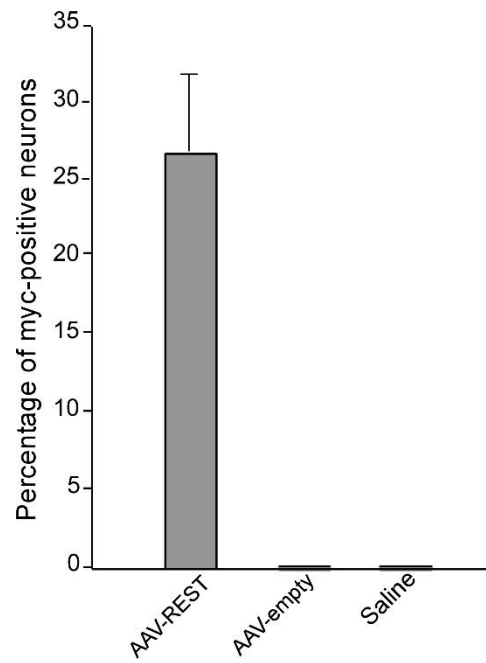
<b>Gene name<sup>1</sup></b>	<b>Subunit</b>	<b>Expression in nociceptors<sup>2</sup></b>	<b>Downregulated in chronic pain model(s)<sup>2</sup></b>
KCNA2	Kv1.2	++	Yes
KCNA4	Kv1.4	+++	Yes
KCNC1	Kv3.1	+	unknown
KCNC3	Kv3.3	-	unknown
KCNC4	Kv3.4	+++	Yes
KCND3	Kv4.3	+++	Yes
KCND2	Kv4.2	+	Yes
KCNH1	EAG	-	unknown
KCNH2	HERG	-	unknown
KCNH4	ELK1	-	unknown
KCNK9	TASK3	+	Yes
KCNMA1	KCa1.1 (SLO1)	++	Yes
KCNN4	KCa3.1 (SK4)	+ <sup>3</sup>	unknown
KCNQ2	Kv7.2	+++	Yes
KCNQ3	Kv7.3	+++	Yes
KCNQ5	Kv7.5	+++	Yes
KCNAB2	BETA-2	++	unknown
KCNIP2	KCHIP2	+++ <sup>4</sup>	unknown
KCNIP4	KCHIP4	-	unknown

<sup>1</sup>RE1-containing K<sup>+</sup> channel genes for which REST binding has been identified by Transcription Factor ChIP-seq Uniform Peaks from ENCODE/Analysis (<http://genome-euro.ucsc.edu>)

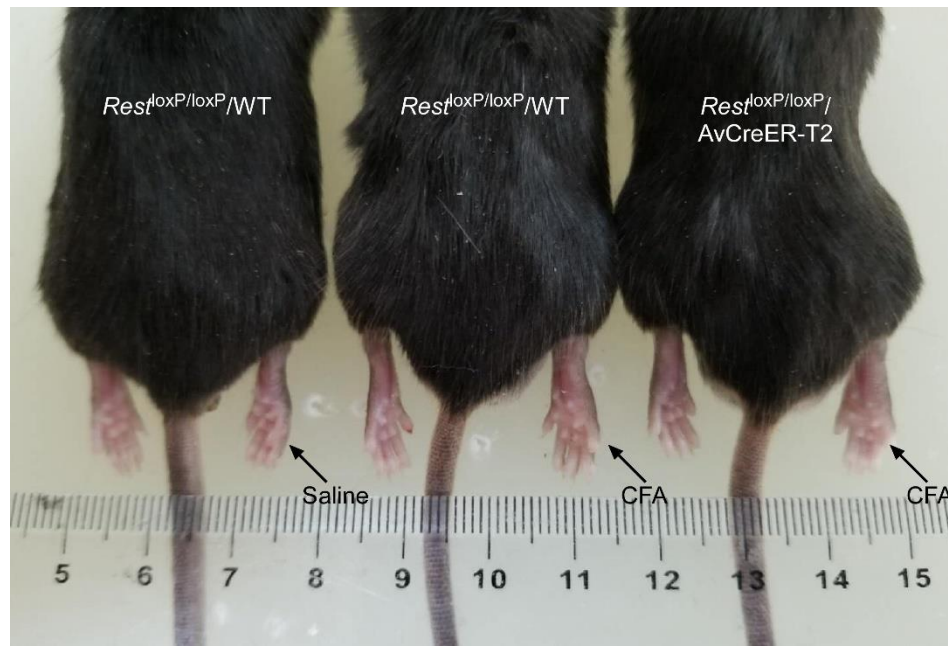
<sup>2</sup>Unless indicated otherwise, data are from Du X & Gamper N (2013) Potassium channels in peripheral pain pathways: expression, function and therapeutic potential. Curr Neuropharmacol 11:621-640.

<sup>3</sup>Lu R, et al. (2017) KCa3.1 channels modulate the processing of noxious chemical stimuli in mice. Neuropharmacology 125:386-395.

