Dataset 1

Figure panel	Assay	Statistical Test; findings	Post-hoc analysis (adjusted p-values)	Number of subjects	Number of subjects excluded (ROUT test)
Fig 1J	Whole cell patch clamp electrophysiology – Peak sodium currents	One Way ANOVA	Holm-Sidak multiple comparison post-hoc test: Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(WT) + TTX + ProTx-II p=0.0017 Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(1.3) + TTX p=0.0003 Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(1.3) + TTX + ProTx-II p=0.0006	Halo-Na_V1.7(WT) + TTX (n=16) Halo-Na_V1.7(WT) + TTX + ProTx-II (n=11) Halo-Na_V1.7(1.3) + TTX (n=15) Halo-Na_V1.7(1.3) + TTX + ProTx-II (n=11)	Halo-Na_V1.7(WT) + TTX excluded n=1
Fig 1K	Whole cell patch clamp electrophysiology – Peak TTX-R currents	Kruskal-Wallis test	Dunn's multiple comparison post-hoc test: Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(WT) + TTX + ProTx-II p >0.9999 Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(1.3) + TTX p>0.9999 Halo-Na_V1.7(WT) + TTX vs. Halo-Na_V1.7(1.3) + TTX + ProTx-II p>0.9999	Halo-Na_V1.7(WT) + TTX (n=16) Halo-Na_V1.7(WT) + TTX + ProTx-II (n=11) Halo-Na_V1.7(1.3) + TTX (n=15) Halo-Na_V1.7(1.3) + TTX + ProTx-II (n=11)	Halo-Na_V1.7(WT) + TTX excluded n=1
Table S1	Biophysical properties of DRG neurons after transfection with Halo-NaV1.7(1.x) constructs	Mann-Whitney test	Halo-Na_V1.7(WT) vs Halo-Na_V1.7(1.1) Activation V1/2, P<0.0001 K, P=0.6152 Inactivation V1/2, P=0.0711 K, P=0.9536 Halo-Na_V1.7(WT) vs Halo-Na_V1.7(1.2) Activation V1/2, P=0.9998 K, P=0.0659 Inactivation V1/2, P=0.5473 K, P=0.4067 Halo-Na_V1.7(WT) vs Halo-Na_V1.7(1.3) Activation V1/2, P=0.1431 K, P=0.7963 Inactivation	Halo-Na_V1.7(WT) (n=15) Halo-Na_V1.7(1.1) (n=16) Halo-Na_V1.7(WT) (n=12) Halo-Na_V1.7(1.2) (n=13) Halo-Na_V1.7(WT) (n=15) Halo-Na_V1.7(1.3) (n=16) Halo-Na_V1.7(WT) (n=18) Halo-Na_V1.7(1.4)	

			V1/2, P=0.3836 K, P=0.9571 Halo-Na$_V$1.7(WT) vs Halo-Na$_V$1.7(1.4) Activation V1/2, P=0.1132 K, P=0.1570 Inactivation V1/2, P=0.2673 K, P=0.6866 Halo-Na$_V$1.7(WT) vs Halo-Na$_V$1.7(1.5) Activation V1/2, P<0.0001 K, P=0.5213 Inactivation V1/2, P=0.7267 K, P=0.3475 Halo-Na$_V$1.7(WT) vs Halo-Na$_V$1.7(1.6) Activation V1/2, P=0.0962 K, P=0.3842 Inactivation V1/2, P=0.9133 K, P=0.6158 Halo-Na$_V$1.7(WT) vs Halo-Na$_V$1.7(1.8) Activation V1/2, P=0.2090 K, P=0.7712 Inactivation V1/2, P=0.9512 K, P=0.7167 Halo-Na$_V$1.7(WT) vs Halo-Na$_V$1.7(1.9) Activation V1/2, P=0.7178 K, P=0.5300 Inactivation V1/2, P=0.8809 K, P=0.5232	(n=20) Halo-Na$_V$1.7(WT) (n=15) Halo-Na$_V$1.7(1.5) (n=14) Halo-Na$_V$1.7(WT) (n=12) Halo-Na$_V$1.7(1.6) (n=15) Halo-Na$_V$1.7(WT) (n=15) Halo-Na$_V$1.7(1.8) (n=17) Halo-Na$_V$1.7(WT) (n=15) Halo-Na$_V$1.7(1.9) (n=15)	
Fig 2C	CRMP2 immunoprecipitation followed by Na$_V$1.7 western blot	Mann-Whitney test	DMSO vs. Myr-TAT-SCR p>0.9999 DMSO vs. Myr-TAT-Na$_V$1.7-CRS p=0.0267	DMSO (n=5) Myr-TAT-SCR (n=5) Myr-TAT-Na$_V$1.7-CRS (n=5)	
Fig 2F	Whole cell patch clamp electrophysiology –	Welch's t-test	Myr-TAT-Na$_V$1.7-CRS vs. Myr-TAT-SCR p=0.0396	Myr-TAT-Na$_V$1.7-CRS (N=15)	

