Supplemental Data

Supplemental Fig 1: Time course of mechanical allodynia induced by SNI. The graph depicts the average withdrawal latencies to innocuous mechanical stimulation at the indicated time points. Significant mechanical allodynia is only observed in SNI-treated animals (compared to Sham-surgery; ***P < 0.001 and **P < 0.01 by two-way ANOVA followed by Bonferroni´s multiple comparison test; pre: 20 animals per condition; week1: 13 animals per condition; week2 and week3: 8 animals per condition; week4: 24 animals per condition; from > 5 independent mouse cohorts)

Supplemental Fig. 2. Composition of the DRG-specific spectral library as revealed by Gene ontology (GO)-based analysis in respect to GO Cellular Component and GO Molecular Function.

Supplemental Fig 3: (A) Schematic representation of the block randomization during the spectral acquisition of all the 12 HRM runs. (B) Total ion chromatograms during HRM acquisition for the four samples integrating the second block replicate

Supplemental Fig 4: Box plot visualization before and after normalization. Globally, little normalization was needed due to the similarity of the samples in protein content and concentration.

Supplemental Fig 5: Coefficient of variation of the quantified signals for all 4 experimental conditions.

Supplemental Fig 6: Assigned Gene Ontology (GO) molecular function (MF) categories and the relative abundance of significantly regulated proteins during inflammatory (left) and neuropathic (right) pain.

Supplemental Fig. 7: Images of full blots. Left, full blot of data shown in Fig. 3A. For humane reasons (reduction of animals needed for this study) we cut Western blots in 4 pieces to enable individual probing with different antibodies (also including those which are not related to the current study labeled in smaller, regular font in the blot). Serca probing was performed on both upper halves of the blot after incubation of blots with Grp94 and NF160. The band corresponding to Serca on both upper halves is indicated by the arrow. Actin (β-Actin) probing was performed on both lower halves after incubation of blots with PDIA6 (left lower half), CNPase (right lower half) and Peripherin (both lower halves). The order of probing was carefully determined in previous experiments considering the molecular weight of each protein and the species primary antibodies were derived from.

Right, in order to demonstrate the specificity of Serca and Actin bands, we show on the right the same blot as left but after initial incubation with antibodies against Grp94 (upper halves), PDIA6 (left lower half) or CNPase (right lower half) and before incubation with the antibody against Serca.

Supplemental Fig. 8: Upregulation of Serca expression in axons of sciatic nerves during inflammatory pain. (A, B) Representative cross sections of big fascicles of sciatic nerves derived from Veh-treated (A) and CFA-treated (B) animals stained for Serca and Tubulin III (a neuronal marker, left panels) or Serca, Peripherin (a marker for unmyelinated C-fibers) and Fluoromyelin (to visualize myelin) in right panels. The merged images of both conditions show prominent colocalization of Serca and Tubulin III (left panels) as well as Serca and Peripherin (right panels) suggesting neuronal expression of Serca in unmyelinated C-fibers within Remak bundles. Note that Serca-label is clearly segregated from Fluoromyelin-positive, i.e. myelinated axons. (C, D) Representative longitudinal sections of big fascicles of sciatic nerves derived from Veh-treated (C) and CFA-treated (D) animals stained for Tubulin III (a neuronal marker) or Fluoromyelin (to visualize myelin) and Serca. In both conditions the majority of Serca-label colocalizes with Tubulin III-positive nerve fibers suggesting neuronal expression of Serca. Note that Serca-label does not overlap with Fluoromyelin, instead Serca-label is found juxtaposed to Fluoromyelin. Asterisks indicate apparent Serca-label in blood vessels.

