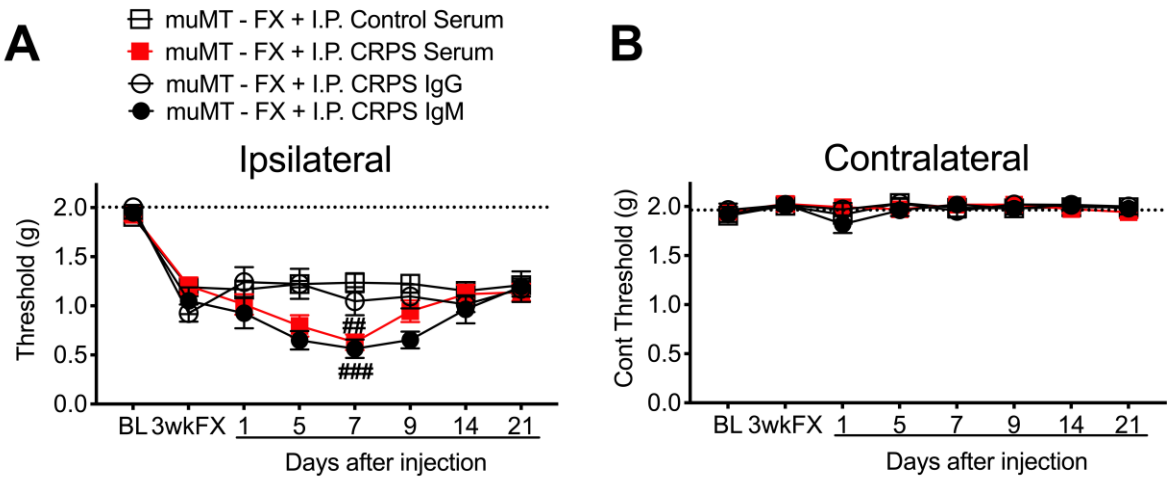
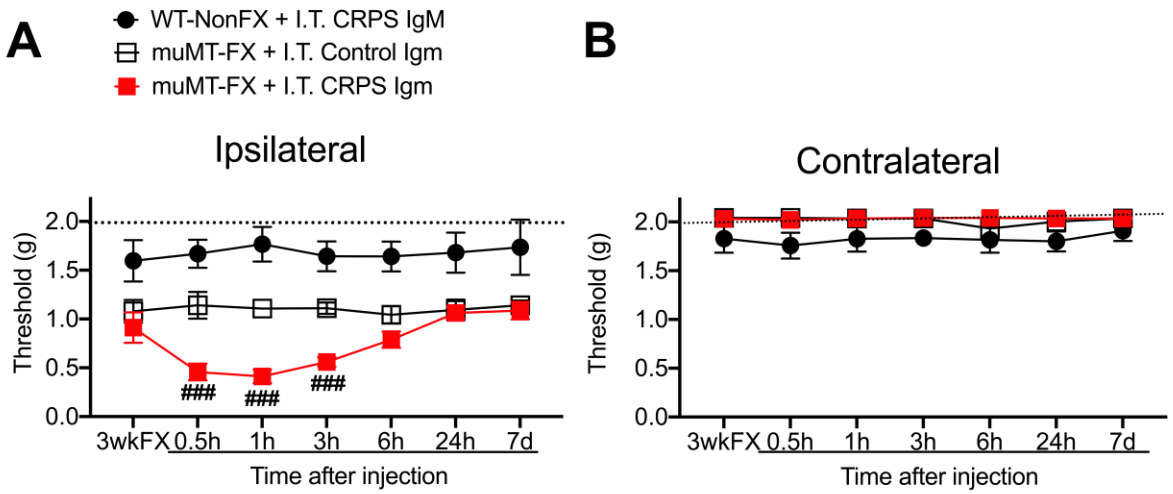
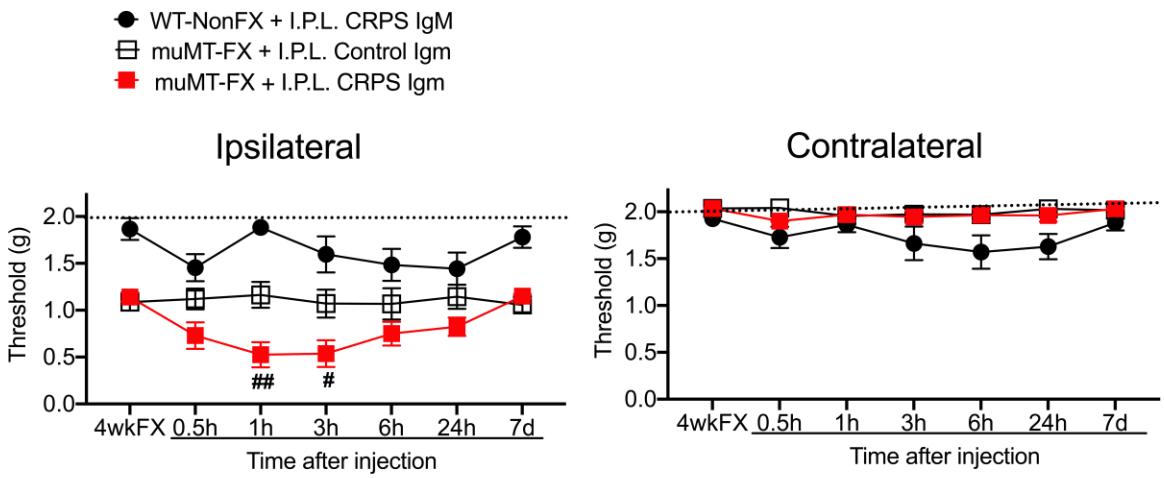