	peak current density			Myr-TAT-SCR (N=13)	
Fig 2G	Whole cell patch clamp electrophysiology – Peak TTX-R current	Mann-Whitney test	Myr-TAT-NaV1.7-CRS vs. Myr-TAT-SCR p=0.8460	Myr-TAT-NaV1.7-CRS (N=16) Myr-TAT-SCR (N=13)	
Fig 2J	Whole cell patch clamp electrophysiology – peak current density	One-way ANOVA	Tukey's multiple comparison post-hoc test: Myr-TAT-SCR + Water vs. Myr-TAT-SCR + 5 nM ProTx-II p=0.0130 Myr-TAT-SCR + Water vs. Myr-TAT-NaV1.7-CRS + Water p=0.0470 Myr-TAT-SCR + Water vs. Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.0012 Myr-TAT-NaV1.7-CRS + Water vs. Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.8197	Myr-TAT-SCR + Water (N=14) Myr-TAT-SCR + 5 nM ProTx-II (N=13) Myr-TAT-NaV1.7-CRS + Water (N=12) Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II (N=8)	
Fig 2M	Whole cell patch clamp electrophysiology – peak current density	One-way ANOVA	Tukey's multiple comparison post-hoc test: Myr-TAT-SCR + Ctrl siRNA vs. Myr-TAT-SCR + CRMP2 siRNA p=0.0416 Myr-TAT-SCR + Ctrl siRNA vs. Myr-TAT-NaV1.7-CRS + Ctrl siRNA p=0.0573 Myr-TAT-SCR + Ctrl siRNA vs. Myr-TAT-NaV1.7-CRS + CRMP2 siRNA p=0.0499 Myr-TAT-NaV1.7-CRS + Ctrl siRNA vs. Myr-TAT-NaV1.7-CRS + CRMP2 siRNA p>0.9999	Myr-TAT-SCR + Ctrl siRNA (n=13) Myr-TAT-SCR + CRMP2 siRNA (n=12) Myr-TAT-NaV1.7-CRS + Ctrl siRNA (n=12) Myr-TAT-NaV1.7-CRS + CRMP2 siRNA (n=13)	
Fig 2O	Total protein western blot	Kruskal-Wallis test	DMSO vs. Myr-TAT-SCR p=0.4620 DMSO vs. Myr-TAT-NaV1.7-CRS p>0.9999	DMSO (n=4) Myr-TAT-SCR (n=4) Myr-TAT-NaV1.7-CRS (n=4)	
Fig 2Q	Cell surface biotinylation	One-way ANOVA	Kruskal-Wallis test: DMSO vs. Myr-TAT-SCR	DMSO (n=5)	

			p=0.8734 DMSO vs. Myr-TAT-Na$_V$1.7-CRS p=0.0178	Myr-TAT-SCR (n=5) Myr-TAT-Na$_V$1.7-CRS (n=5)	
Fig 2T	Whole cell patch clamp electrophysiology – peak current density	One-way ANOVA p=0.0022	Kurskal-Wallis multiple comparison post-hoc test: Myr-TAT-SCR peptide + 0.1% DMSO vs. Myr-TAT-SCR peptide + 20 μM Pitstop2 p>0.9999 Myr-TAT-SCR peptide + 0.1% DMSO vs. Myr-TAT-Na$_V$1.7-CRS peptide + 0.1% DMSO p=0.0033 Myr-TAT-SCR peptide + 20uM Pitstop2 vs. Myr-TAT-Na$_V$1.7-CRS peptide + 20 μM Pitstop2 p>0.9999 Myr-TAT-Na$_V$1.7-CRS peptide + 0.1% DMSO vs. Myr-TAT-Na$_V$1.7-CRS peptide + 20 μM Pitstop2 p=0.0109	Myr-TAT-SCR peptide + 0.1% DMSO (n=15) Myr-TAT-SCR peptide + 20uM Pitstop2 (n=7) Myr-TAT-Na$_V$1.7-CRS peptide + 0.1% DMSO (n=12) Myr-TAT-Na$_V$1.7-CRS peptide + 20uM Pitstop2 (n=14)	
Table S2	Biophysical properties of DRG neurons after treatment with interfering peptide	Mann-Whitney test	<u>V1/2 Values</u>: Activation Myr-TAT-SCR vs Myr-TAT-NaV1.7-CRS p=0.0299 Inactivation Myr-TAT-SCR vs Myr-TAT-NaV1.7-CRS p=0.6919 <u>Slope values:</u> Activation Myr-TAT-SCR vs Myr-TAT-Na$_V$1.7-CRS p=0.0057 Inactivation Myr-TAT-SCR vs Myr-TAT-Na$_V$1.7-CRS p=0.1398	Myr-TAT-SCR Activation V1/2 (n=10) K (n=10) Inactivation V1/2 (n=14) K (n=14) Myr-TAT-NaV1.7-CRS Activation V1/2 (n=9) K (n=9) Inactivation V1/2 (n=13) K (n=13)	
	Biophysical properties of DRG neurons	One-way ANOVA	<u>V1/2 Values</u>: Activation Myr-TAT-SCR + Vehicle vs Myr-TAT-SCR +	Myr-TAT-SCR + Vehicle Activation V1/2 (n=12)	

	after treatment with interfering peptide and treated with ProTx-II		5 nM ProTx-II p<0.0001 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.0119 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.0001 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.0165 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.9383 Myr-TAT-NaV1.7-CRS + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.3200 Inactivation Myr-TAT-SCR + Vehicle vs Myr-TAT-SCR + 5 nM ProTx-II p=0.9981 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.1077 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.0120 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.1501 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.0174 Myr-TAT-NaV1.7-CRS + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.6028 Slope Values : Activation Myr-TAT-SCR + Vehicle vs Myr-TAT-SCR + 5 nM ProTx-II p=0.2535 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.9772 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.5347 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.1318 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.9913 Myr-TAT-NaV1.7-CRS + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.3469 Inactivation Myr-TAT-SCR + Vehicle vs Myr-TAT-SCR +	K (n=12) Inactivation V1/2 (n=11) K (n=11) Myr-TAT-SCR + 5 nM ProTx-II Activation V1/2 (n=11) K (n=11) Inactivation V1/2 (n=11) K (n=11) Myr-TAT-NaV1.7-CRS + Vehicle Activation V1/2 (n=11) K (n=11) Inactivation V1/2 (n=10) K (n=10) Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II Activation V1/2 (n=7) K (n=7) Inactivation V1/2 (n=6) K (n=6)	

