Supporting Information

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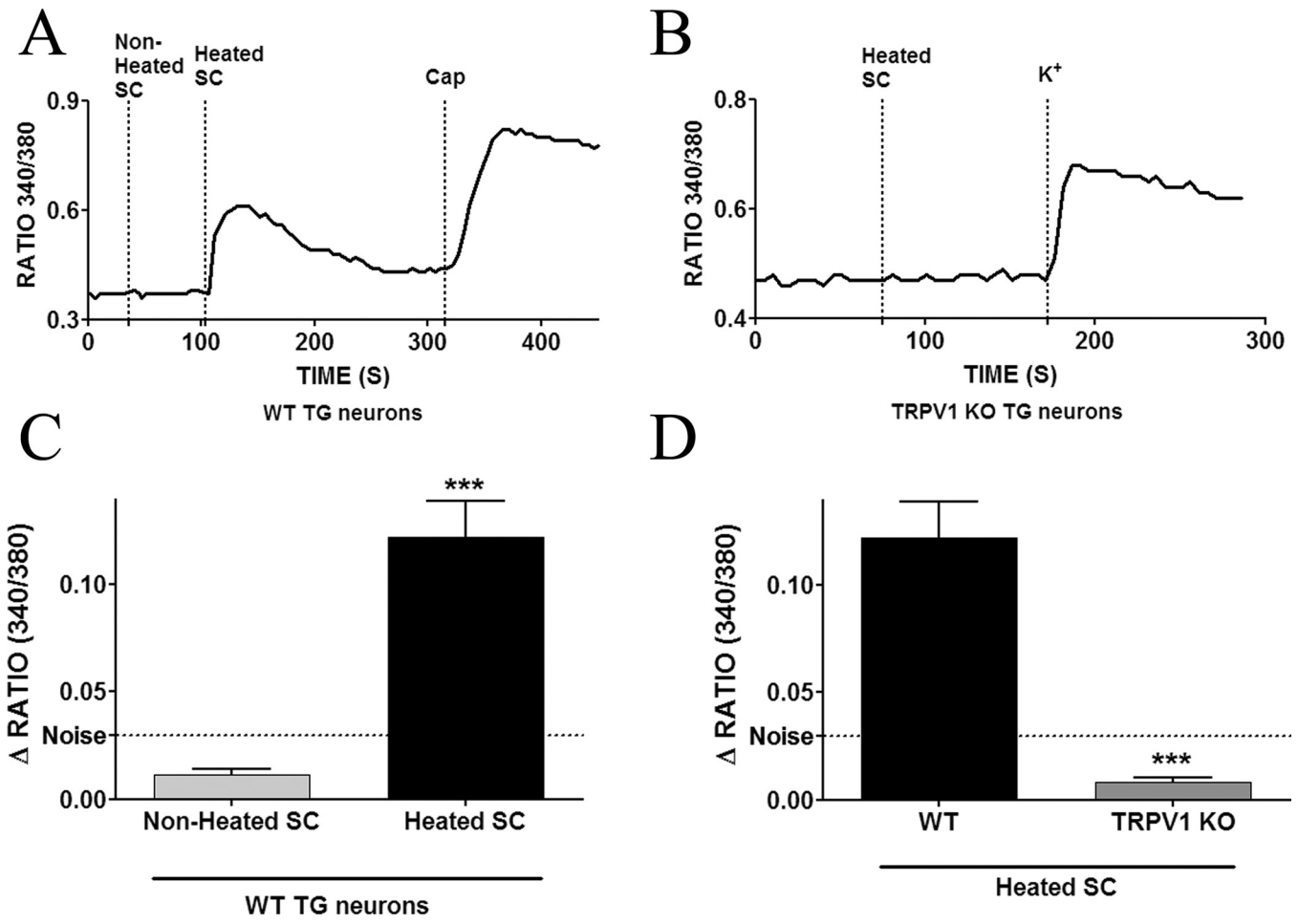

