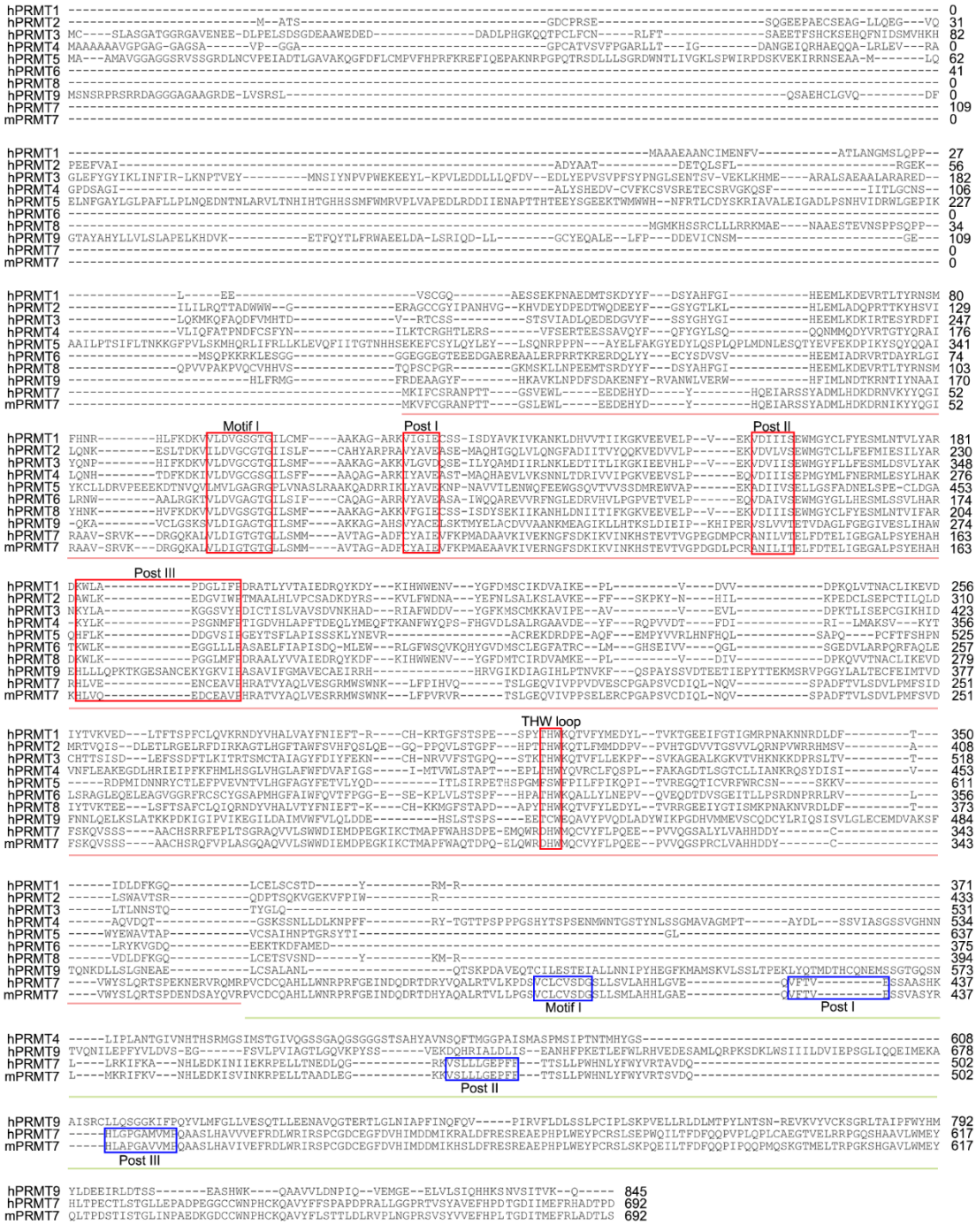

Figure S1. Sequence alignment of human PRMTs and mouse PRMT7

The amino acid sequences of PRMTs are compared here using ClustalW. The signature conserved sequence motifs (Motif I; Post I, II, III; and 'THW' loops) are indicated by the boxes. Two PRMT7 core domains are underlined in pink and green. The UniProt IDs for the aligned sequences are as follows: hPRMT1: Q99873; hPRMT2: P55345;

hPRMT3: O60678; hPRMT4: Q86X55; hPRMT5: O14744; hPRMT6: Q96LA8; hPRMT7: Q9NVM4; hPRMT8: Q9NR22; hPRMT9: Q6P2P2; and mPRMT7: Q922X9.