			5 nM ProTx-II p=0.5017 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.9991 Myr-TAT-SCR + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.9965 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + Vehicle p=0.6064 Myr-TAT-SCR + 5 nM ProTx-II vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.7658 Myr-TAT-NaV1.7-CRS + Vehicle vs Myr-TAT-NaV1.7-CRS + 5 nM ProTx-II p=0.9997		
	Biophysical properties of DRG neurons after treatment with interfering peptide and treated with CRMP2 siRNA		V1/2 Activation Myr-TAT-SCR + siRNA-Control vs Myr-TAT-SCR + siRNA-CRMP2 p=0.5071 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.0489 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.9975 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.5149 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.5793 Myr-TAT-NaV1.7-CRS + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.0533 Inactivation Myr-TAT-SCR + siRNA-Control vs Myr-TAT-SCR + siRNA-CRMP2 p=0.1480 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.3691 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.3810 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.8987 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.8708 Myr-TAT-NaV1.7-CRS + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p>0.9999 Slope Values	Myr-TAT-SCR + siRNA-Control Activation V1/2 (n=8) K (n=8) Inactivation V1/2 (n=10) K (n=10) Myr-TAT-SCR + siRNA-CRMP2 Activation V1/2 (n=10) K (n=10) Inactivation V1/2 (n=7) K (n=7) Myr-TAT-NaV1.7-CRS + siRNA-Control Activation V1/2 (n=10) K (n=10) Inactivation V1/2 (n=10) K (n=10) Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 Activation V1/2 (n=10) K (n=10) Inactivation V1/2 (n=11) K (n=11)	

			Activation Myr-TAT-SCR + siRNA-Control vs Myr-TAT-SCR + siRNA-CRMP2 p=0.9986 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.8907 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.9976 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.9345 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p>0.9999 Myr-TAT-NaV1.7-CRS + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.9438 Inactivation Myr-TAT-SCR + siRNA-Control vs Myr-TAT-SCR + siRNA-CRMP2 p=0.9027 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.8246 Myr-TAT-SCR + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.9949 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-Control p=0.9997 Myr-TAT-SCR + siRNA-CRMP2 vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.7964 Myr-TAT-NaV1.7-CRS + siRNA-Control vs Myr-TAT-NaV1.7-CRS + siRNA-CRMP2 p=0.6771		
	Biophysical properties of DRG neurons after treatment with interfering peptide and treated with Pitstop2	One-way ANOVA	V1/2 Activation Myr-TAT-SCR + DMSO vs Myr-TAT-SCR + 20 µM Pitstop2 p=0.0328 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + DMSO p=0.8854 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p>0.9999 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + DMSO p=0.1618 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.0378	Myr-TAT-SCR + DMSO Activation V1/2 (n=14) K (n=14) Inactivation V1/2 (n=9) K (n=9) Myr-TAT-SCR + 20 µM Pitstop2 Activation V1/2 (n=7) K (n=7) Inactivation	

			Myr-TAT-NaV1.7-CRS + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.9006 Inactivation Myr-TAT-SCR + DMSO vs Myr-TAT-SCR + 20 µM Pitstop2 p=0.0008 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + DMSO p=0.0006 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.0004 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + DMSO p>0.9999 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.9982 Myr-TAT-NaV1.7-CRS + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.9992 Slope Values Activation Myr-TAT-SCR + DMSO vs Myr-TAT-SCR + 20 µM Pitstop2 p=0.5518 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + DMSO p=0.0561 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.1489 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + DMSO p=0.7943 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.9646 Myr-TAT-NaV1.7-CRS + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.9475 Inactivation Myr-TAT-SCR + DMSO vs Myr-TAT-SCR + 20 µM Pitstop2 p=0.0295 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + DMSO p=0.7778 Myr-TAT-SCR + DMSO vs Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 p=0.3964 Myr-TAT-SCR + 20 µM Pitstop2 vs Myr-TAT-NaV1.7-CRS + DMSO p=0.2181	V1/2 (n=7) K (n=7) Myr-TAT-NaV1.7-CRS + DMSO Activation V1/2 (n=11) K (n=11) Inactivation V1/2 (n=8) K (n=8) Myr-TAT-NaV1.7-CRS + 20 µM Pitstop2 Activation V1/2 (n=13) K (n=13) Inactivation V1/2 (n=10) K (n=10)	

			Myr-TAT-SCR + 20 μM Pitstop2 vs Myr-TAT-NaV1.7-CRS + 20 μM Pitstop2 p=0.4333 Myr-TAT-NaV1.7-CRS + DMSO vs Myr-TAT-NaV1.7-CRS + 20 μM Pitstop2 p=0.9398		
Fig 3B	Whole cell patch clamp electrophysiology – evoked action potentials	Multiple Mann-Whitney tests	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS 0 pA, p>0.9999 10 pA, p=0.1593 20 pA, p=0.1023 30 pA, p=0.0167 40 pA, p=0.0353 50 pA, p=0.0167 60 pA, p=0.0538 70 pA, p=0.0276 80 pA, p=0.0112 90 pA, p=0.0364 100 pA, p=0.0632 110 pA, p=0.0097 120 pA, p=0.0153	Myr-TAT-SCR (n=26) Myr-TAT-Na_V1.7-CRS (n=26)	
Fig 3C	Whole cell patch clamp electrophysiology – resting membrane potential	Mann-Whitney tests	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS p=0.7462	Myr-TAT-SCR (n=26) Myr-TAT-Na_V1.7-CRS (n=26)	
Fig 3E	Whole cell patch clamp electrophysiology – rheobase	Mann-Whitney tests	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS p=0.0035	Myr-TAT-SCR (n=26) Myr-TAT-Na_V1.7-CRS (n=26)	
Fig 3F	Whole cell patch clamp electrophysiology – Input resistance	Mann-Whitney tests	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS p=0.7336	Myr-TAT-SCR (n=26) Myr-TAT-Na_V1.7-CRS (n=26)	
Fig 3H	Spinal cord CGRP release assay	Two-Way ANOVA	Sidak's multiple comparisons test Fraction 1 Control vs. Myr-TAT-SCR p=0.8968 Control vs. Myr-TAT-Na_V1.7-CRS p=0.1324 Myr-TAT-SCR vs Myr-TAT-Na_V1.7-CRS p=0.4010 Fraction 2 Control vs. Myr-TAT-SCR p=0.2430	DMSO (n=4) Myr-TAT-SCR (n=4) Myr-TAT-Na_V1.7-CRS (n=4)	

