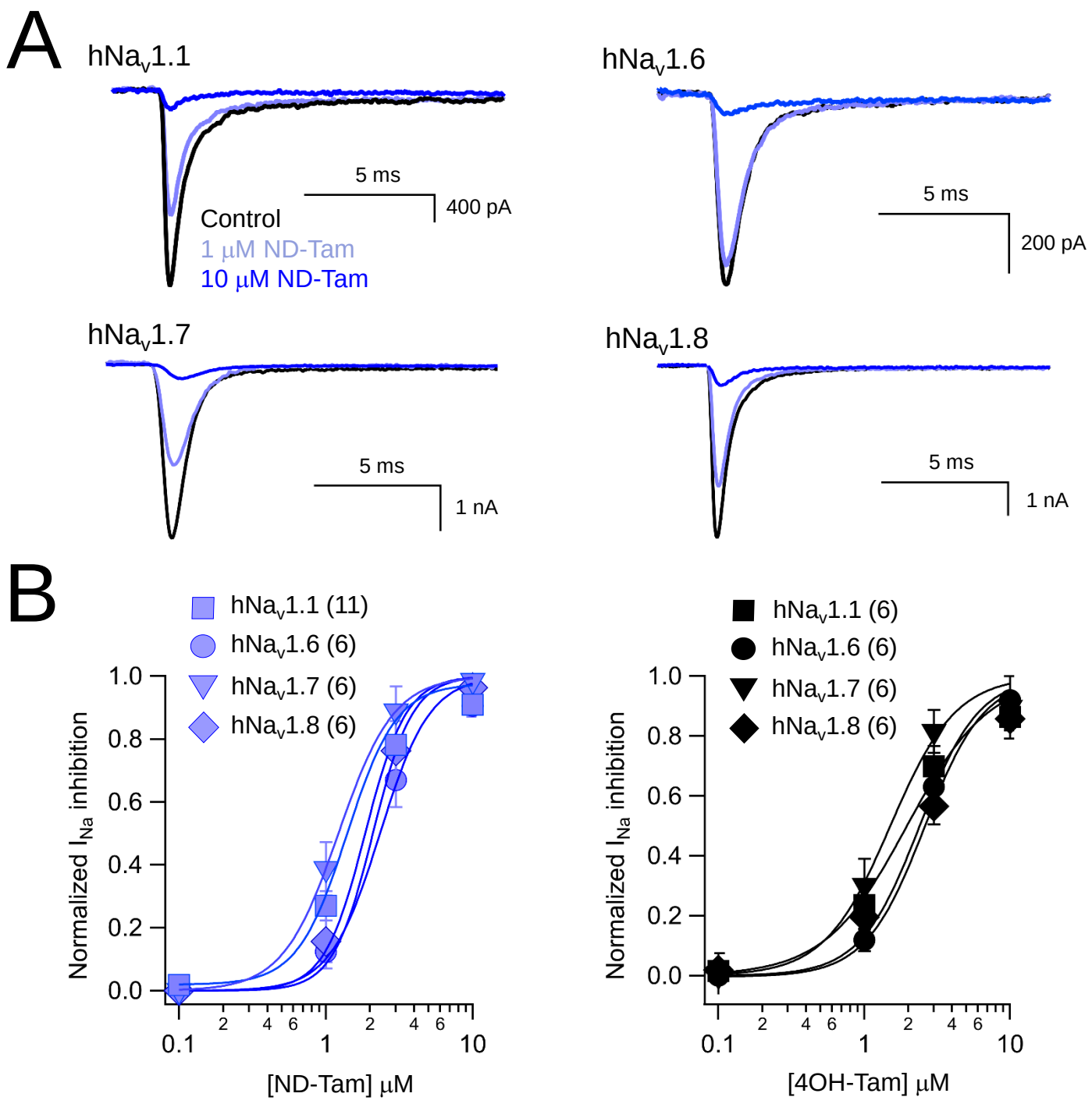