Supplemental Figure 1. CRPS patient serum and IgM had pronociceptive effects in B cell deficient fracture mice. This figure presents the time course of the raw von Frey fiber withdrawal threshold data in the ipsilateral and contralateral hindpaws that were presented as side-to-side difference scores in Figure 1A of this paper. At 3 weeks after tibia fracture and casting (FX) muMT mice lacking B cells and IgM exhibited ipsilateral hindpaw von Frey allodynia (**A**) with no effects in the contralateral hindpaw (**B**). After intraperitoneal injection of early (1-12 months post injury) CRPS patient serum (0.5ml, I.P) or IgM (500ug/1ml, I.P.) into 3 weeks post FX muMT mice, the mice gradually developed increased allodynia in the ipsilateral hindpaw over the ensuing week, and consistent with the 6 day half-life of IgM, these pronociceptive effects resolved by 2 weeks post-injection. The pronociceptive effects of the CRPS serum were restricted to the FX limb. No pronociceptive effects were observed after intraperitoneal injection of early CRPS patient IgG (5mg/1ml, I.P.) or after injection of control subject serum (0.5ml, I.P.) in 3 weeks post-FX mice. A 2-way repeated measures analysis of variance was used to test the effects of each treatment group on the dependent variables over time, using a Sidak correction test for post hoc contrasts. Data are expressed as mean values ± SEM, n = 5 patients per cohort and each patients serum or immunoglobulin was injected into 3 mice for a total n of 15 mice. ## $P < 0.01$, and ### $P < 0.001$ for each injection cohort vs the control serum treatment group. MuMT: mice lacking B cells, FX: fracture, BL: baseline, 3wkFX: 3 weeks after fracture



Supplemental Figure 2. CRPS patient IgM had pronociceptive effects in the spinal cord of B cell deficient fracture mice. This figure presents the time course of the raw von Frey fiber withdrawal threshold data in the ipsilateral and contralateral hindpaws that were presented as side-to-side difference scores in Figure 2A of this paper. After intrathecal injection of early (1-12 months post injury) CRPS patient IgM (5ug/5ul, I.T.) into 3 weeks post fracture (FX) muMT mice, the mice exhibited increased von Frey allodynia in the ipsilateral hindpaw (**A**), but not the contralateral hindpaw (**B**) that rapidly developed within 30 minutes and resolved over the ensuing 6 hours. The pronociceptive effects of the intrathecal IgM injection were restricted to the FX limb and there were no pronociceptive effects when early CRPS IgM was injected intrathecally into nonfracture wildtype mice. No pronociceptive effects were observed after intrathecal injection of control subject IgM. A 2-way repeated measures analysis of variance was used to test the effects of each treatment group on the dependent variables over time, using a Sidak correction test for post hoc contrasts. Data are expressed as mean values ± SEM, n = IgM was eluted from sera pooled from 8 early CRPS patients or 8 control subjects and injected intrathecally into 7 mice per cohort. ## $P < 0.01$, and ### $P < 0.001$ for the CRPS IgM cohort vs the control IgM treatment group, WT: wildtype mice, MuMT: mice lacking B cells, FX: fracture, NonFX: nonfractured mice, 3wkFX: 3 weeks after fracture.



Supplemental Figure 3. CRPS patient IgM had pronociceptive effects in the skin of B cell deficient fracture mice. This figure presents the time course of the raw von Frey fiber withdrawal threshold data in the ipsilateral and contralateral hindpaws that were presented as side-to-side difference scores in Figure 2C of this paper. After intraplantar injection of early (1-12 months post injury) CRPS patient IgM (5ug/5ul, I.T.) into 3 weeks post fracture (FX) muMT mice, the mice exhibited increased von Frey allodynia in the ipsilateral hindpaw (**A**), but not the contralateral hindpaw (**B**) that rapidly developed within 1 hour and resolved over the ensuing 3-6 hours. The pronociceptive effects of the intraplantar IgM injection were restricted to the FX limb and there were no pronociceptive effects when early CRPS IgM was injected intraplantarly into nonfracture wildtype mice. No pronociceptive effects were observed after intraplantar injection of control subject IgM. A 2-way repeated measures analysis of variance was used to test the effects of each treatment group on the dependent variables over time, using a Sidak correction test for post hoc contrasts. Data are expressed as mean values ± SEM, n = IgM was eluted from sera pooled from 8 early CRPS patients or 8 control subjects and injected intraplantarly into 7 mice per cohort. # $P < 0.05$, and ## $P < 0.01$ for the CRPS IgM cohort vs the control IgM treatment group, WT: wildtype mice, MuMT: mice lacking B cells, FX: fracture, NonFX: nonfractured mice, 4wkFX: 4 weeks after fracture