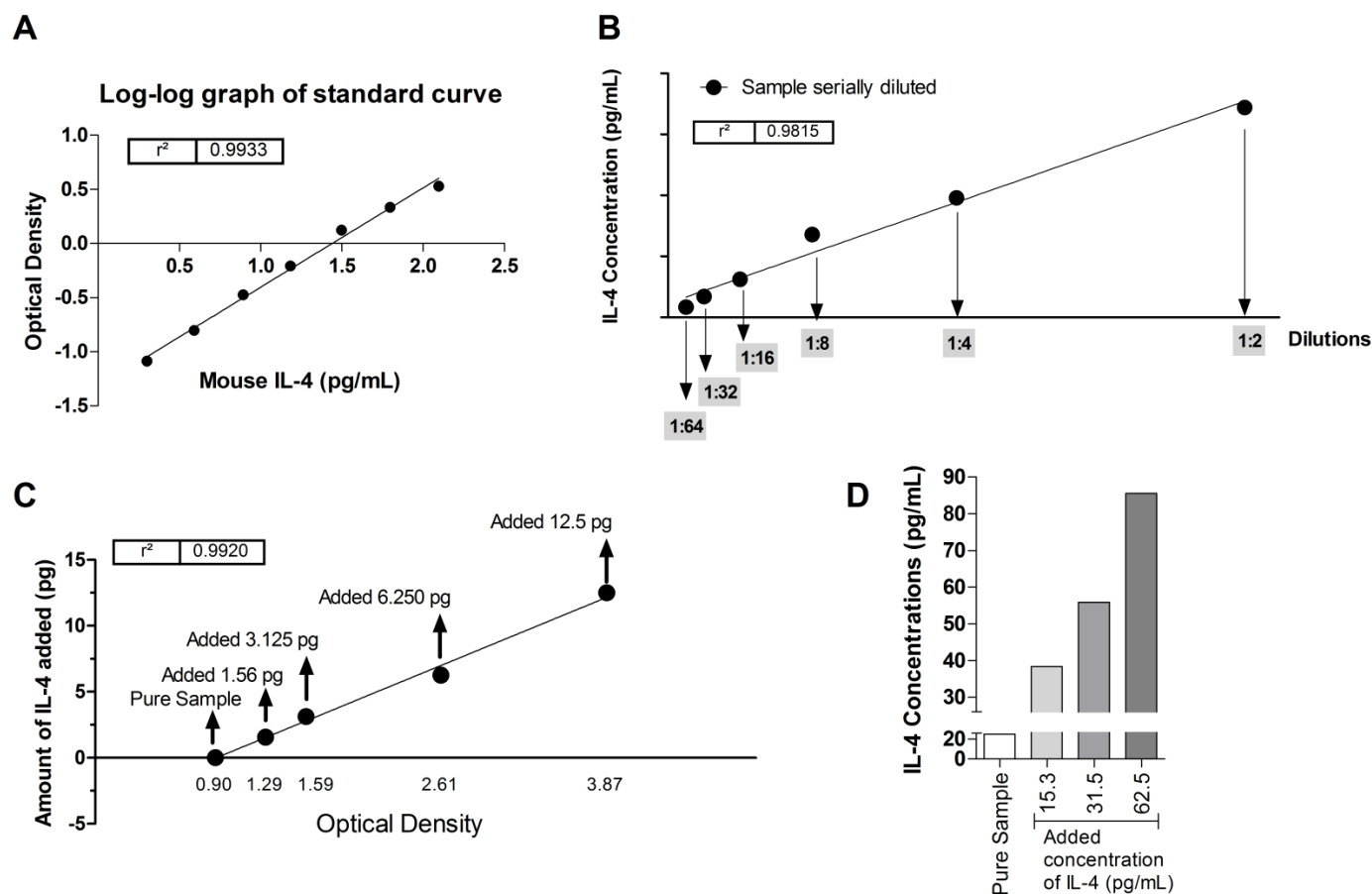
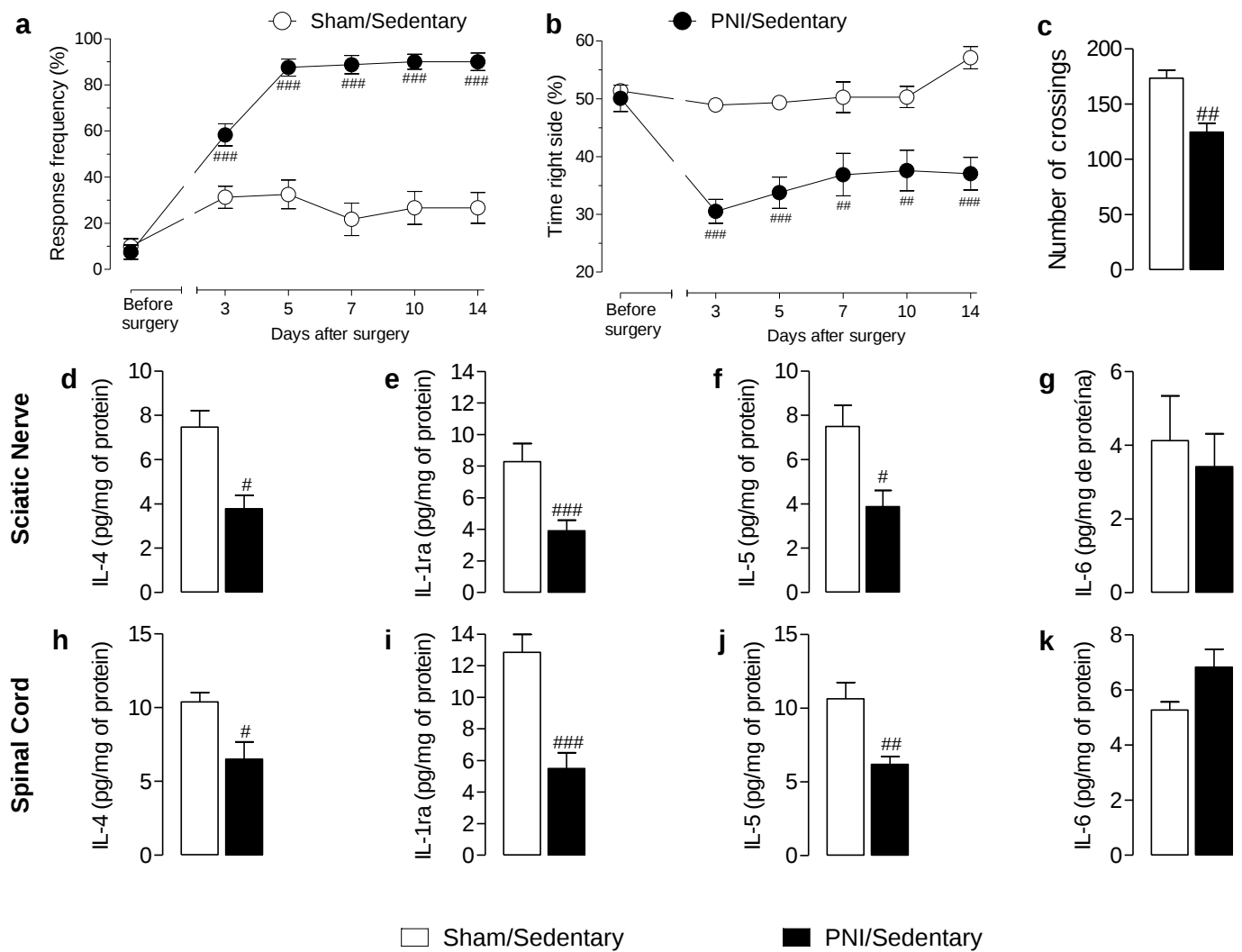