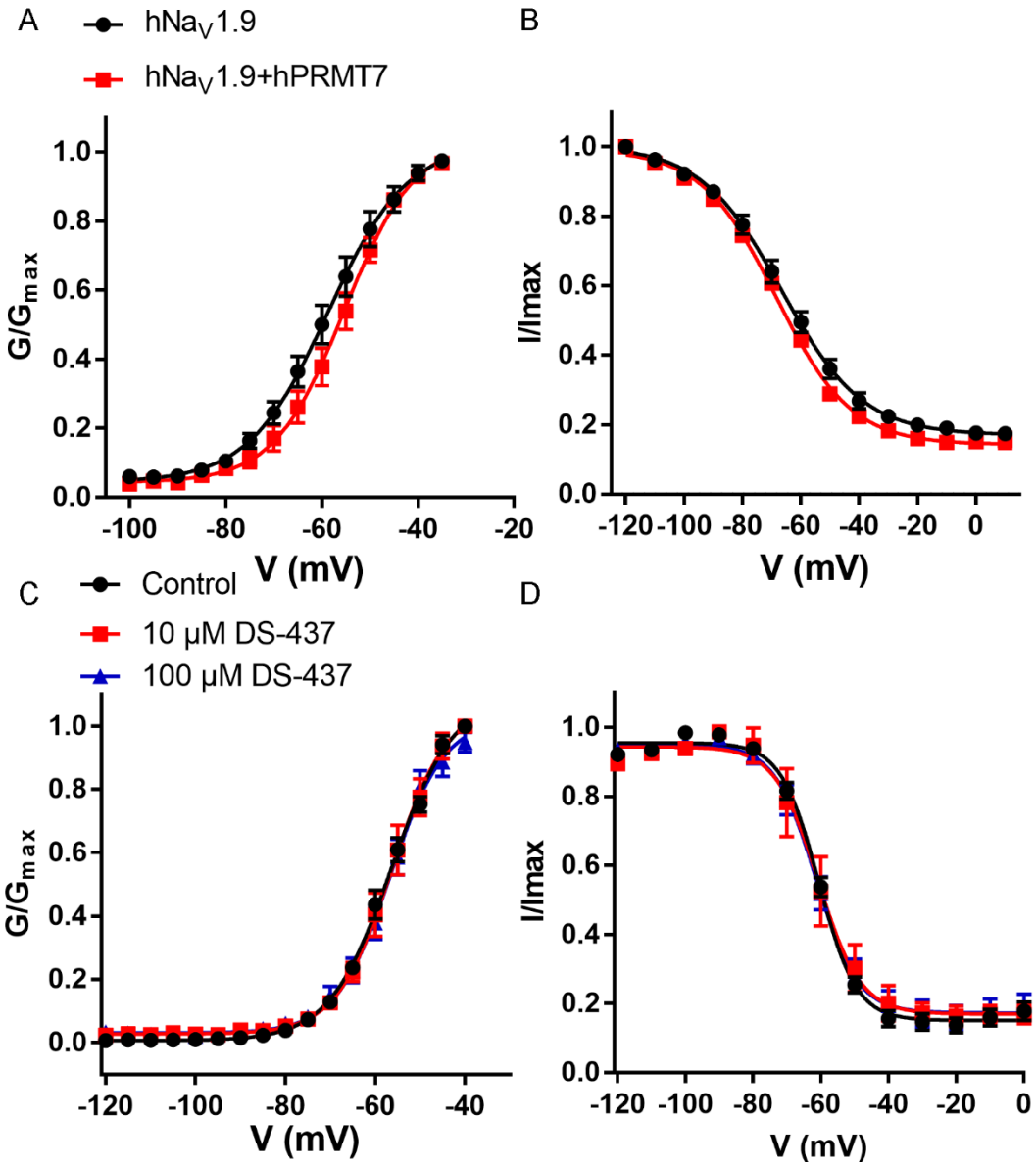

Figure S2. Functional effects of PRMT7 on Nav1.9 channel

Normalized conductance-voltage relationship (A) and steady-state fast inactivation curves (B) of neurons transfected with hNav1.9, or Nav1.9 and PRMT7. Normalized conductance-voltage relationship (C) and steady-state fast inactivation curves (D) of neurons in experimental (DS-437) and control groups.