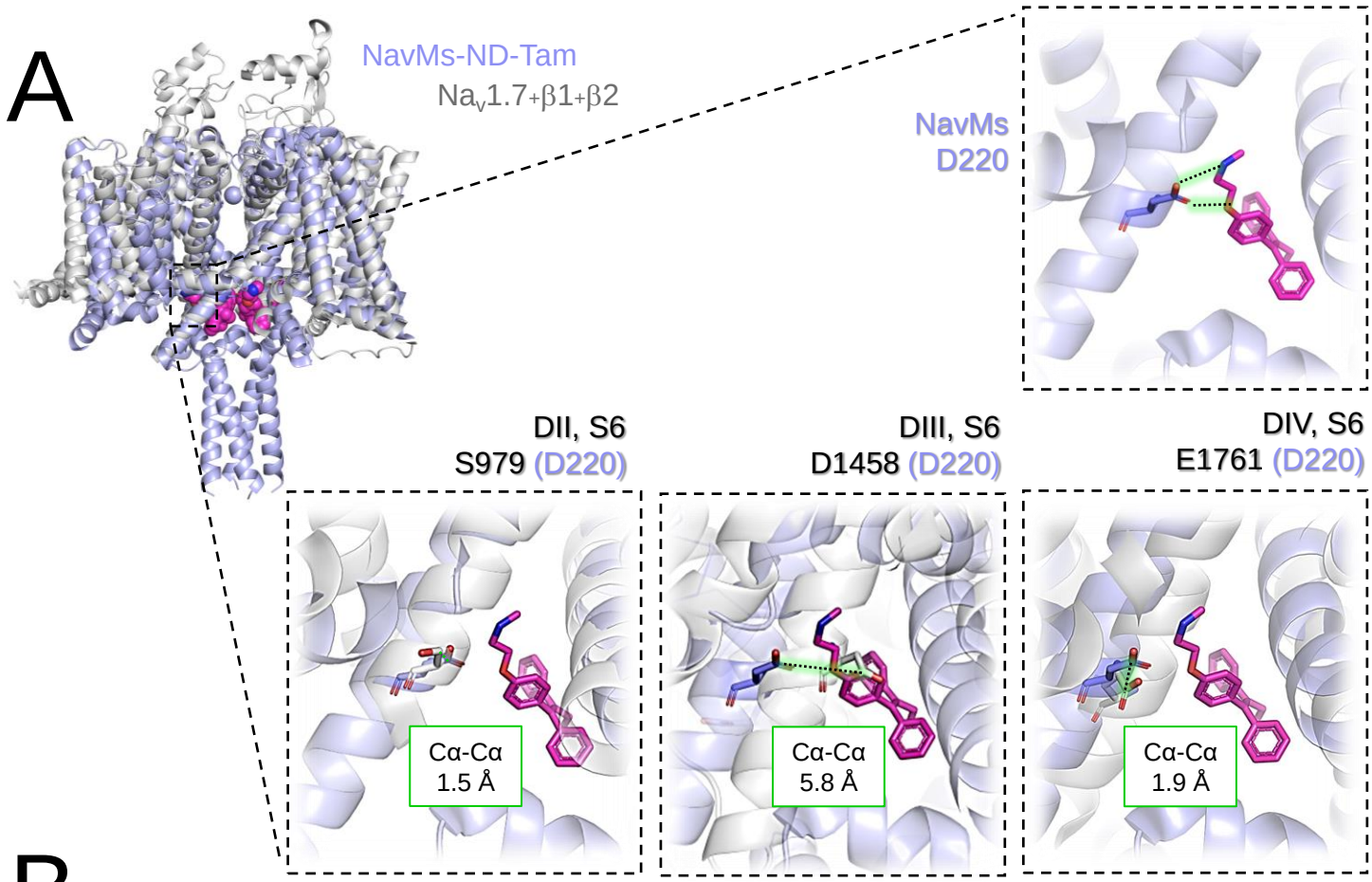
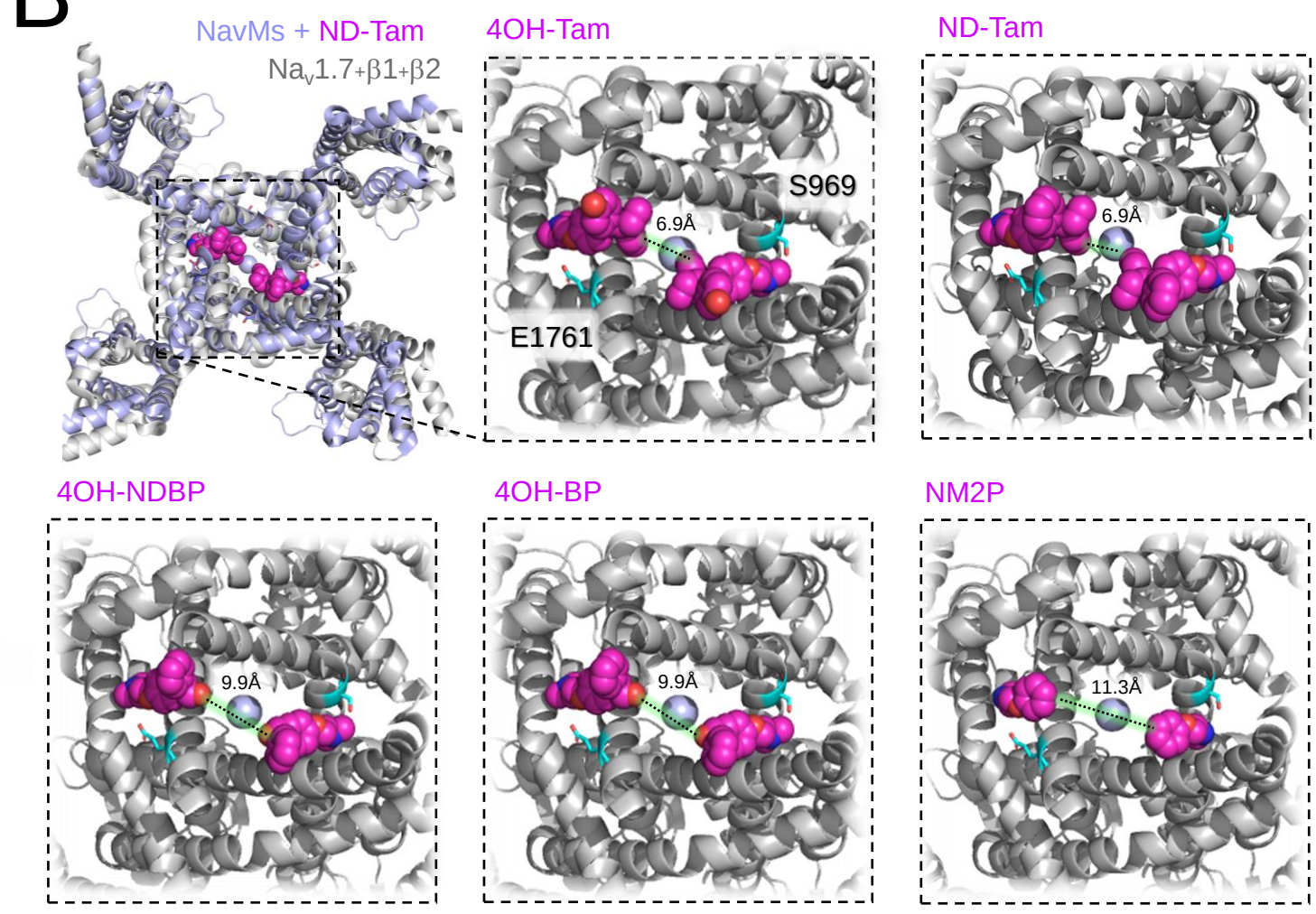
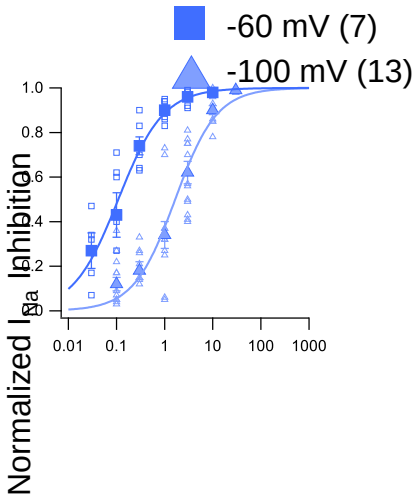