# Supplemental Digital Content 1 - Figure 1



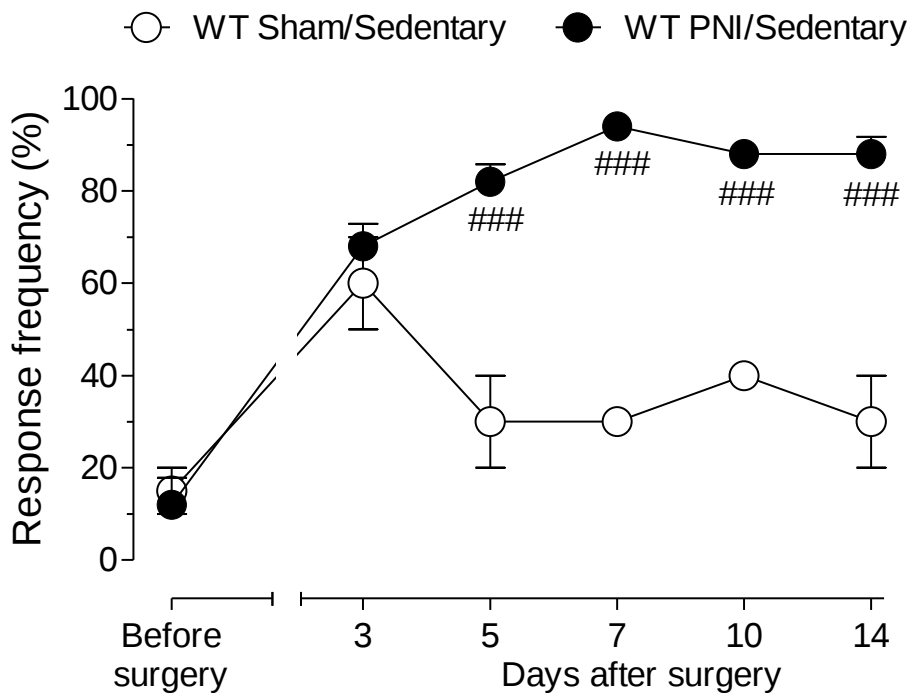
**SDC1 Fig. 1.** (A) Mouse IL-4 Standard curve on log-log graph. (B) Optical densities of a sample for IL-4 that was serially diluted. (C) Optical density of a pure sample and samples with known concentrations of IL-4 (1.56, 3.125, 6.250 and 12.5 pg of IL-4). (D) IL-4 concentrations (pg/mL) of the same sample shown in Panel C. Pure sample concentration is initially demonstrated (white bar). Subsequent bars show addition of increasing concentration of IL-4 to the sample (15.3, 31.5 and 62.5 pg/mL).

# Supplemental Digital Content 1 - Figure 2



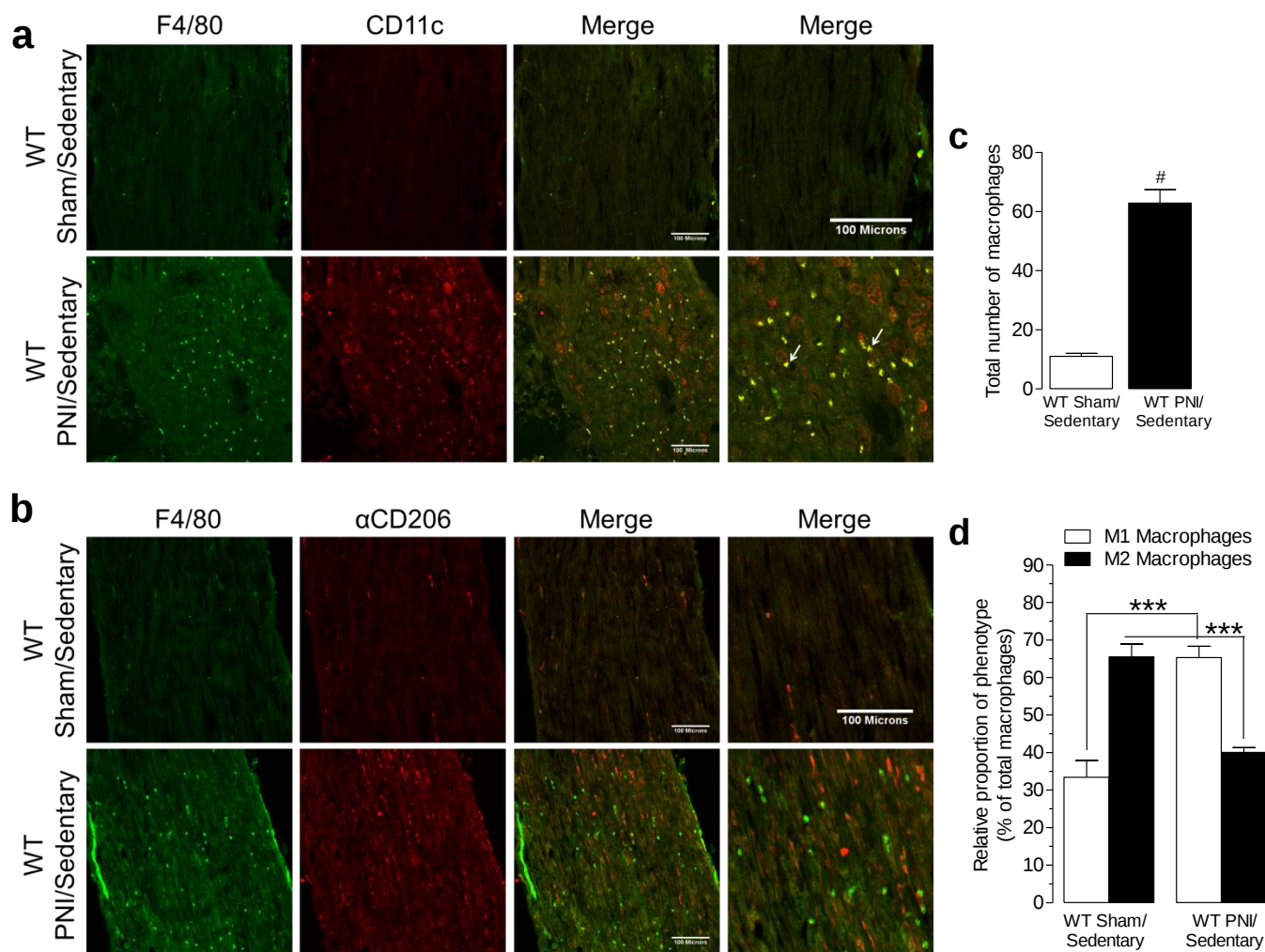
**SDC1 Fig. 2.** Effect of sciatic nerve injury on mechanical hyperalgesia, escape/avoidance test, spontaneous locomotor activity, and peripheral and central neuroimmunomodulation in Swiss sedentary mice with peripheral nerve injury (PNI) or sham-operated. (a) Withdrawal response frequency of mouse hind paw to application of a 0.4 g von Frey filament before and after surgery, for up to 14 days post-PNI. (b) Graph shows results of the escape/avoidance test and represents the time spent on the right side of the chamber when the right paw was stimulated, before and after surgery for up to 14 days post-PNI. (c) Graph shows results of the open field test and represents the number of locomotion units covered by the animal in six minutes, expressed as the number of crossings on day 14 post-PNI. (d, e, f and g) Graphs show IL-4, IL-1ra, IL-5 and IL-6 cytokine levels in the sciatic nerve tissue, respectively. (h, i, j and k) Graphs show IL-4, IL-1ra, IL-5 and IL-6 cytokine levels in lumbar (L1 to L6) spinal cord, respectively. Each point represents the mean of five to eight animals and error bars indicate  $\pm$  SEM. Hash marks denote significance levels, when compared with Sham/Sedentary group (#P<.05, ###P<.01 and ####P<.001).