Scale bars: 10 μm

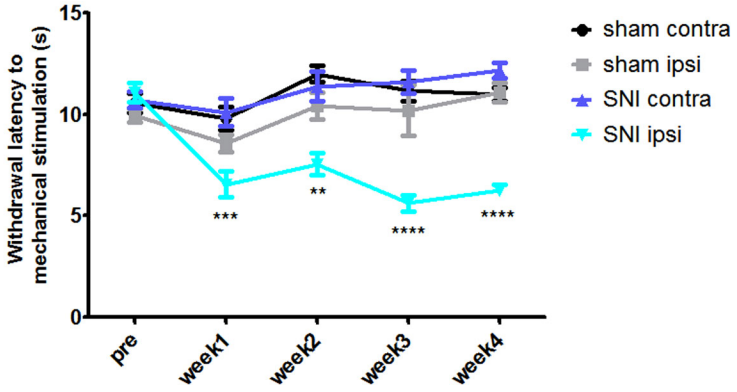
Supplemental Table 1: Mouse DRG spectral library ("Spectral library" tab) containing information for 161605 peptides corresponding to 3067 proteins. Column legends are explained in the "Legend" tab.

Supplemental Table 2: List of ion channels and receptors present in the spectral library and previously shown to be involved in somatosensation and pain.

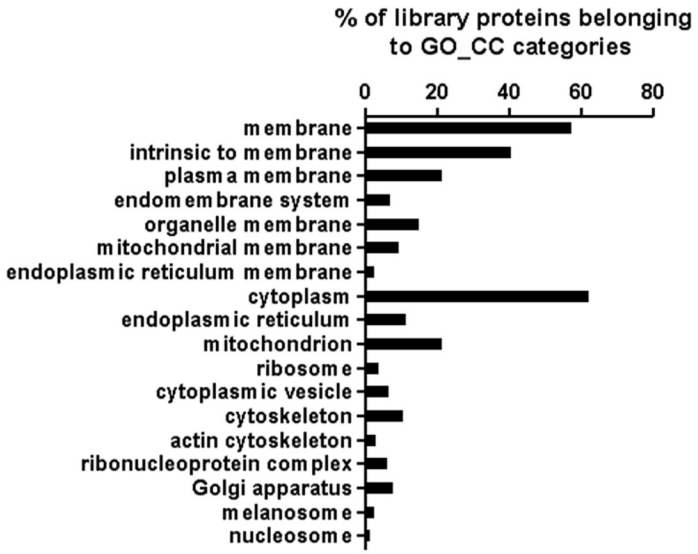
Supplemental Table 3: Statistical analysis of proteins profiled in this study in both inflammatory ("comparison CFA versus Vehicle" tab) and neuropathic ("comparison SNI versus Sham" tab) pain conditions. Column legends are explained in the "Legend" tab.

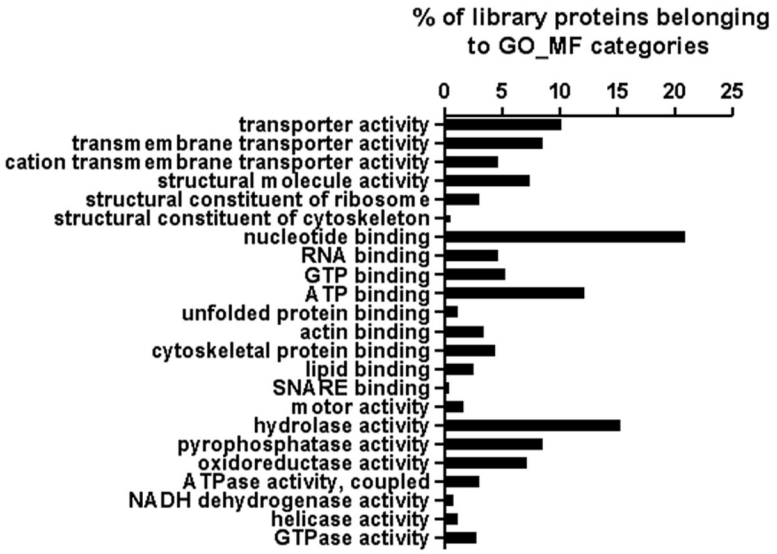
Supplemental Table 4: Overlapping proteins identified in both, inflammatory and neuropathic pain conditions. Differentially regulated proteins are highlighted in orange color.