			Control vs. Myr-TAT-Na$_V$1.7-CRS p=0.1495 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.8924 Fraction 3 Control vs. Myr-TAT-SCR p=0.9219 Control vs. Myr-TAT-Na$_V$1.7-CRS p=0.0026 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.0012 Fraction 4 Control vs. Myr-TAT-SCR p=0.2418 Control vs. Myr-TAT-Na$_V$1.7-CRS p<0.0001 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p<0.0001 Fraction 5 Control vs. Myr-TAT-SCR p=0.5405 Control vs. Myr-TAT-Na$_V$1.7-CRS p=0.0191 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.4724 Fraction 6 Control vs. Myr-TAT-SCR p=0.9613 Control vs. Myr-TAT-Na$_V$1.7-CRS p=0.7229 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.9202		
Fig 4A	CRMP2 binding to peptide 141	Mann-Whitney test	WT vs. CRMP2$^{K374A/K374A}$ p<0.0001	WT (n=4) CRMP2$^{K374A/K374A}$ (n=4)	
Fig 4B	SNI female rats – paw withdrawal threshold	Multiple Mann-Whitney tests	Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (Pre-SNI, p>0.9999) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=0, p=0.9675) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=0.5, p>0.9999) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=1, p=0.8918) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=2, p=0.0173) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=3, p=0.0022) Myr-TAT-SCR female vs. Myr-TAT-Na$_V$1.7-CRS female (t=4, p=0.0152)	Myr-TAT-SCR female (n=6) Myr-TAT-Na$_V$1.7-CRS female (n=6)	

			Myr-TAT-SCR female vs. Myr-TAT-Na_V1.7-CRS female (t=5, p=0.0649)		
	SNI male rats – paw withdrawal threshold		Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (Pre-SNI, p>0.9999) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=0, p=0.3095) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=0.5, p=0.4643) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=1, p=0.0833) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=2, p=0.0119) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=3, p=0.0119) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=4, p=0.0119) Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male (t=5, p=0.0119)	Myr-TAT-SCR male (n=6) Myr-TAT-Na_V1.7-CRS male (n=6)	
Fig 4C	Paw withdrawal threshold rats – area under the curve	Mann-Whitney test	Myr-TAT-SCR female vs. Myr-TAT-Na_V1.7-CRS female p=0.0087 Myr-TAT-SCR male vs. Myr-TAT-Na_V1.7-CRS male p=0.0152	Myr-TAT-SCR female (n=6) Myr-TAT-Na_V1.7-CRS female (n=6) Myr-TAT-SCR male (n=6) Myr-TAT-Na_V1.7-CRS male (n=6)	
Fig 4D	Mouse thermal nociception – hot plate	Kruskal-Wallis test	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS (females) p=0.1177 Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS (males) p=0.5540	Female Myr-TAT-SCR (n=10) Female Myr-TAT-Na_V1.7-CRS (n=10) Male Myr-TAT-SCR (n=10) Male Myr-TAT-Na_V1.7-CRS (n=10)	
Fig 4E	Mouse thermal nociception – tail flick	Kruskal-Wallis test	Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS (females) p>0.9999 Myr-TAT-SCR vs. Myr-TAT-Na_V1.7-CRS (males) p>0.9999	Female Myr-TAT-SCR (n=10) Female Myr-TAT-Na_V1.7-CRS (n=10) Male Myr-TAT-SCR (n=10) Male Myr-TAT-Na_V1.7-CRS (n=10)	

Fig 4F	Motor coordination in rats - rotarod	Multiple Mann-Whitney tests	Males Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (baseline) p=0.4009 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (60 min post injection) p=0.8298 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (120 min post injection) p=0.3176 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (180 min post injection) p=0.7103 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (240 min post injection) p=0.9015 Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS (300 min post injection) p=0.6859	Myr-TAT-SCR (n=7) Myr-TAT-Na$_V$1.7-CRS (n=7)	
Fig 5C	Whole cell patch clamp electrophysiology – peak current density	Welch's t-test	Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.0002	Myr-TAT-SCR (n=12) Myr-TAT-Na$_V$1.7-CRS (n=12)	
Fig 5D	Whole cell patch clamp electrophysiology – TTX-R current density	Mann-Whitney test	Myr-TAT-SCR vs. Myr-TAT-Na$_V$1.7-CRS p=0.6194	Myr-TAT-SCR (n=12) Myr-TAT-Na$_V$1.7-CRS (n=12)	
Fig 5G	Whole cell patch clamp electrophysiology – peak current density	One-way ANOVA	pAAV-SCR +Vehicle vs. pAAV-SCR + ProTx p=0.0024 pAAV-SCR +Vehicle vs. pAAV-Na$_V$1.7-CRS + vehicle p=0.0213 pAAV-SCR +Vehicle vs. pAAV-Na$_V$1.7-CRS + ProTx p=0.0003 pAAV-Na$_V$1.7-CRS + Vehicle vs. pAAV-Na$_V$1.7-CRS + ProTx p>0.9999	pAAV-SCR +Vehicle (n=15) pAAV-SCR + Protox (n=12) pAAV-Na$_V$1.7-CRS + Vehicle (n=13) pAAV-Na$_V$1.7-CRS + Protox (n=15)	
Fig 5J	Whole cell patch clamp electrophysiology – peak current density	One-way ANOVA	pAAV-SCR +Vehicle vs. pAAV-SCR + Pitstop2 p>0.9999 pAAV-SCR +Vehicle vs. pAAV-Na$_V$1.7-CRS + Vehicle p>0.0018 pAAV-SCR +Vehicle vs. pAAV-Na$_V$1.7-CRS + Pitstop2 p>0.9999 pAAV-Na$_V$1.7-CRS + Vehicle v.s pAAV-Na$_V$1.7-CRS + Pitstop2 p=0.0115	pAAV-SCR +Vehicle (n=12) pAAV-SCR + Pitstop2 (n=15) pAAV-Na$_V$1.7-CRS + Vehicle (n=15) pAAV-Na$_V$1.7-CRS + Pitstop2 (n=9)	