## Supplemental Digital Content 1 - Figure 3



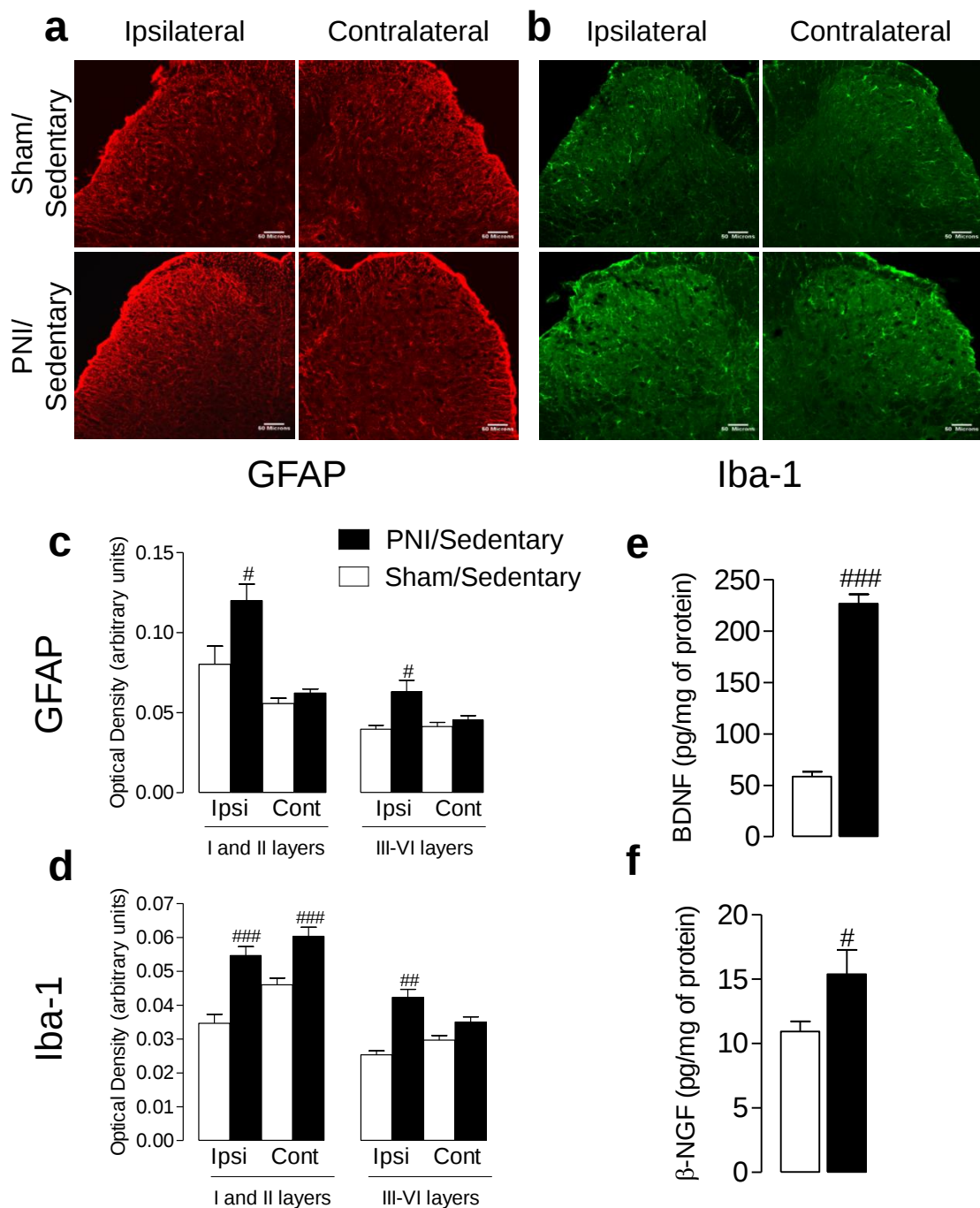
**SDC1 Fig. 3.** Effect of sciatic nerve injury on mechanical hyperalgesia in Balb/cJ Wild-type (WT) sedentary mice with peripheral nerve injury (PNI) compared with sedentary sham-operated mice, before and after surgery up to day 14. Each point represents the mean of five to six animals and error bars indicate  $\pm$  SEM. Hash marks denote significance levels, when compared with the WT Sham/Sedentary group (###  $P < .001$ ).