Supplementary Figure 1

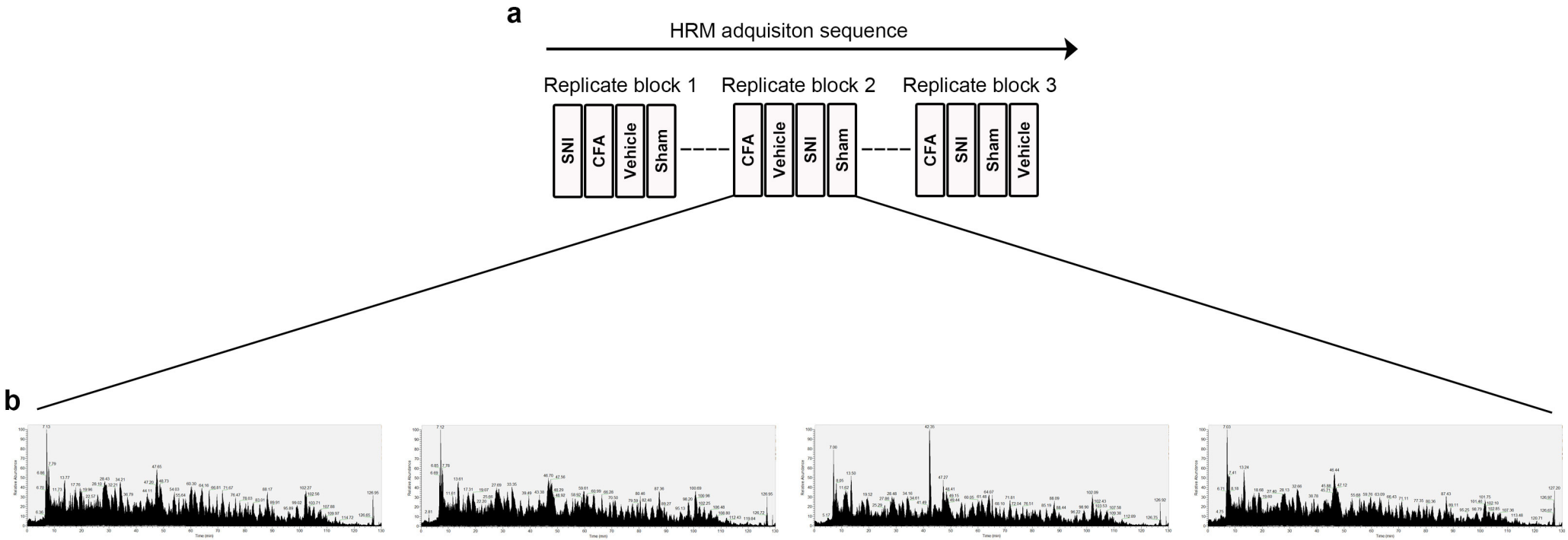


Supplemental Figure 2

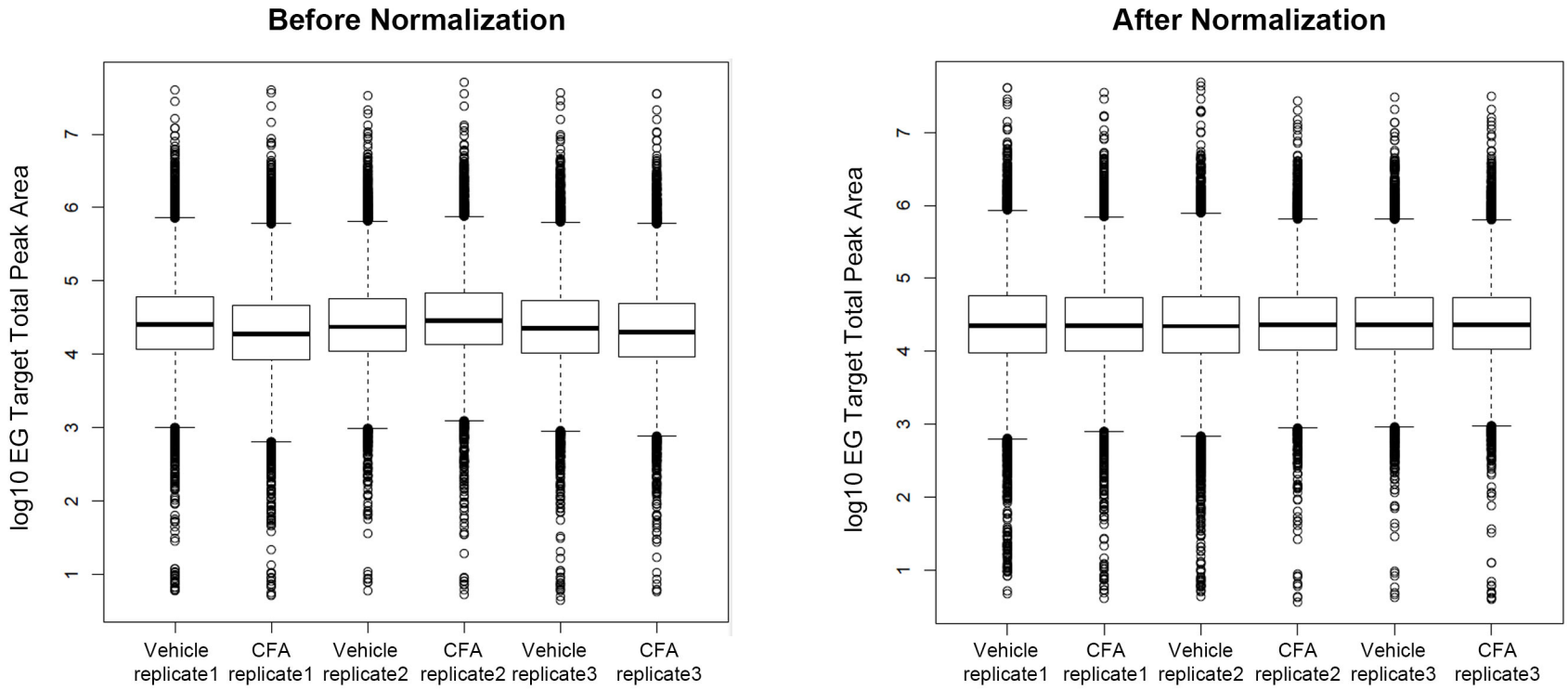




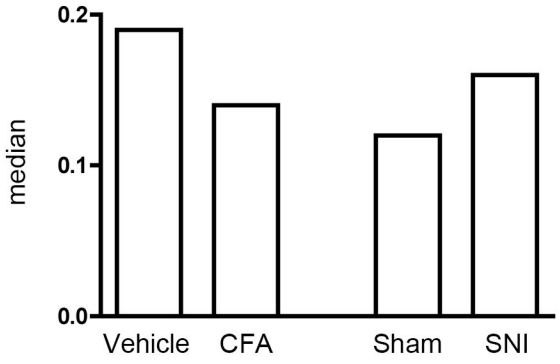
Supplemental Figure 3



Supplemental Figure 4

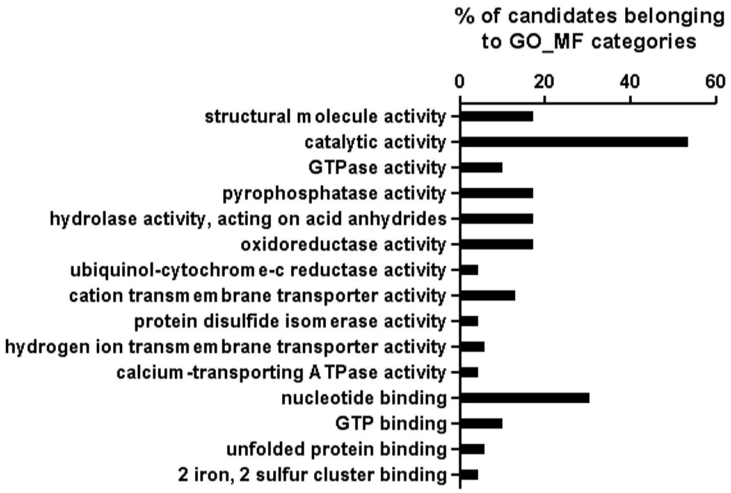


Supplemental Figure 5

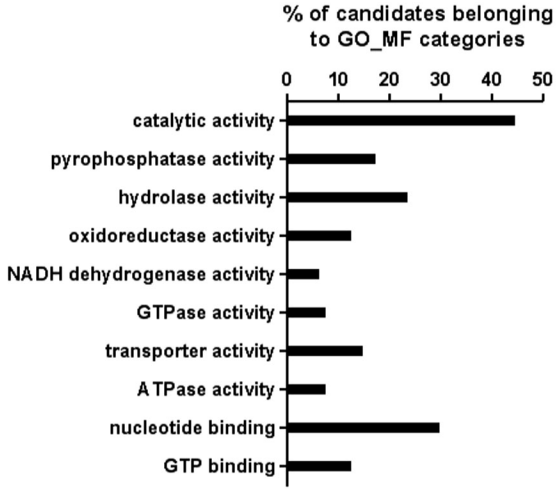


Supplemental Figure 6

Inflammatory

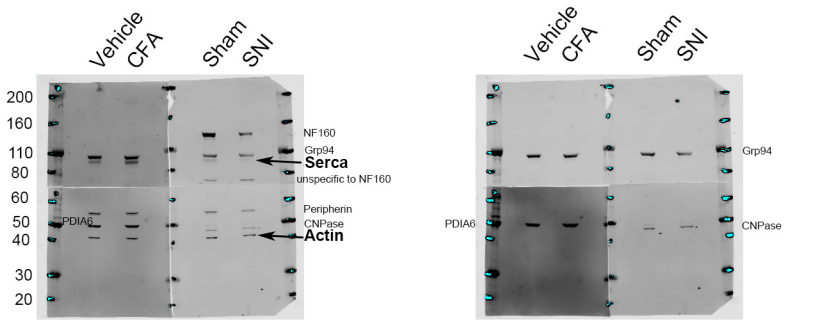


Neuropathic



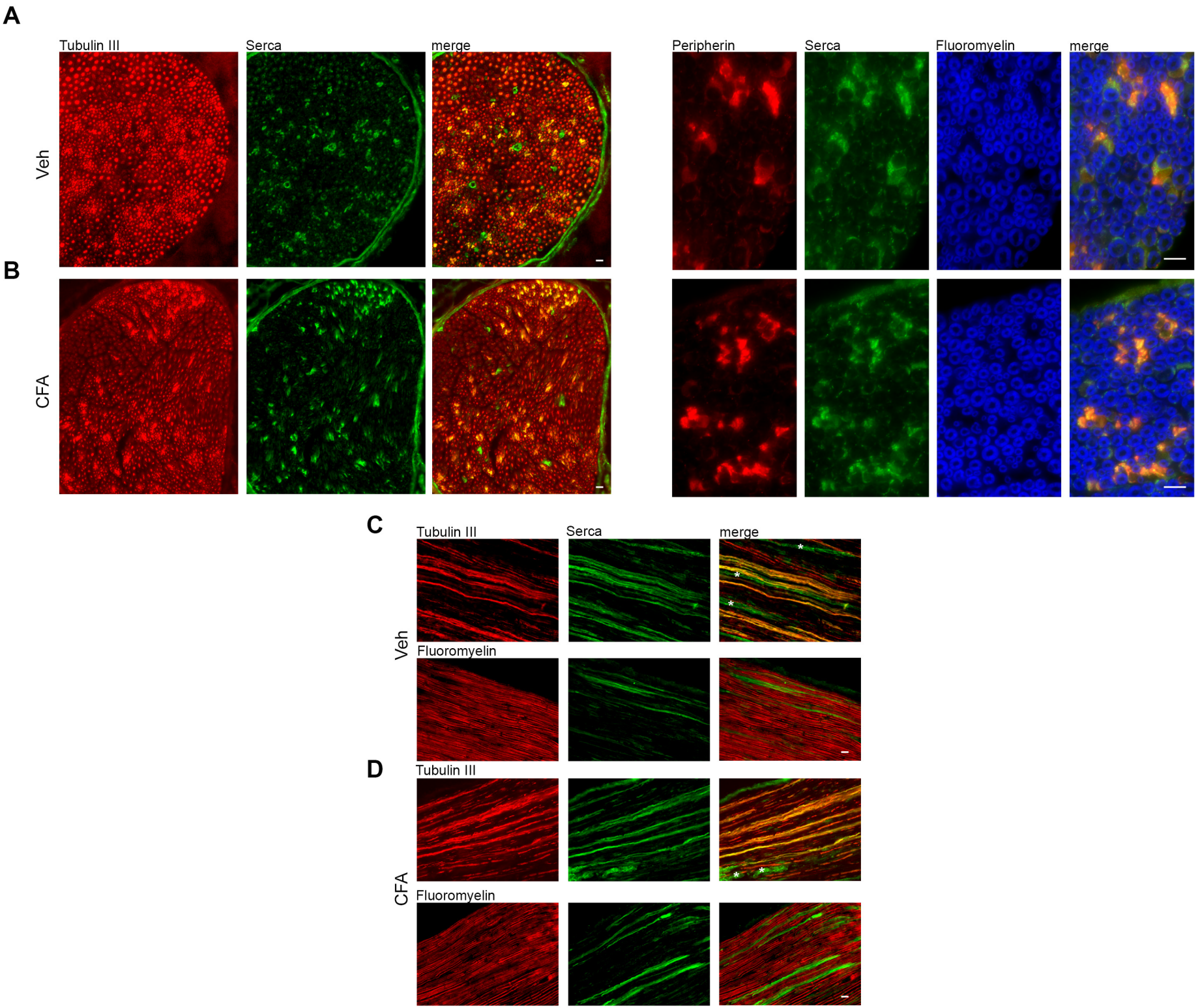
Supplementary Figure 7

Original blot from Figure 4



same blot as left after initial incubation with antibodies against Grp94 (upper halves) and PDIA6 (left lower half) or CNPase (right lower half)