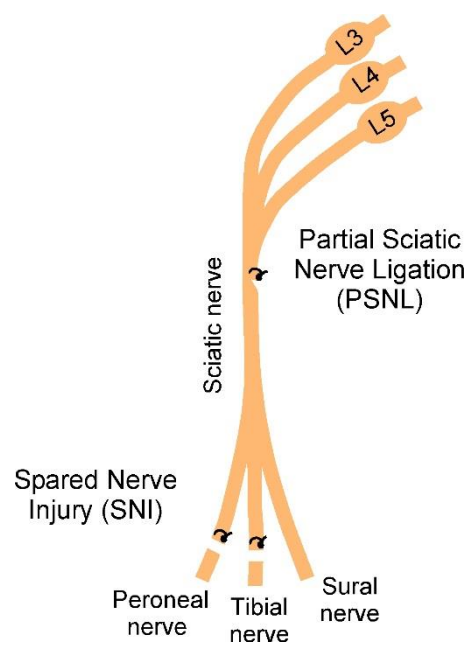
<sup>4</sup>Kuo YL, et al. (2017) K<sup>+</sup> Channel Modulatory Subunits KCHIP and DPP Participate in Kv4-Mediated Mechanical Pain Control. J Neurosci 37:4391-4404.



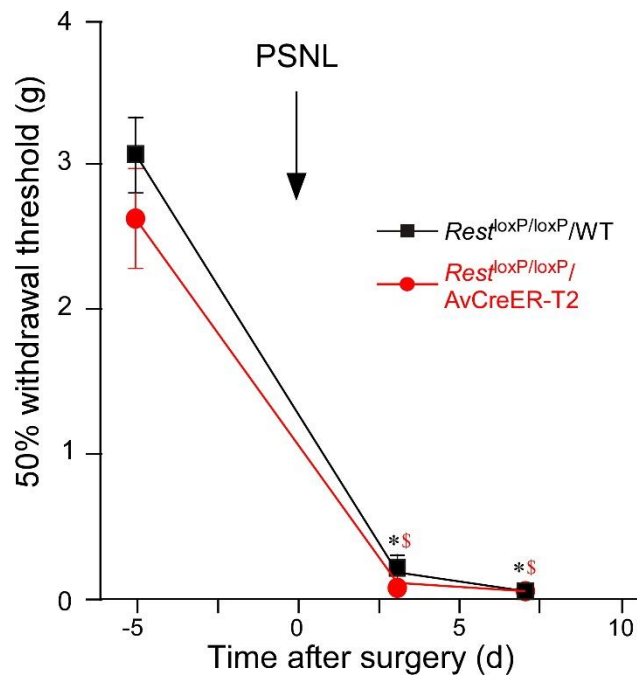
**Supplemental Figure 1.** Quantification of immunohistochemical analysis of Myc expression in L4 DRG of mice DRG-injected with AAV2/9-REST, empty AAV2/9 particles or saline (example images are presented in Fig. 1C); for each conditions 3 mice, 5-6 sections were analysed.



**Supplemental Figure 2. Deletion of Rest does not affect paw edema.** Hind-paw injection of the Complete Freund's Adjuvant (CFA, 20  $\mu$ l) produced similar degree of paw swelling in the tamoxifen-injected *Rest*<sup>loxP/loxP</sup>/AvCreER-T2 and *Rest*<sup>loxP/loxP</sup>/WT mice; injection of saline produced no swelling. Photographs are taken 2 weeks after the CFA injection.



**Supplemental Figure 3.** Schematic of neuropathic pain models used.



**Supplemental Figure 4.** In the absence of tamoxifen  $Rest^{loxP/loxP}/AvCreER-T2$  mice have normal mechanical threshold and develop hyperalgesia following partial sciatic nerve ligation (PSNL) similarly to the WT littermates.  $Rest^{loxP/loxP}/AvCreER-T2$  (red symbols, lines; n=10);  $Rest^{loxP/loxP}/WT$  (black symbols, lines; n=10).\*, \$ different from the pre-injury measurements in the same animal;  $P < 0.05$  (two-way repeated measures ANOVA with Tukey post-hoc test).

**Supplemental Movie 1.** Wild-type mice *in vivo* injected with AAV2/9 REST into the right L4 DRG display paw dragging and change of gait. Video was recorded on day 34 after the injection.

**Supplemental Movie 2.** Control wild-type mice *in vivo* injected with empty AAV2/9 into the right L4 DRG display normal gait. Video was recorded on day 34 after the injection.

**Supplemental Movie 3.** Tamoxifen-injected  $Rest^{loxP/loxP}/WT$  (control) mice after SNI displayed dragging of injured (right) paw and changed gait. Video was recorded on day 21 after the surgery.

**Supplemental Movie 4.** Tamoxifen-injected *Rest*<sup>loxP/loxP</sup>/AvCreER-T2 mice after SNI displayed nearly normal gait and no dragging of the injured (right) paw. Video was recorded on day 21 after the surgery.