# Supplemental Digital Content 1 - Figure 4



**SDC1 Fig. 4.** Confocal micrographs of the sciatic nerve in Balb/cJ wild-type (WT) sedentary mice with peripheral nerve injury (PNI) compared with sham-operated mice two weeks after surgery, and quantification of the macrophages. (a) Sections show immunohistochemical labeling for macrophages with F4/80 (green) and labeling for M1 macrophages with CD11c (red), merged pictures in columns 3 and 4 (higher magnification) show the co-localization of F4/80 and CD11c as yellow (arrows). (b) Sections show immunohistochemical labeling for macrophages with F4/80 (green) and labeling for M2 macrophages with  $\alpha$ CD206 (red), merged pictures in columns 3 and 4 (higher magnification) show the co-localization of F4/80 and  $\alpha$ CD206 as yellow (arrows). (c and d) Graphs show the quantification of the total number of macrophages per group and percentage of macrophage types, respectively that are labeled as M1 or M2. Each column represents the mean of six mice  $\pm$  SEM. Hash mark denotes the level of significance compared with WT Sham/Sedentary group ( $\#P < .05$ ). Asterisk denotes the level of significance from M1 or M2 macrophages comparing WT Sham/Sedentary with WT PNI/Sedentary groups ( $***P < .001$ ). Scale bar: 100  $\mu$ m.

# Supplemental Digital Content 1 - Figure 5



**SDC1 Fig. 5.** Confocal micrographs of the spinal cord dorsal horn in sedentary mice with peripheral nerve injury (PNI) compared with sham-operated mice two weeks after surgery, and quantification of the glial cells and BDNF and  $\beta$ -NGF levels in lumbar spinal cord. (a and b) Sections show immunohistochemical labeling for GFAP (red) and Iba-1 (green), respectively, for the ipsilateral and contralateral sides of the spinal cord dorsal horn. (c and d) Graphs show the quantification of the GFAP and Iba-1 optical density (arbitrary units), respectively, for the ipsilateral and contralateral sides of the spinal cord dorsal horn. Quantification using optical density readings was done for the superficial laminae (I and II) and in the deep laminae (III - VI). (e and f) Graphs show BDNF and  $\beta$ -NGF levels in lumbar spinal cord, respectively. Each column represents the mean of six to eight mice  $\pm$  SEM. Hash marks denote significance levels, when compared with Sham/Sedentary group ( $\#P < .05$ ,  $##P < .001$  and  $###P < .001$ ). Scale bar: 50  $\mu$ m.