Supplemental Figure 8



UniProt ID	Protein ID	Full name
Q8BLA8	TRPA1	Transient receptor potential ion channel A1
Q9QZC1	TRPC3	Transient receptor potential ion channel C3
Q704Y3	TRPV1	Transient receptor potential ion channel V1
Q9WTR1	TRPV2	Transient receptor potential ion channel V2
Q6QIY3	Nav 1.8, Scn10a	Sodium channel, voltage-gated, type 10, subunit alpha
Q9R053	Nav 1.9, Scn11a	Sodium channel, voltage-gated, type 11, subunit alpha
O08532	Cacna2d1	calcium channel, voltage-dependent, alpha2/delta subunit 1
O55017	Cacna1b	calcium channel, voltage-dependent, N type, alpha 1B subunit, Cav2.2
P97445	Cacna1a	calcium channel, voltage-dependent, P/Q type, alpha 1A subunit, Cav 2.1
P48302	Ednrb	endothelin receptor type B
Q9WV18	Gabbr1	gamma-aminobutyric acid (GABA) B receptor, 1
Q60934	Grik1	glutamate receptor, ionotropic, kainate 1; GluR5
Q6ZPR4	Kcnt1	potassium channel, subfamily T, member 1
Q9JM63	Kcnj10	potassium inwardly-rectifying channel, subfamily J, member 10
Q03717	Kcnb1	potassium voltage gated channel, Shab-related subfamily, member 1
A6H8H5	Kcnb2	potassium voltage gated channel, Shab-related subfamily, member 2
P16388	Kcna1	potassium voltage-gated channel, shaker-related subfamily, member 1
P63141	Kcna2	potassium voltage-gated channel, shaker-related subfamily, member 2
Q9JJX6	P2rx4	purinergic receptor P2X, ligand-gated ion channel 4
Q3UR32	P2rx3	purinergic receptor P2X, ligand-gated ion channel, 3
Q9Z1M0	P2rx7	purinergic receptor P2X, ligand-gated ion channel, 7
Q8CD54	Piezo2	Piezo-Type Mechanosensitive Ion Channel Component 2
P70263	Ptgdr	prostaglandin D receptor
Q01279	Egfr	epidermal growth factor receptor
Q9Z0W1	Ngfr	nerve growth factor receptor
Q99MB1	Tlr3	toll-like receptor 3
P97785	Gfra1	glial cell line derived neurotrophic factor family receptor alpha 1
P05622	Pdgfrb	platelet derived growth factor receptor, beta polypeptide

Supplemental Table 2: List of ion channels and receptors present in the spectral library and previously shown to be involved in somatosensation and pain.