Fig. S1. Depolarization of isolated rat spinal cord with noxious heat releases endogenous TRPV1 agonist(s). (*A*) Freshly isolated rat spinal cords (9) were washed for 50 min in Hanks buffer and a basal sample (20 min in Hanks, 37 °C, Non-Heated-SC) was collected. Spinal cords were then depolarized with preheated buffer (20 min, 48 °C, Heated-SC). Both supernatants were passed through C_{18} SepPak columns and washed with water/0.05 TFA. The substances adsorbed onto the column were eluted with 90% acetonitrile/0.05% TFA. The eluates were dried under a flow of nitrogen and reconstituted in Hanks buffer. Using a fura-2 calcium imaging set up, a representative tracer demonstrates the effect of the application of reconstituted eluates to a TG neuron from WT mice that also responded to capsaicin (100 nM). Ratiometric data are shown. (*B*) A representative tracer demonstrating the effect of the same eluate (from heat-depolarized spinal cords) to a neuron from TRPV1 KO mice. The viability of the cell was assessed using buffer containing 50 mM potassium. (*C*) Comparison of calcium accumulation in TG neurons from WT mice evoked by applying eluates from nonheated versus heat-depolarized spinal cords ($n = 34$ for nonheated and 40 for heated SC eluate, ***, $= P < 0.001$, *t*-test). (*D*) Comparison of calcium accumulation in in TG neurons from WT versus TRPV1 KO mice evoked by applying eluates from heat-depolarized spinal cords ($n = 40$ for WT and 23 for KO neurons, ***, $= P < 0.001$, *t*-test).

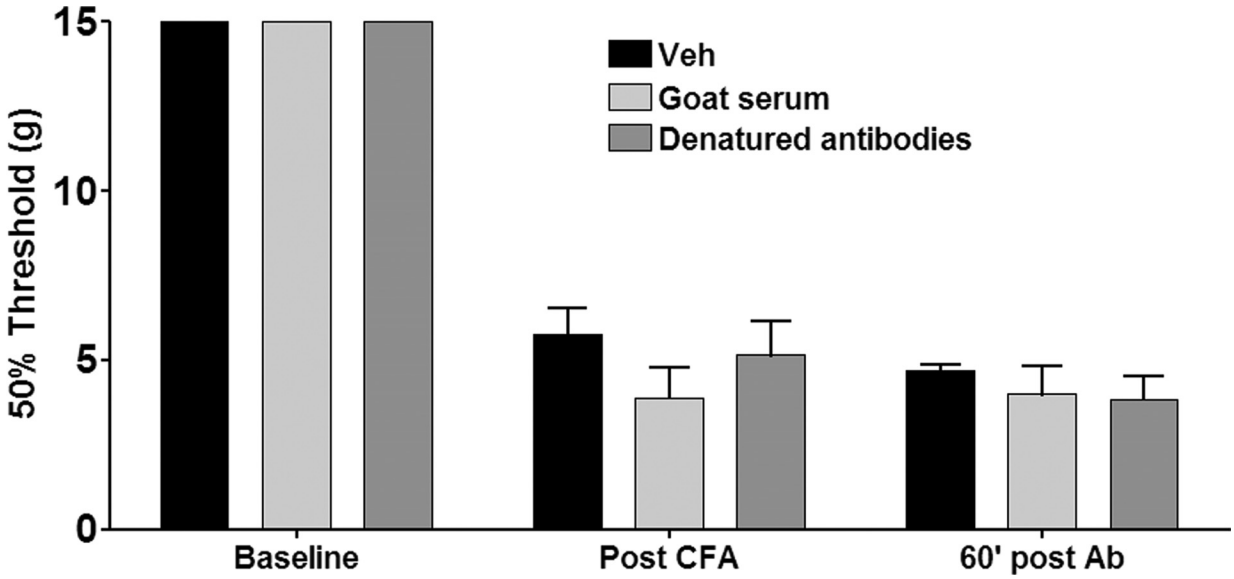

Fig. S2. Control studies demonstrating specificity of 9-HODE and 13-HODE antibodies. In an experimental design similar to Fig. 4*C*, tactile withdrawal thresholds were obtained for unilateral CFA injected animals 24 h post CFA treatment. Then the animals were injected either with vehicle, preimmune goat serum, or heat (95 °C) denatured antibodies against 9- and 13-HODE (30 μg each). Paw withdrawal thresholds were obtained in both ipsilateral and contralateral paws 60 min after i.t. injections.