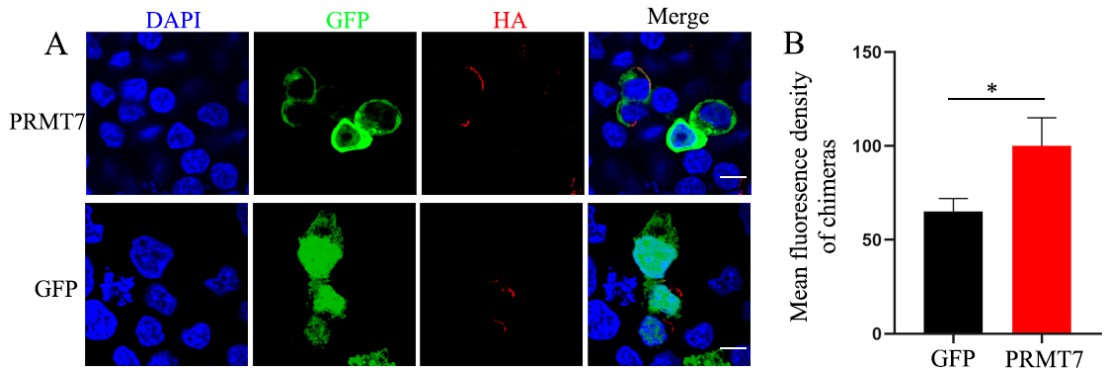

Figure S3. PRMT7 promotes chimera expression on the cell surface

(A) HEK293T cells co-transfected with chimeric construct and an expression plasmid encoding either GFP-PRMT7 or GFP were analyzed by non-permeabilized immunofluorescence labeling with antibodies against HA (red), and nuclei (blue) were labeled with DAPI. Scale bar, 10 μm. (B) Quantitative analyses of the relative mean fluorescence intensity of cells co-expressing chimeric protein and PRMT7 or GFP with the ROI Manager tool of ImageJ software. At least 100 cells co-expressing the two proteins were counted. The independent student's *t* test was used to analyze statistical significance, *p <0.05.

