**SUPPLEMENTAL INFORMATION**

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**Supplemental Fig 1. Acute SSZ treatment attenuates spontaneous CIBP-related behaviors.** Animal femurs were inoculated with breast cancer cells (66.1) after baseline (Pre-surgery) behavioral measurements. On day 10 after femoral inoculation, mice demonstrated bone cancer–induced flinching and guarding. Bone cancer–induced spontaneous flinches ***(A)*** and guarding ***(B)*** were attenuated in mice administered the system xc- inhibitor sulfasalazine (SSZ, 3, 10 or 30 mg/kg, i.p.), as compared to vehicle-treated animals (two-way repeated measure ANOVA Fflinching(3,5) = 7.979, Fguarding(3,5) = 5.041, pflinching <0.001, pguarding = 0.0083). Vehicle (10% DMSO, 10% Tween-80, and 80% saline, 10 ml/kg, i.p.) treatment did not significantly alter flinching or guarding behaviors. Results are represented as the mean ± S.E.M. of 7-8 animals per group.



**Supplemental Fig 2. Nitrated β-actin, a marker for peroxynitrite generation, increased in CIBP.** There is an apparent elevation in nitrosative stress in the bone tumor microenvironment as evidenced by an increase in nitrated β-actin in the bone marrow exudates from cancer-bearing animals as compared to sham controls (Mann-Whitney test for unpaired experimental data, p = 0.0424). Animals were inoculated intrafemorally with breast cancer cells (66.1) or cell-free media (Sham). On day 14 after femoral inoculation ipsilateral animal femurs were extracted and flushed. Femur contents from 2-4 animals/treatment were pooled per sample. Pooled femur extrudates were analyzed for expression of total and nitrated β-actin. Briefly, marrow exudates (50 µg) were incubated with 10 µg of agarose conjugated anti-3-nitrotyrosine beads (Millipore, Billerica, MA). The immunoprecipitate was released and denatured with 15 µl of 2X Laemmli buffer, boiled for 5 min, and centrifuged 12,000 x g for 1 min at room temperature. Total protein (40 µg, denatured in Laemmli buffer and boiled for 5 min) and immunoprecipitate fractions were resolved in 4-20% TGX mini-gels in Towbin’s running buffer. The gels were equilibrated in Towbin’s buffer with 20% methanol and electroblotted to PVDF in Towbin’s buffer with 20% methanol. Membranes were blocked with 1% BSA (Sigma, A7030) in 1X PBS-T with 0.01% Tween-20 and 0.1% thimerasol and total and nitrated proteins were detected using mouse anti-β-actin (Sigma, A5441). Results are represented as the mean % nitrated / total β-actin ± S.E.M. of 4 (Sham) or 7 (66.1) pools of marrow extrude; \*p<0.05.



**Supplemental Fig 3. Acute FeTMPyP treatment attenuates spontaneous CIBP-related behaviors.** Animal femurs were inoculated with breast cancer cells (66.1) after baseline (Pre-surgery) behavioral measurements. On day 10-12 after femoral inoculation animals demonstrated bone cancer–induced flinching and guarding. Bone cancer–induced spontaneous flinches ***(A)*** andguarding ***(B)*** were attenuated in animals administered the peroxynitrite composition catalyst FeTMPyP, as compared to vehicle-treated animals (two-way repeated measure ANOVA Fflinching(5,9) = 60.95, Fguarding(5,9) = 68.59, pflinching <0.0001, pguarding < 0.0001). Vehicle (saline, 10 ml/kg, i.p.) treatment did not significantly alter flinching or guarding behaviors. Results are represented as the mean ± S.E.M. of 7-8 animals per group.



**Supplemental Fig 4. FeTMPyP does not alter rotarod performace or animal weight.** Drug-induced sedation/motor impairment was measured using the Rotarod apparatus (Columbus 4/8). Briefly, naïve mice were trained to remain on a 22-mm diameter rod rotating at 5 rpm during three two-minute training periods each separated by 10 min of rest. Animals were then administered FeTMPyP (10 mg/kg, i.p.) or vehicle (Saline) and placed on the Rotarod for trials 30 – 360 min post injection. Each trial lasted for two minutes, or until the animal fell off the rod. Time spent on the rod in each two minute period was recorded. Results are represented as the mean ± S.E.M. of 8 animals per group. Time on rotarod did not differ between the treatment groups as determined by two-way repeated measure ANOVA F(1,6) = 0.8410, p = 0.3758 ***(A)***.Animals were inoculated intrafemorally with breast cancer cells (66.1) or cell-free media (Sham). Once daily administration of FeTMPyP (10 mg/kg, i.p., q.d.) or vehicle (saline, 10 ml/kg, i.p., q.d.) began on post-surgery day 7 and continued until post-surgery day 14. Neither tumor- nor non-tumor-bearing animals receiving FeTMPyP had significantly altered body weight as compared to vehicle-treated controls as determined by two-way ANOVA FSham(1,8) = 0.08219, F66.1(1,8) = 0.01683, psham = 0.7816, p66.1 = 0.9000 ***(B)***.

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**Supplemental Fig 5. Acute SRI10 treatment attenuates spontaneous CIBP-related behaviors.** Animal femurs were inoculated with breast cancer cells (66.1) after baseline (Pre-surgery) behavioral measurements. On day 7 after femoral inoculation animals demonstrated bone cancer–induced flinching and guarding. Bone cancer–induced spontaneous flinches ***(A)*** andguarding ***(B)*** were attenuated in animals administered the SRI10 (3 mg/kg, i.p.), as compared to vehicle-treated animals (two-way repeated measure ANOVA Fflinching(1,6) = 30.08, Fguarding(1,6) = 14.32, pflinching <0.0001, pguarding = 0.0002). Vehicle (10% DMSO, 10% Tween-80, and 80% saline, 10 ml/kg, i.p.) treatment did not significantly alter flinching or guarding behaviors. Results are represented as the mean ± S.E.M. of 12 animals per group.