Fig 5L	Slice patch clamp electrophysiology – Frequency of sEPSC	Mann-Whitney test	pAAV-SCR vs. pAAV-Na$_V$1.7-CRS p=0.0305	pAAV-SCR (n=12) pAAV-Na$_V$1.7-CRS (n=11)	
Fig 5L	Slice patch clamp electrophysiology – Amplitud of sEPSC	Mann-Whitney test	pAAV-SCR vs. pAAV-Na$_V$1.7-CRS p=0.0357	pAAV-SCR (n=11) pAAV-Na$_V$1.7-CRS (n=10)	
Table S3	Biophysical properties of DRG neurons after treatment with AAV	Mann-Whitney test	*AAV-SCR vs AAV-Na$_V$1.7-CRS* V1/2 Activation P=0.6571 Inactivation P=0.8627 *AAV-SCR vs AAV-Na$_V$1.7-CRS* Slope Activation P=0.5775 Inactivation P=0.4563	*AAV-SCR* Activation V1/2 (n=12) K (n=12) Inactivation V1/2 (n=12) K (n=12) *AAV-Na$_V$1.7-CRS* Activation V1/2 (n=12) K (n=12) Inactivation V1/2 (n=12) K (n=12)	
	Biophysical properties of DRG neurons after treatment with AAV and ProTx-II	One-Way ANOVA	V1/2 Activation AAV-SCR + Vehicle vs. AAV-SCR + 5 nM ProTx-II P<0.0001 AAV-SCR + Vehicle vs. AAV-Na$_V$1.7-CRS + Vehicle P=0.3475 AAV-SCR + Vehicle vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P=0.9865 AAV-SCR + 5 nM ProTx-II vs. AAV-Na$_V$1.7-CRS + Vehicle P<0.0001 AAV-SCR + 5 nM ProTx-II vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P<0.0001 AAV-Na$_V$1.7-CRS + Vehicle vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P=0.2012 Inactivation AAV-SCR +	AAV-SCR + Vehicle Activation V1/2 (n=15) K (n=15) Inactivation V1/2 (n=15) K (n=15) AAV-SCR + 5 nM ProTx-II Activation V1/2 (n=12) K (n=12) Inactivation V1/2 (n=12) K (n=12) AAV-NaV1.7-CRS + Vehicle Activation V1/2 (n=13) K (n=13) Inactivation V1/2 (n=13) K (n=13)	

			Vehicle vs. AAV-SCR + 5 nM ProTx-II P=0.0493 AAV-SCR + Vehicle vs. AAV-Nav1.7-CRS + Vehicle P=0.1129 AAV-SCR + Vehicle vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.9991 AAV-SCR + 5 nM ProTx-II vs. AAV-Nav1.7-CRS + Vehicle P<0.0001 AAV-SCR + 5 nM ProTx-II vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.0363 AAV-Nav1.7-CRS + Vehicle vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.1468 Slope Values Activation AAV-SCR + Vehicle vs. AAV-SCR + 5 nM ProTx-II P=0.6643 AAV-SCR + Vehicle vs. AAV-Nav1.7-CRS + Vehicle P=0.9836 AAV-SCR + Vehicle vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.2070 AAV-SCR + 5 nM ProTx-II vs. AAV-Nav1.7-CRS + Vehicle P=0.4754 AAV-SCR + 5 nM ProTx-II vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.8856 AAV-Nav1.7-CRS + Vehicle vs. AAV-Nav1.7-CRS + 5 nM ProTx-II P=0.1176	AAV-NaV1.7-CRS + 5 nM ProTx-II Activation V1/2 (n=15) K (n=15) Inactivation V1/2 (n=15) K (n=15)	

			Inactivation AAV-SCR + Vehicle vs. AAV-SCR + 5 nM ProTx-II P=0.9961 AAV-SCR + Vehicle vs. AAV-Na$_V$1.7-CRS + Vehicle P=0.7893 AAV-SCR + Vehicle vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P=0.9997 AAV-SCR + 5 nM ProTx-II vs. AAV-Na$_V$1.7-CRS + Vehicle P=0.6553 AAV-SCR + 5 nM ProTx-II vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P=0.9971 AAV-Na$_V$1.7-CRS + Vehicle vs. AAV-Na$_V$1.7-CRS + 5 nM ProTx-II P=0.7396		
	Biophysical properties of DRG neurons after treatment with AAV and Pitstop 2	One-Way ANOVA	V1/2 Activation AAV-SCR + DMSO vs. AAV-SCR + 20 µM Pitstop2 P=0.9961 AAV-SCR + DMSO vs. AAV-Na$_V$1.7-CRS + DMSO p>0.9999 AAV-SCR + DMSO vs. AAV-Na$_V$1.7-CRS + 20 µM Pitstop2 P=0.9973 AAV-SCR + 20 µM Pitstop2 vs. AAV-Na$_V$1.7-CRS + DMSO P=0.9995 AAV-SCR + 20 µM Pitstop2 vs. AAV-Na$_V$1.7-CRS + 20 µM Pitstop2 P=0.9913 AAV-Na$_V$1.7-CRS + DMSO vs. AAV-Na$_V$1.7-CRS +	AAV-SCR + DMSO Activation V1/2 (n=12) K (n=12) Inactivation V1/2 (n=12) K (n=12) AAV-SCR + 20 µM Pitstop2 Activation V1/2 (n=15) K (n=15) Inactivation V1/2 (n=15) K (n=15) AAV-NaV1.7-CRS + DMSO Activation V1/2 (n=15) K (n=15)	