Supplemental Figure 1

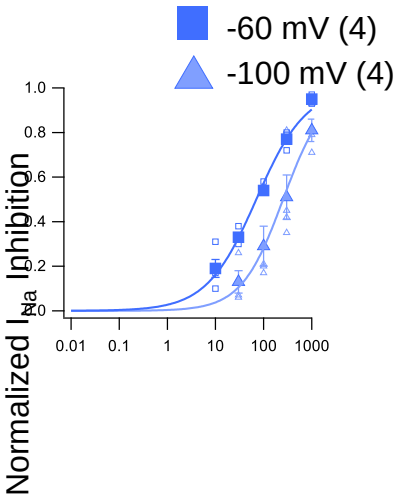




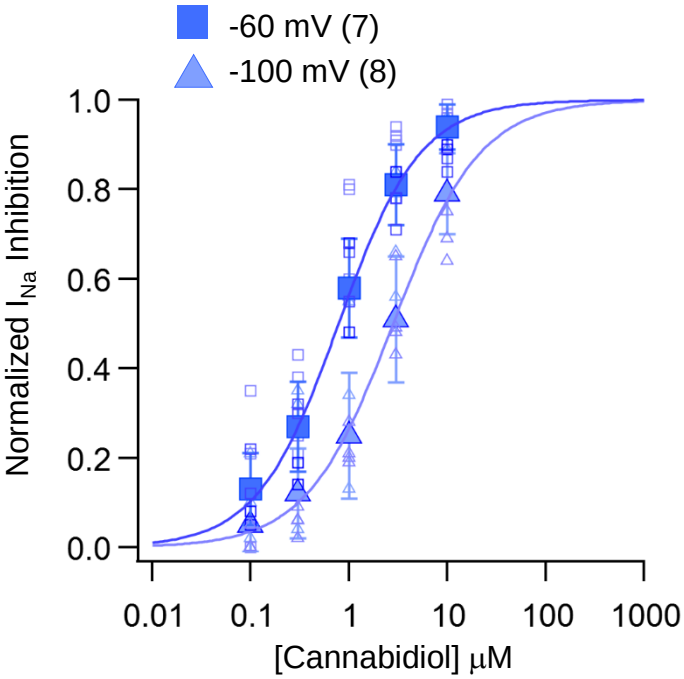
Supplemental Figure 2

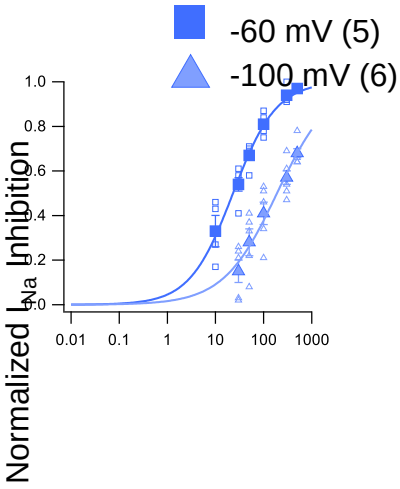


[ND-Tam] μM



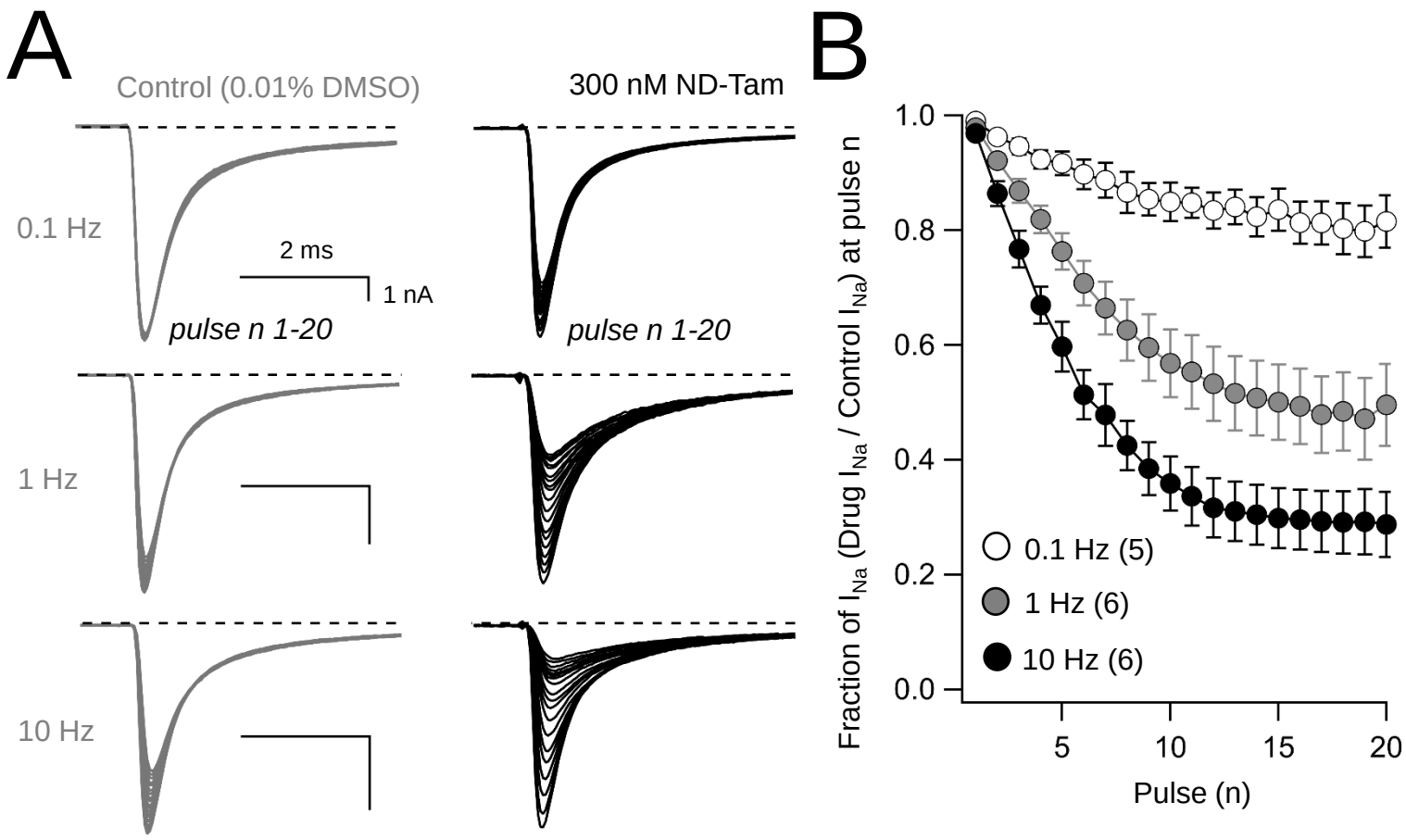
[Carbamazepine] μM



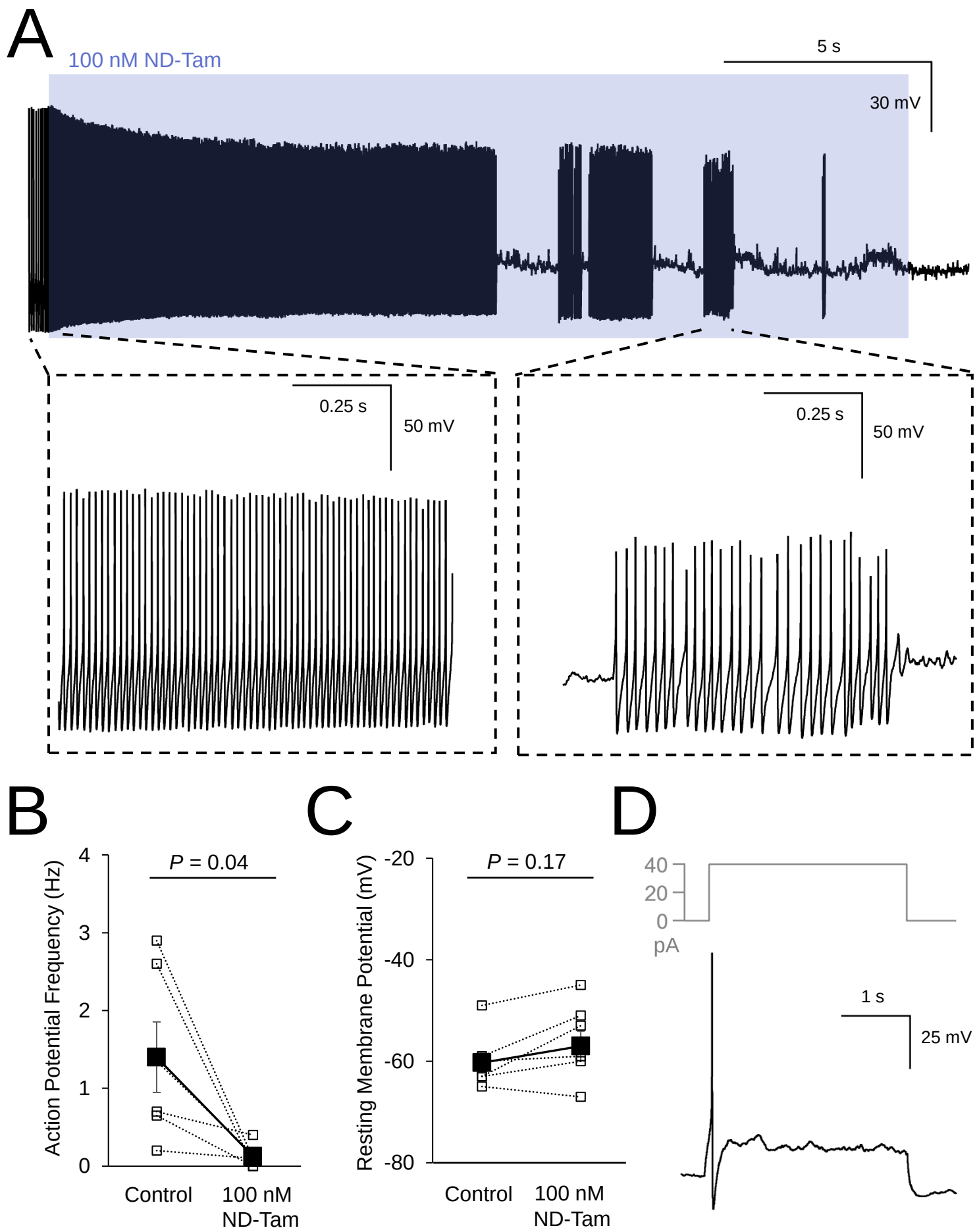


[Lidocaine] μM

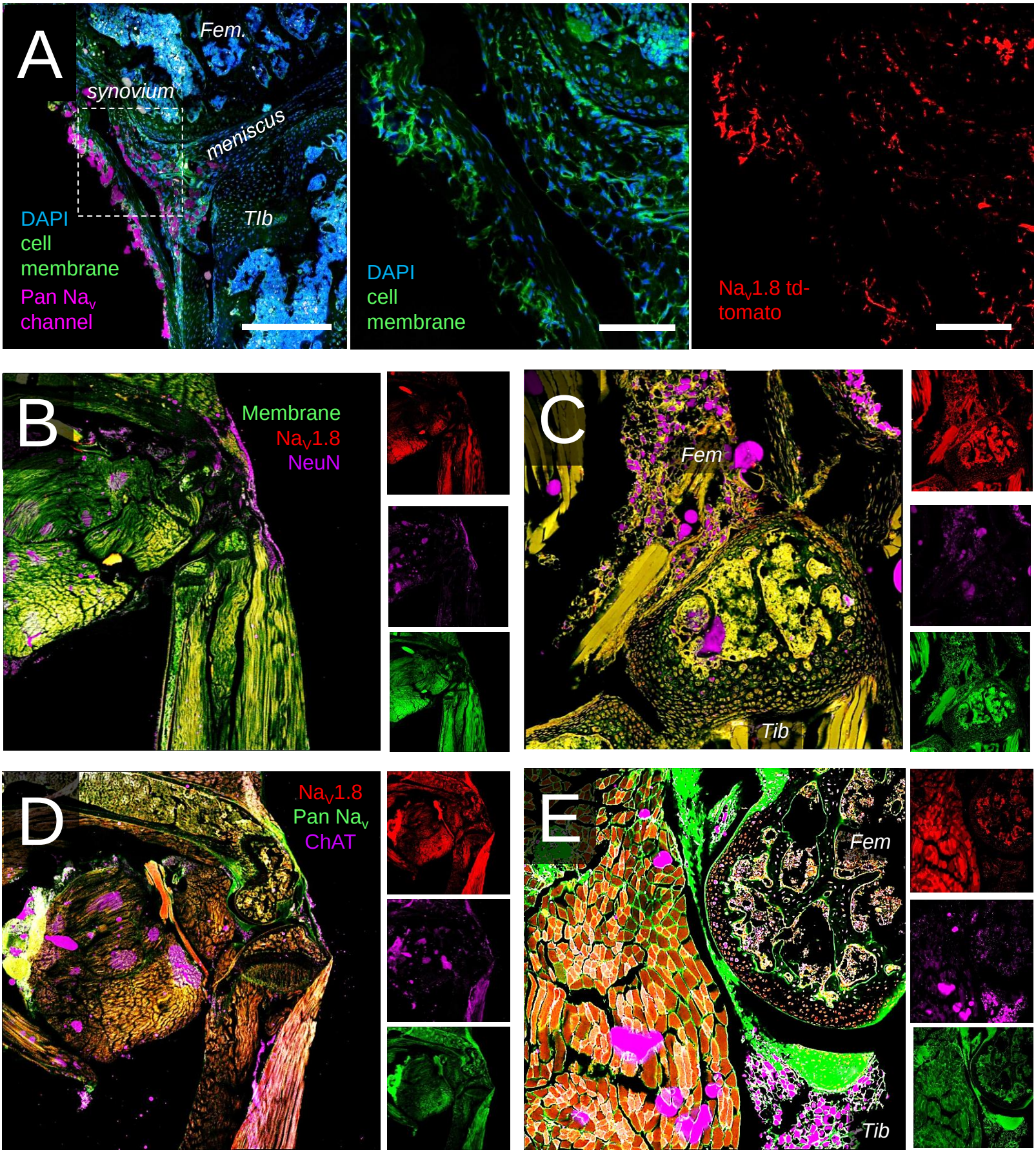
Supplemental Figure 3



Supplemental Figure 4



Supplemental Figure 5



Supplemental Figure 6