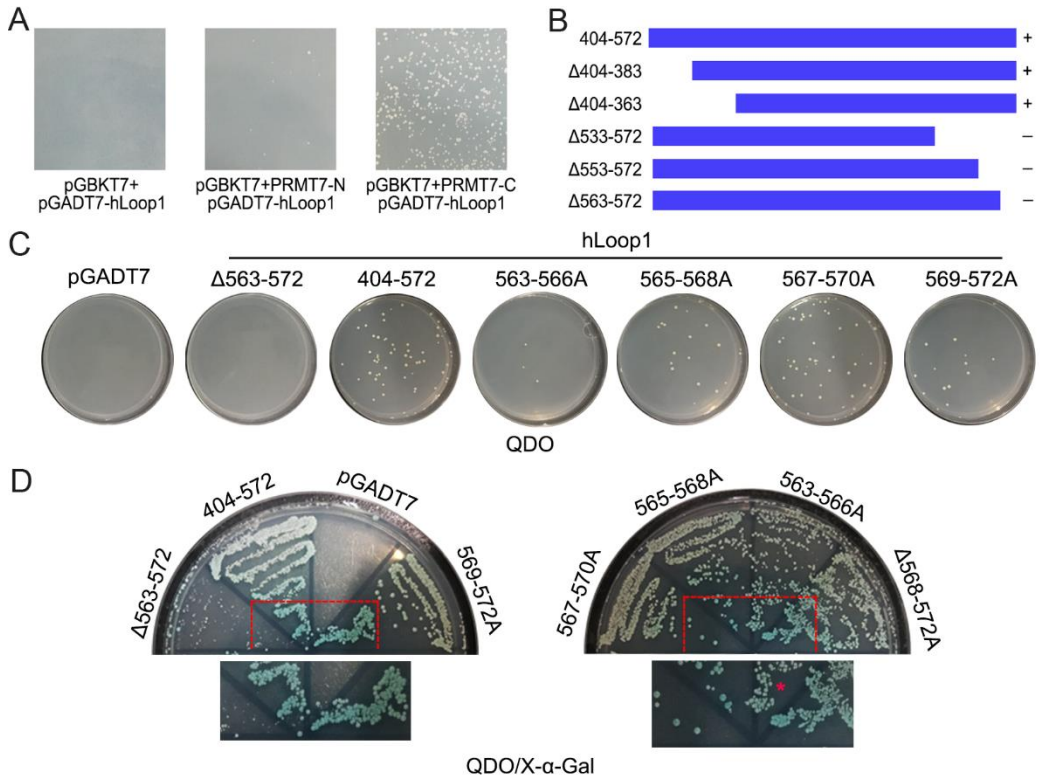

Figure S4. Mapping and verification of the PRMT7 binding site on hLoop1

(A) The interaction of hLoop1 with the N- (residues 1–363) and C-terminal core (residues 364–692) of PRMT7 in Y2H. (B) Diagram of truncated hLoop1 constructs assayed for interaction with the PRMT7-C-terminal core using the Y2H assay. +, growth on QDO plates; -, no growth. (C) Representative Y2H interactions of the PRMT7-C-terminal core with the indicated hybrid constructs. Interactors were analyzed by growth on QDO agar plates. (D) Y2H analysis showing the growth of indicated yeast cells on QDO/X-α-gal agar plates. Yeast β-galactosidase assays confirming protein-protein interactions. Asterisks indicate the lightest blue signals of mutant (residues 563-566A of hLoop1) in the magnified view (red box).

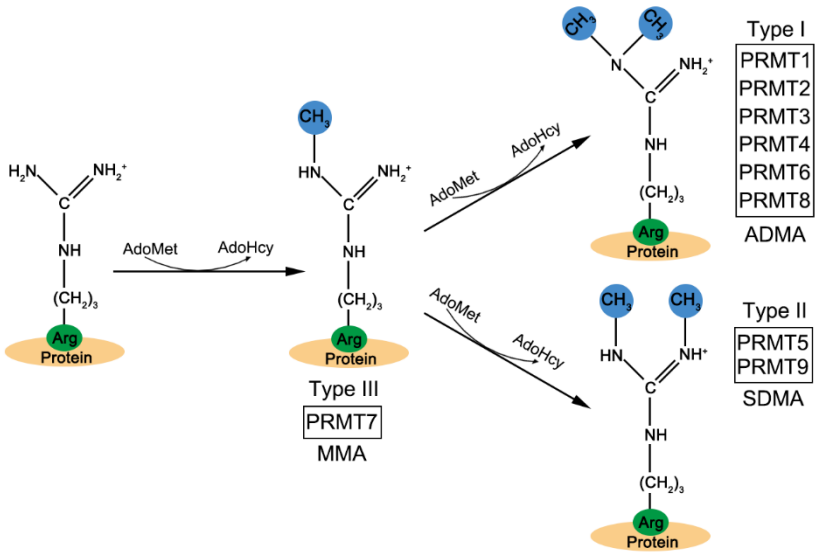

Figure S5. Types of protein arginine methylation catalyzed by PRMTs

Mammalian PRMTs catalyze the transfer of the methyl group onto the terminal nitrogen atom of arginine residues forming monomethylarginine (MMA), asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) by type I, type II and type III enzymes, respectively.

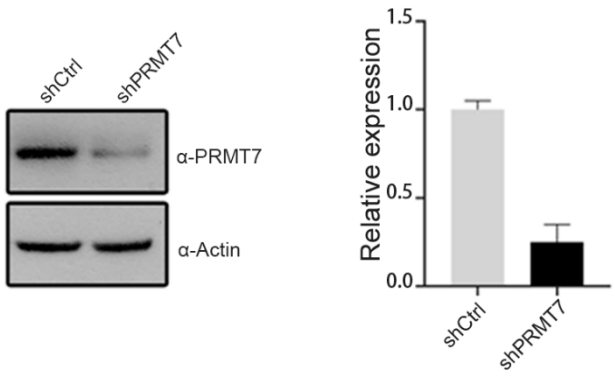

Figure S6. Western blot analyses of PRMT7 expression in HEK293T-shCtrl and shPRMT7 cells