			20 μM Pitstop2 P=0.9974 Inactivation AAV-SCR + DMSO vs. AAV-SCR + 20 μM Pitstop2 P=0.8802 AAV-SCR + DMSO vs. AAV-Nav1.7-CRS + DMSO P=0.0517 AAV-SCR + DMSO vs. AAV-Nav1.7-CRS + 20 μM Pitstop2 P=0.9997 AAV-SCR + 20 μM Pitstop2 vs. AAV-Nav1.7-CRS + DMSO P=0.0042 AAV-SCR + 20 μM Pitstop2 vs. AAV-Nav1.7-CRS + 20 μM Pitstop2 P=0.9378 AAV-Nav1.7-CRS + DMSO vs. AAV-Nav1.7-CRS + 20 μM Pitstop2 P=0.0675 Slope Values Activation AAV-SCR + DMSO vs. AAV-SCR + 20 μM Pitstop2 P=0.9522 AAV-SCR + DMSO vs. AAV-Nav1.7-CRS + DMSO P=0.9973 AAV-SCR + DMSO vs. AAV-Nav1.7-CRS + 20 μM Pitstop2 P=0.7382 AAV-SCR + 20 μM Pitstop2 vs. AAV-Nav1.7-CRS + DMSO P=0.8693 AAV-SCR + 20 μM Pitstop2 vs. AAV-Nav1.7-CRS + 20 μM Pitstop2 P=0.9365 AAV-Nav1.7-CRS + DMSO vs. AAV-Nav1.7-CRS + 20 μM Pitstop2	Inactivation V1/2 (n=15) K (n=15) AAV-NaV1.7-CRS + 20 μM Pitstop2 Activation V1/2 (n=9) K (n=9) Inactivation V1/2 (n=9) K (n=9)	

			P=0.6006 Inactivation AAV-SCR + DMSO vs. AAV-SCR + 20 µM Pitstop2 P=0.9716 AAV-SCR + DMSO vs. AAV-Na$_V$1.7-CRS + DMSO P=0.9428 AAV-SCR + DMSO vs. AAV-Na$_V$1.7-CRS + 20 µM Pitstop2 P=0.8158 AAV-SCR + 20 µM Pitstop2 vs. AAV-Na$_V$1.7-CRS + DMSO P=0.9992 AAV-SCR + 20 µM Pitstop2 vs. AAV-Na$_V$1.7-CRS + 20 µM Pitstop2 P=0.9547 AAV-Na$_V$1.7-CRS + DMSO vs. AAV-Na$_V$1.7-CRS + 20 µM Pitstop2 P=0.9776		
Fig 6D	Males SNI reversal – paw withdrawal thresholds	Two-way anova	AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (Pre-SNI, p>0.9999) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=0d, p>0.9999) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=4d, p=0.0173) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=7d, p=0.0087) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=11d, p=0.0152) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=14d, p=0.0087) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=20d, p=0.0238) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=24d, p=0.0866)	AAV-CMV-eGFP-Na$_V$1.7-CRS (n=5) AAV-CMV-eGFP-SCR (n=6)	

			AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=31d, p=0.1212)		
Fig 6E	Males SNI reversal – area under the curve	Mann-Whitney test	AAV-CMV-eGFP-Na$_V$1.7-CRS vs AAV-CMV-eGFP-SCR (p=0.0043)	AAV-CMV-eGFP-Na$_V$1.7-CRS (n=5) AAV-CMV-eGFP-SCR (n=6)	
Fig 6F	Males SNI-Reversal Locomotor activity	Mann-Whitney test	AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.9307	AAV9-CMV-eGFP-SCR (n=6) AAV9-CMV-eGFP-Na$_V$1.7 (n=5)	
Fig 6G	Males SNI-Reversal Open field test	Multiple Mann-Whitney tests	Time in Periphery AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.2786 Time in Center AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.2786	AAV9-CMV-eGFP-SCR (n=6) AAV9-CMV-eGFP-Na$_V$1.7 (n=5)	
Fig 6H	Females SNI reversal – paw withdrawal thresholds	Two-way anova	AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (Pre-SNI, p>0.9999) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=7d, p=0.3770) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=11d, p=0.0275) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=14d, p=0.021) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=18d, p<0.0001) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=27d, p<0.0001) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=38d, p=0.004)	AAV-CMV-eGFP-SCR (n=8) AAV-CMV-eGFP-Na$_V$1.7-CRS (n=9)	
Fig 6I	Females SNI reversal – area	Mann-Whitney test	AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (p<0.0001)	AAV-CMV-eGFP-SCR (n=8)	

	under the curve			AAV-CMV-eGFP-Na$_V$1.7-CRS (n=9)	
Fig 6J	Females SNI reversal - Locomotor activity	Mann-Whitney test	AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.1520	AAV9-CMV-eGFP-SCR (n=7) AAV9-CMV-eGFP-Na$_V$1.7 (n=8)	
Fig 6K	Females SNI-reversal Open field test	Multiple Mann-Whitney tests	Time in Periphery AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.8665 Time in Center AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.8665		
Fig 6L	Males SNI prevention – paw withdrawal thresholds	Two-way anova	AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (BL1, p>0.9999) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (BL2, p>0.9999) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=6d, p=0.0424) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=8d, p=0.0002) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=12d, p=0.0005) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=19d, p=0.0005) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=21d, p=0.0015) AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (t=54d, p=0.0038)	AAV-CMV-eGFP-SCR (n=7) AAV-CMV-eGFP-Na$_V$1.7-CRS (n=9)	
Fig 6M	Males SNI prevention – area under the curve	Mann-Whitney test	AAV-CMV-eGFP-Na$_V$1.7-CRS vs. AAV-CMV-eGFP-SCR (p=0.0002)	AAV-CMV-eGFP-SCR (n=7) AAV-CMV-eGFP-Na$_V$1.7-CRS (n=9)	