I_{Na} Source	ND-Tam IC_{50}; *Slope*	4OH-Tam IC_{50}; *Slope*	CBD IC_{50}; *Slope*	CBZ IC_{50}; *Slope*	Lidocaine IC_{50}; *Slope*
DRG -40 mV	3.9 nM ± 0.7; *1.1* (5)	Not tested	Not tested	Not tested	Not tested
DRG -60 mV	112 nM ± 15; *1.4* (6)	Not tested	1.1 μM ± 0.2; *1.6* (7)	70 μM ± 8 *0.9* (4-5)	23 μM ± 2 *1.2* (4-5)
DRG -100 mV	1.7 μM ± 0.2; *1.6* (13)	3.3 μM ± 0.6; *1.5* (8)	3.3 μM ± 0.8 *1.4* (8)	254 μM ± 20 *1.1* (4-5)	190 μM ± 18 *1.1* (4-6)
$hNa_v1.1$	2.2 μM ± 0.2; *1.9* (8)	3.1 μM ± 0.5; *1.7* (6)	Not tested	Not tested	Not tested
$hNa_v1.6$	2.4 μM ± 0.5; *1.9* (6)	2.2 μM ± 0.2; *1.8* (6)	Not tested	Not tested	Not tested
$hNa_v1.7$	1.7 μM ± 0.3; *2.2* (11)	1.9 μM ± 0.4; *1.8* (6)	Not tested	Not tested	Not tested
$hNa_v1.7$ S969A	12 μM ± 0.3; *1.3* (5)	Not tested	Not tested	Not tested	Not tested
$hNa_v1.7$ E1468A	1.8 μM ± 0.2; *2.3* (6)	Not tested	Not tested	Not tested	Not tested
$hNa_v1.7$ D1761A	5.1 μM ± 0.9; *1.4* (8)	Not tested	Not tested	Not tested	Not tested
$hNa_v1.7$ S969A:D1761A	36 μM ± 1.1; *0.9* (6)	Not tested	Not tested	Not tested	Not tested
hNav1.7 F1748A	1.1 μM ± 0.9; *2.1* (6)	Not tested	Not tested	Not tested	Not tested
hNav1.7 Y1755A	1.9 μM ± 0.8; *2.2* (6)	Not tested	Not tested	Not tested	Not tested
$hNa_v1.8$	2.3 μM ± 0.2 *2.1* (4-5)	3.4 μM ± 0.1 (4-5)	Not tested	Not tested	Not tested

