



Supplementary material

Table S1. Summary of mechanical paw withdrawal thresholds measured at baseline and at 2 and 4 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	Vehicle			EA (2 mg/kg)			EA (4 mg/kg)		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	0.88 \pm 0.07	-		0.94 \pm 0.02	-	>.999	0.98 \pm 0.02	-	1.00
2	0.19 \pm 0.07	<.001		0.42 \pm 0.14	0.00	0.58	0.68 \pm 0.10	0.28	0.01
4	0.11 \pm 0.02	<.001		0.25 \pm 0.11	<.001	0.96	0.96 \pm 0.55	0.03	0.02

Table S2. Summary of thermal paw withdrawal thresholds measured at baseline and at 1 and 3 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	Vehicle			EA (2 mg/kg)			EA (4 mg/kg)		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	9.48 \pm 0.98	-		8.01 \pm 0.38	-	0.86	8.61 \pm 1.44	-	0.99
1	5.84 \pm 0.98	0.04		6.97 \pm 1.32	0.98	0.96	9.84 \pm 0.93	0.94	0.02
3	4.83 \pm 0.81	0.00		6.26 \pm 0.92	0.71	0.88	4.79 \pm 0.29	0.02	>0.99

Table S3. Summary of thermal paw withdrawal thresholds measured at baseline and at 1 and 3 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	Vehicle			EA (2 mg/kg)		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle
0	7.98 \pm 0.06	-		7.82 \pm 0.07	-	0.9949
1	4.46 \pm 0.40	<0.0001		4.71 \pm 0.32	<0.0001	0.9696
3	3.58 \pm 0.23	<0.0001		6.41 \pm 0.18	0.0154	<0.0001

Supplementary table 4: Summary of mechanical paw withdrawal thresholds measured at baseline and at 2 and 4 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	WT Vehicle			WT EA			TRPC5 KO Vehicle			TRPC5 KO EA		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	1.00 \pm 0.01	-		0.98 \pm 0.02	-	>.999	0.99 \pm 0.01	-	>.999	0.98 \pm 0.01	-	>.999
2	0.46 \pm 0.11	<.001		0.98 \pm 0.02	>.999	<.001	0.43 \pm 0.09	<.001	>.999	0.87 \pm 0.06	0.972	0.001
4	0.20 \pm 0.04	<.001		0.60 \pm 0.13	0.003	0.002	0.22 \pm 0.07	<.001	>.999	0.88 \pm 0.06	0.992	<.001

Supplementary table 5: Summary of thermal paw withdrawal thresholds measured at baseline and at 1 and 3 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	WT Vehicle			WT EA			TRPC5 KO Vehicle			TRPC5 KO EA		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	9.70 \pm 0.73	-		8.58 \pm 0.47	-	1.00	9.50 \pm 0.93	-	>0.9999	8.32 \pm 0.99	-	1.00
2	5.45 \pm 1.14	0.11		9.26 \pm 1.42	>0.9999	0.21	7.11 \pm 0.82	0.83	0.98	9.21 \pm 1.13	>0.9999	0.23
4	4.75 \pm 0.95	0.03		7.15 \pm 0.98	1.00	0.82	4.28 \pm 0.59	0.04	>0.9999	6.85 \pm 1.70	0.99	0.92

Supplementary table 6: Summary of mechanical paw withdrawal thresholds measured at baseline and at 2 and 4 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	Veh+Veh			Veh+EA			ML204+Veh			ML204+EA		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	0.99 \pm 0.01	-		0.96 \pm 0.04	-	>.999	0.98 \pm 0.04	-	>.999	0.96 \pm 0.03	-	>.999
2	0.38 \pm 0.17	<.001		0.86 \pm 0.11	1.00	0.00	0.53 \pm 0.07	0.01	0.95	0.72 \pm 0.05	0.45	0.11
4	0.28 \pm 0.06	<.001		0.79 \pm 0.12	0.89	0.00	0.28 \pm 0.05	<.001	>.999	0.54 \pm 0.11	0.02	0.40

Supplementary table 7: Summary of thermal paw withdrawal thresholds measured at baseline and at 1 and 3 hours after intra-plantar injections of carrageenan in the left hindpaw.

Time (h)	Veh+Veh			Veh+EA			ML204+Veh			ML204+EA		
	Mean \pm SEM	vs baseline		Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle	Mean \pm SEM	vs baseline	vs vehicle
0	8.19 \pm 0.74	-		7.67 \pm 1.06	-	>0.9999	9.37 \pm 2.58	-	>0.9999	6.86 \pm 0.84	-	1.00
2	6.83 \pm 0.65	1.00		10.69 \pm 1.89	0.88	0.62	5.77 \pm 0.89	0.71	>0.9999	11.41 \pm 1.23	0.40	0.39
4	4.45 \pm 1.24	0.67		8.04 \pm 1.72	>0.9999	0.72	4.34 \pm 1.47	0.26	>0.9999	7.00 \pm 3.07	>0.9999	0.96

Supplementary table 8: Summary of dose-response curve of cultured primary sensory neurons from WT and KO mice to increasing concentration of Englerin-A.

Englerin-A concentration (nM)	WT	TRPC5 KO
0.1	0.00	0.00
0.3	10.04 \pm 6.17	3.67 \pm 9.17
1	21.20 \pm 8.26	23.81 \pm 0.39
3	30.49 \pm 15.98.17	26.66 \pm 11.87
10	53.48 \pm 1.90	52.12 \pm 3.80
30	79.80 \pm 9.00	85.07 \pm 6.86
100	76.41 \pm 6.50	81.75 \pm 15.64