Supplementary file 1.: MTM pretreatment decreases oxaliplatin-induced mechanical hypersensitivity. MTM (100 μg/kg ip) administered on days -1 and 0, decreased oxaliplatin-induced mechanical hypersensitivity at 24 hrs, 48 hrs and day 3 (**** p < 0.0001); n=9. Statistical Comparison: 2-way RM ANOVA with Tukey post hoc test. Mean values ± SEM.
**Supplementary Figure 2:** Sex differences in MTM reversal of hypersensitivity. (A) Percent (%) efficacy of MTM reversal of heat hyperalgesia in male (black) versus female (grey) mice following CFA-induced inflammation. MTM-treated male mice had greater efficacy to reverse inflammatory heat hyperalgesia than similarly treated females; day 3 (* p = 0.021), day 4 (*p = 0.014), day 6 (**) p = 0.0013) and day 10 (* p = 0.017); n=17. (B) MTM-treated male mice had greater efficacy to reverse oxaliplatin-induced cold (10°C) on day 6 (* p = 0.010) and 10 (* p = 0.034) than MTM-treated female mice. (C) Efficacy of MTM to reverse oxaliplatin-induced cold (4°C) and mechanical (D) hypersensitivity in male and female mice; n= 6. Multiple Mann-Whitney tests. Mean values ± SEM.
Supplementary Figure 3.: Mithramycin (MTM) induces apoptosis in ovarian OVCAR3 cancer cell line and increases apoptosis of oxaliplatin-treated colon cancer cell line HCT116. (A) MTM (50 nM, 200nM, 400nM) treatment of OVCAR cells at 24 hours increased apoptosis (**** p < 0.0001); n=3 independent experiments. (B) MTM (50 nM) with 10 or 20 μM oxaliplatin (OX), increased apoptosis in HCT116 cells in an additive manner (**** p < 0.0001); n=9. Apoptosis (Relative Luminescence Units - RLU) was normalized to vehicle control. Statistical Comparison: one-way ANOVA with Tukey post hoc test. Mean values ± SEM.
Supplementary Figure 4]: Heat map (top) (A) and table (bottom) (B) of overlapping 61 DEGs present in both oxaliplatin (OX) only and OX plus mithramycin (MTM) treatment groups. OM: indicates OX treatment followed by MTM rescue, OV indicates OX treatment only. Distinct genes are upregulated (red) and downregulated (blue) between treatment groups. FDR < 0.05, logFC > 0.38 (fold change greater than 1.5). Color key indicates logFC.
Supplementary Figure 5.: Mitochondrial differentially expressed genes identified from DRG following oxaliplatin plus MTM rescue (left) versus oxaliplatin treatment alone (right). A protein-atlas database was searched to confirm the indicated DEG product has experimentally validated mitochondrial subcellular localization. Downregulated (- blue) and upregulated (red) DEGs are shown.