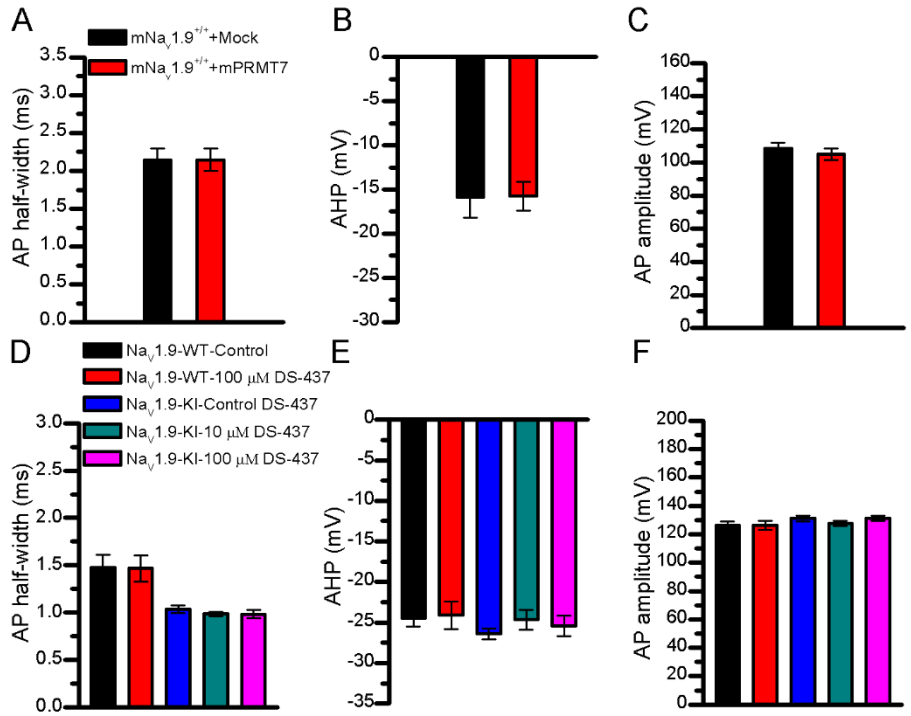

Figure S7. The effects of treatments on AP properties in DRG neuron

(A) Half-width, (B) AHP (after hyperpolarization) and (C) amplitude of APs in *Scn11a*$^{-/-}$ mouse DRG neurons transfected with the empty vector pcDNA3.1/GFP (mock) and pcDNA3.1-*Prmt7*/GFP (*Prmt7*). Data were statistically analysed by unpaired Student's t tests. (D) Half-width, (E) AHP (after hyperpolarization) and (F) amplitude of APs in *Scn11a*$^{A796G/A796G}$ mouse DRG neurons incubated with or without DS-437. Data were statistically analysed by one-way ANOVA.

Table S1. Primer sequences for PRMT7 shRNA

Name	Sequence
PRMT7 shRNA	Sense: 5'-GATCCGGATGCAGTGTGTGTACTTCCTTC AAGAGAGGAAGTACACACACTGCATCCTTTTTG-3' Antisense: 5'-AATTCAAAAAGGATGCAGTGTGTGTACT TCCTCTCTTGAAGGAAGTACACACACTGCATCCG-3'

Table S2. The effects of PRMT7 on activation and inactivation of $Na_V1.9$

	Voltage dependence of Activation (mV)			Voltage dependence of Inactivation (mV)		
	$V_{1/2}$	k	n	$V_{1/2}$	k	n
$hNa_V1.9$	-59.4 ± 1.76	6.16 ± 0.31	10	-66.84 ± 2.02	-13.5 ± 0.85	11
$hNa_V1.9$+hPRMT7	-56.5 ± 1.57	6.24 ± 0.43	12	-68.78 ± 1.17	-13.9 ± 1.04	11

Table S3. The effects of DS-437 on activation and inactivation of $Na_V1.9$

	Voltage dependence of Activation (mV)			Voltage dependence of Inactivation (mV)		
	$V_{1/2}$	k	n	$V_{1/2}$	k	n
Control	-56.37 ±0.74	6.88 ± 0.46	15	-60.64 ± 0.55	-5.57 ± 0.49	9
10 μM	-56.31 ± 1.21	6.16 ± 0.73	13	-60.83 ± 1.43	-6.28 ± 1.26	5
100 μM	-56.66 ± 1.02	6.04 ± 0.67	16	-61.41 ± 0.98	-6.14 ± 0.86	11