Fig 6N	Males SNI prevention - Locomotor activity	Mann-Whitney test	AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-$Na_V1.7$ p=0.7577	AAV-CMV-eGFP-SCR (n=7) AAV-CMV-eGFP-$Na_V1.7$-CRS (n=9)	
Fig 6O	Males SNI-Prevention Open field test	Multiple Mann-Whitney tests	Time in Periphery AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-$Na_V1.7$ P=0.1141 Time in Center AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-$Na_V1.7$ P=0.1141	AAV-CMV-eGFP-SCR (n=7) AAV-CMV-eGFP-$Na_V1.7$-CRS (n=9)	
Fig 6P	Females SNI prevention – paw withdrawal thresholds	Two-way anova	AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (BL1, p>0.9999) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (BL2, p=0.2058) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (t=8d, p=0.0024) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (t=12d, p=0.0005) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (t=16d, p=0.0256) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (t=20d, p=0.0069) AAV-CMV-eGFP-$Na_V1.7$-CRS vs. AAV-CMV-eGFP-SCR (t=54d, p=0.0107)	AAV-CMV-eGFP-SCR (n=9) AAV-CMV-eGFP-$Na_V1.7$-CRS (n=8)	
Fig 6Q	Females SNI prevention – area under the curve	Mann-Whitney test	AAV-CMV-eGFP-$Na_V1.7$-CRS vs AAV-CMV-eGFP-SCR (p<0.0001)	AAV-CMV-eGFP-SCR (n=9) AAV-CMV-eGFP-$Na_V1.7$-CRS (n=8)	
Fig 6R	Females SNI prevention - Locomotor activity	Mann-Whitney test	AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-$Na_V1.7$ p=0.3704	AAV-CMV-eGFP-SCR (n=9) AAV-CMV-eGFP-$Na_V1.7$-CRS (n=8)	
Fig 6S	Females SNI-prevention	Multiple Mann-Whitney tests	Time in Periphery AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-$Na_V1.7$ p=0.5414	AAV-CMV-eGFP-SCR (n=9)	

	Open field test		Time in Center AAV9-CMV-eGFP-SCR vs. AAV9-CMV-eGFP-Na$_V$1.7 p=0.5414	AAV-CMV-eGFP-Na$_V$1.7-CRS (n=8)	
Fig 7A	Paclitaxel paw withdrawal threshold	Three-way ANOVA	Holm-Sidak post-hoc test: Time p<0.0001 Treatment Tx p<0.0001 Virus Tx p<0.0001 Time x Treatment Tx p<0.0001 Time x Virus Tx p=0.0002 Treatment Tx x Virus Tx p=0.0077 Time x Treatment Tx x Virus Tx p=0.0708 7 days: Veh + AAV9-CMV-eGFP-SCR vs. 7 days: Pac + AAV9-CMV-eGFP-SCR p=0.0024 14 days: Veh + AAV9-CMV-eGFP-SCR vs. 14 days: Pac + AAV9-CMV-eGFP-SCR p=0.0827 16 days: Veh + AAV9-CMV-eGFP-SCR vs. 16 days: Pac + AAV9-CMV-eGFP-SCR p=0.0136 21 days: Veh + AAV9-CMV-eGFP-SCR vs. 21 days: Pac + AAV9-CMV-eGFP-SCR p=0.0360 7 days: Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS vs. 7 days: Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p<0.0001 7 days: Pac + AAV9-CMV-eGFP-SCR vs. 7 days: Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p>0.9999 14 days: Pac + AAV9-CMV-eGFP-SCR vs. 14 days: Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.2977 16 days: Pac + AAV9-CMV-eGFP-SCR vs. 16 days: Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.0096 21 days: Pac + AAV9-CMV-eGFP-SCR vs. 21 days: Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.0345	Veh + AAV9-CMV-eGFP-SCR (n=8) Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS (n=8) Pac + AAV9-CMV-eGFP-SCR (n=8) Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS (n=8)	
Fig 7B	Paclitaxel paw withdrawal threshold – area under the curve	One-way ANOVA	Veh + AAV9-CMV-eGFP-SCR vs. Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.4799 Veh + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-SCR p<0.0001 Veh + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.1597 Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS vs. Pac + AAV9-CMV-eGFP-SCR p<0.0001	Veh + AAV9-CMV-eGFP-SCR (n=8) Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS (n=8) Pac + AAV9-CMV-eGFP-SCR (n=8) Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS	

			Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS vs. Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0062 Pac + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p<0.0001	(n=8)	
Fig 7C	Paclitaxel time aversive response	Three-way ANOVA	Holm-Sidak post-hoc test: Time p<0.0001 Treatment Tx p<0.0001 Virus Tx p<0.0001 Time x Treatment Tx p<0.0001 Time x Virus Tx p<0.0001 Treatment Tx x Virus Tx p<0.0001 Time x Treatment Tx x Virus Tx p<0.0001 8 days: Veh + AAV9-CMV-eGFP-SCR vs. 8 days: Pac + AAV9-CMV-eGFP-SCR p=0.0024 15 days: Veh + AAV9-CMV-eGFP-SCR vs. 15 days: Pac + AAV9-CMV-eGFP-SCR p=0.0024 17 days: Veh + AAV9-CMV-eGFP-SCR vs. 17 days: Pac + AAV9-CMV-eGFP-SCR p=0.0190 22 days: Veh + AAV9-CMV-eGFP-SCR vs. 22 days: Pac + AAV9-CMV-eGFP-SCR p=0.0027 8 days: Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS vs. 8 days: Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0033 8 days: Pac + AAV9-CMV-eGFP-SCR vs. 8 days: Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p>0.9999 15 days: Pac + AAV9-CMV-eGFP-SCR vs. 15 days: Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0049 17 days: Pac + AAV9-CMV-eGFP-SCR vs. 17 days: Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0227 22 days: Pac + AAV9-CMV-eGFP-SCR vs. 22 days: Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0108	Veh + AAV9-CMV-eGFP-SCR (n=8) Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS (n=8) Pac + AAV9-CMV-eGFP-SCR (n=8) Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS (n=8)	
Fig 7D	Paclitaxel time aversive response – area under the curve	One-way ANOVA	Veh + AAV9-CMV-eGFP-SCR vs. Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.9336 Veh + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-SCR p<0.0001 Veh + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-$Na_V1.7$-CRS p=0.0025 Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS vs. Pac + AAV9-CMV-eGFP-SCR p<0.0001	Veh + AAV9-CMV-eGFP-SCR (n=8) Veh + AAV9-CMV-eGFP-$Na_V1.7$-CRS (n=8) Pac + AAV9-CMV-eGFP-SCR (n=8)	

			Veh + AAV9-CMV-eGFP-Na$_V$1.7-CRS vs. Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p=0.0005 Pac + AAV9-CMV-eGFP-SCR vs. Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS p<0.0001	Pac + AAV9-CMV-eGFP-Na$_V$1.7-CRS (n=8)	
Fig 8B	Na$_V$1.7 pull down from Macaque DRG	Mann-Whitney test	Na$_V$1.7-CRS vs. Scramble p=0.0286	Na$_V$1.7-CRS (n=4) Scramble (n=4)	
Fig 8E	Macaque DRG whole cell patch clamp electrophysiology – peak current density	Kruskal-Wallis Test; p<0.0001 Kruskal-Wallis statistic = 22.99	AAV-CMV-SCR vs. AAV-CMV-SCR + Protox, p=0.0154 AAV-CMV-SCR vs. AAV-CMV-Na$_V$1.7, p=0.0010 AAV-CMV-SCR vs. AAV-CMV-Na$_V$1.7 + Protox, p<0.0001 AAV-CMV-SCR + Protox vs. AAV-CMV-Na$_V$1.7, p>0.9999 AAV-CMV-SCR + Protox vs. AAV-CMV-Na$_V$1.7 + Protox, p>0.9999 AAV-CMV-Na$_V$1.7 vs. AAV-CMV-Na$_V$1.7 + Protox, p>0.9999	AAV9-SCR (n=13) AAV9-Na$_V$1.7-CRS (n=12) AAV9-SCR + 5nM ProTx-II (n=17) AAV9-Na$_V$1.7-CRS + 5nM ProTx-II (n=16)	
Fig 8I	Macaque DRG whole cell patch clamp electrophysiology – TTX-R peak current density	Mann-Whitney test	AAV9-Na$_V$1.7-CRS + 300 nM TTX vs. AAV9-SCR + 300 nM TTX p=0.4865	AAV9-SCR + 300 nM TTX (n=11) AAV9-Na$_V$1.7-CRS (n=11)	
Table S4	Macaque DRG whole cell patch clamp electrophysiology – TTX-R channel kinetics	Mann-Whitney test	*AAV9-SCR + TTX vs AAV9-Na$_V$1.7-CRS+ TTX* Activation V1/2 P=0.7026 K P=0.5853	AAV9-SCR + TTX Activation V1/2 (n=11) K (n=11) AAV9-NaV1.7-CRS+ TTX Activation V1/2 (n=11) K (n=11)	
	Macaque DRG whole cell patch clamp electrophysiology – ProTx-II	One-Way ANOVA	V1/2 Activation AAV9-SCR + Vehicle vs AAV9-SCR + 5 nM ProTx-II P=0.0037	AAV9-SCR + Vehicle Activation V1/2 (n=13) K (n=13)	

	channel kinetics		AAV9-SCR + Vehicle vs AAV9-Na$_V$1.7-CRS+ Vehicle P=0.9790 AAV9-SCR + Vehicle vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II P=0.1558 AAV9-SCR + 5 nM ProTx-II vs AAV9-Na$_V$1.7-CRS+ Vehicle P=0.0175 AAV9-SCR + 5 nM ProTx-II vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II P=0.2996 AAV9-Na$_V$1.7-CRS+ Vehicle vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II P=0.3917 <u>Slope Values</u> AAV9-SCR + Vehicle vs AAV9-SCR + 5 nM ProTx-II P=0.7661 AAV9-SCR + Vehicle vs AAV9-Na$_V$1.7-CRS+ Vehicle P=0.7296 AAV9-SCR + Vehicle vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II P=0.7412 AAV9-SCR + 5 nM ProTx-II vs AAV9-Na$_V$1.7-CRS+ Vehicle P=0.2656 AAV9-SCR + 5 nM ProTx-II vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II p>0.9999 AAV9-Na$_V$1.7-CRS+ Vehicle vs AAV9-Na$_V$1.7-CRS+ 5 nM ProTx-II P=0.2151	AAV9-SCR + 5 nM ProTx-II Activation V1/2 (n=13) K (n=13) AAV9-NaV1.7-CRS+ Vehicle Activation V1/2 (n=17) K (n=17) AAV9-NaV1.7-CRS+ 5 nM ProTx-II Activation V1/2 (n=14) K (n=14)	