Supplemental Table 1

Chemical	DRG I_{Na}, HP = -100 mV IC_{50}	human $Na_v1.7$ Ki
ND-Tam	1.7 μM ± 0.2 (13)	0.96 μM ± 0.1 (4)
4OH-Tam	3.3 μM ± 0.6 (8)	1.2 μM ± 0.1 (4)
TPE	No inhibition EC_{50} > 10 μM, (4)	No binding, Ki > 10 μM, (4)
NM2P	No inhibition EC_{50} > 10 μM, (4)	2.9 μM ± 0.1 (4)
NDBP	No inhibition EC_{50} > 10 μM, (4)	1.8 μM ± 0.1 (4)
4HBP	No inhibition EC_{50} > 10 μM, (4)	1.5 μM ± 0.1 (4)

Supplemental Table 2

Source	ND-Tam IC_{50}	CBD IC_{50}	CBZ IC_{50}	Lid. IC_{50}
DRG Peak Amp.	0.7 μM ± 0.3 (7)	3.2 μM ± 0.8 (6)	419 μM ± 216 (6)	16 μM ± 1.3 (6)
DRG Frequency	119 nM ± 22 (7)	1.8 μM ± 0.3 (6)	432 μM ± 209 (6)	7 μM ± 1.2 (6)

Supplemental Table 3

A

two-way repeated measures ANOVA with Sidak's post test

Comparison	Pre-injection	30 min	1h	2h	24
Vehicle-ND-Tam	*P* = 0.93	***P* = 0.008**	*P* = 0.12	*P* = 0.97	*P* = 0.94

B

two-way repeated measures ANOVA with Tukey's post test

Comparison	Pre-injection	30 min	1h	2h	3h	24h
Vehicle-ND-Tam	*P* = 0.98	***P* = 0.003**	*P* = 0.09	*P* = 0.29	***P* = 0.03**	*P* = 0.71
Vehicle-CBD	*P* = 0.84	***P* < 0.0001**	*P* = 0.77	*P* = 0.98	***P* = 0.02**	*P* = 0.57
Vehicle-Lidocaine	*P* = 0.99	***P* < 0.0001**	*P* = 0.23	*P* = 0.08	***P* = 0.03**	*P* = 0.40
ND-Tam-CBD	*P* = 0.92	***P* = 0.03**	*P* = 0.39	*P* = 0.06	*P* = 0.34	*P* = 0.99
ND-Tam-Lidocaine	*P* = 0.98	***P* = 0.003**	*P* = 0.87	*P* = 0.67	*P* = 0.90	*P* = 0.83

C

one-way ANOVA with Tukey's post test

Comparison	AUC
Vehicle-ND-Tam	***P* < 0.0001**
Vehicle-CBD	***P* = 0.001**
Vehicle-Lidocaine	***P* < 0.0001**
ND-Tam-CBD	*P* = 0.17
ND-Tam-Lidocaine	*P* = 0.13
CBD-Lidocaine	***P* = 0.002**

Supplemental Table 4

D

two-way repeated measures ANOVA with Tukey's post test

Comparison	Pre-DMM	Pre-injection	0h	30 min	1h	2h	3.5h	24h
Vehicle-ND-Tam	*P* = 0.34	*P* = 0.48	*P* = 0.97	***P* = 0.03**	***P* = 0.0004**	***P* = 0.0009**	*P* = 0.12	*P* = 0.90
Vehicle-Lidocaine	*P* = 0.62	*P* = 0.61	*P* = 0.86	***P* = 0.004**	***P* = 0.005**	*P* = 0.91	*P* = 0.89	*P* = 0.99
ND-Tam-Lidocaine	*P* = 0.91	*P* = 0.74	*P* = 0.61	***P* = 0.001**	***P* = 0.0007**	***P* < *0.0001***	*P* = 0.47	*P* = 0.97

E

one-way ANOVA with Tukey's post test

Comparison	AUC
Vehicle-ND-Tam	***P* < 0.0001**
Vehicle-Lidocaine	***P* = 0.001**
ND-Tam-Lidocaine	***P* = 0.0001**

Supplemental Table 4 cont.