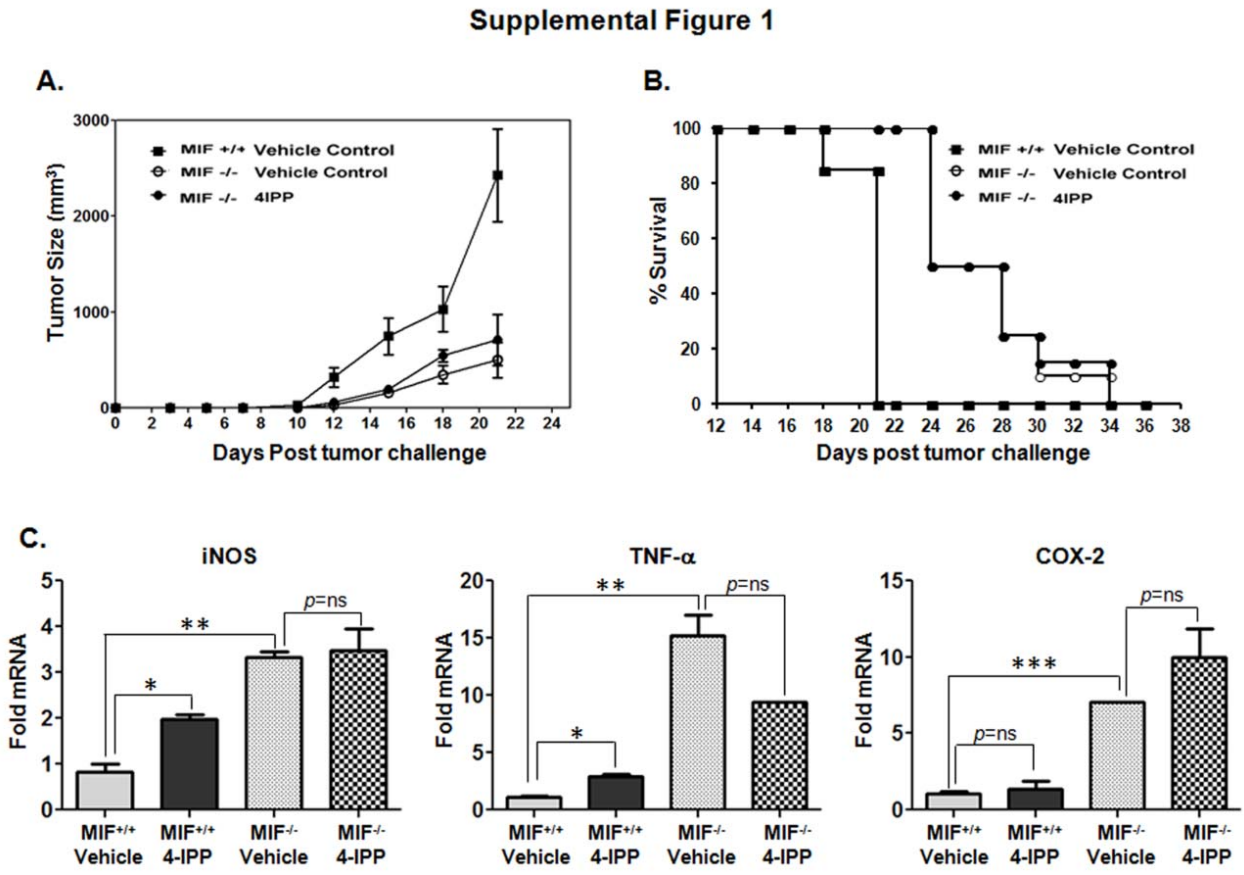
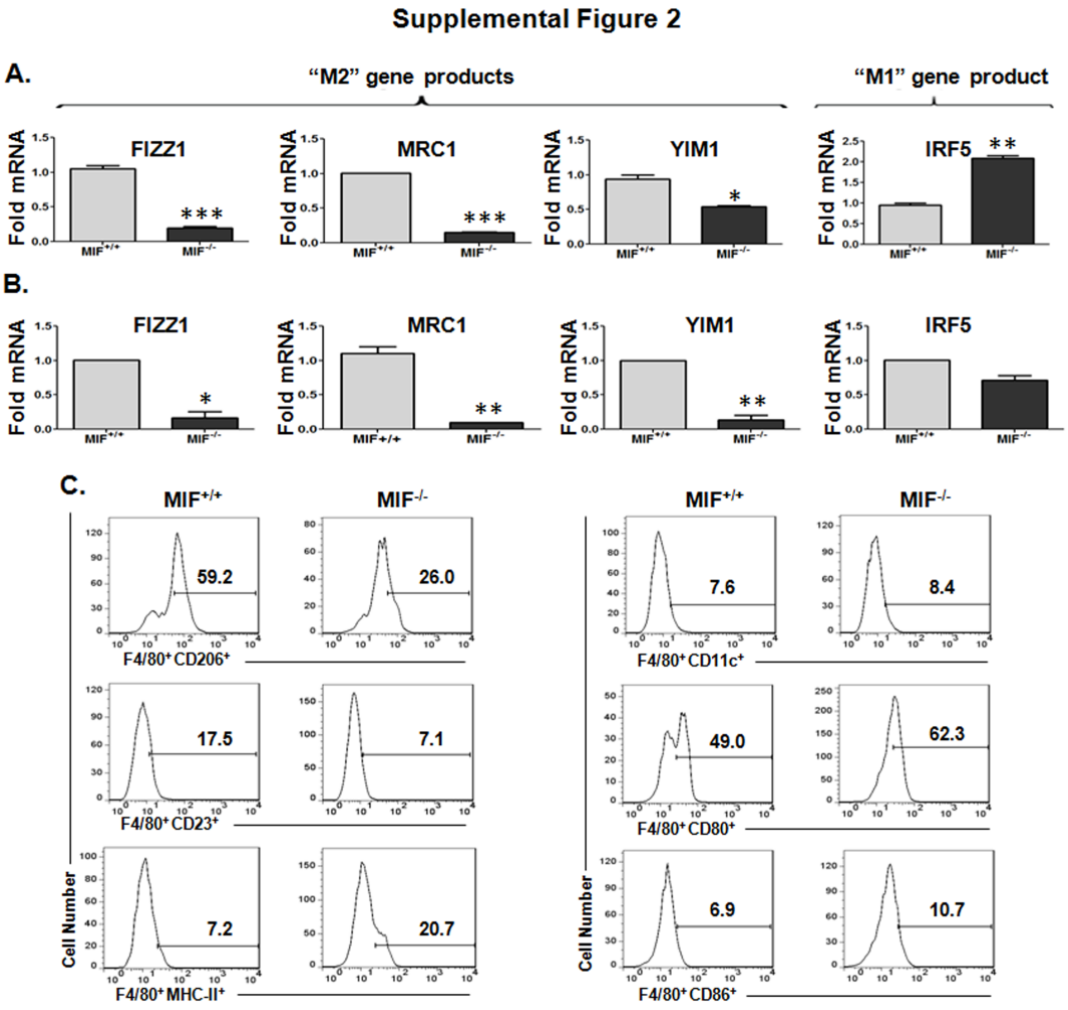
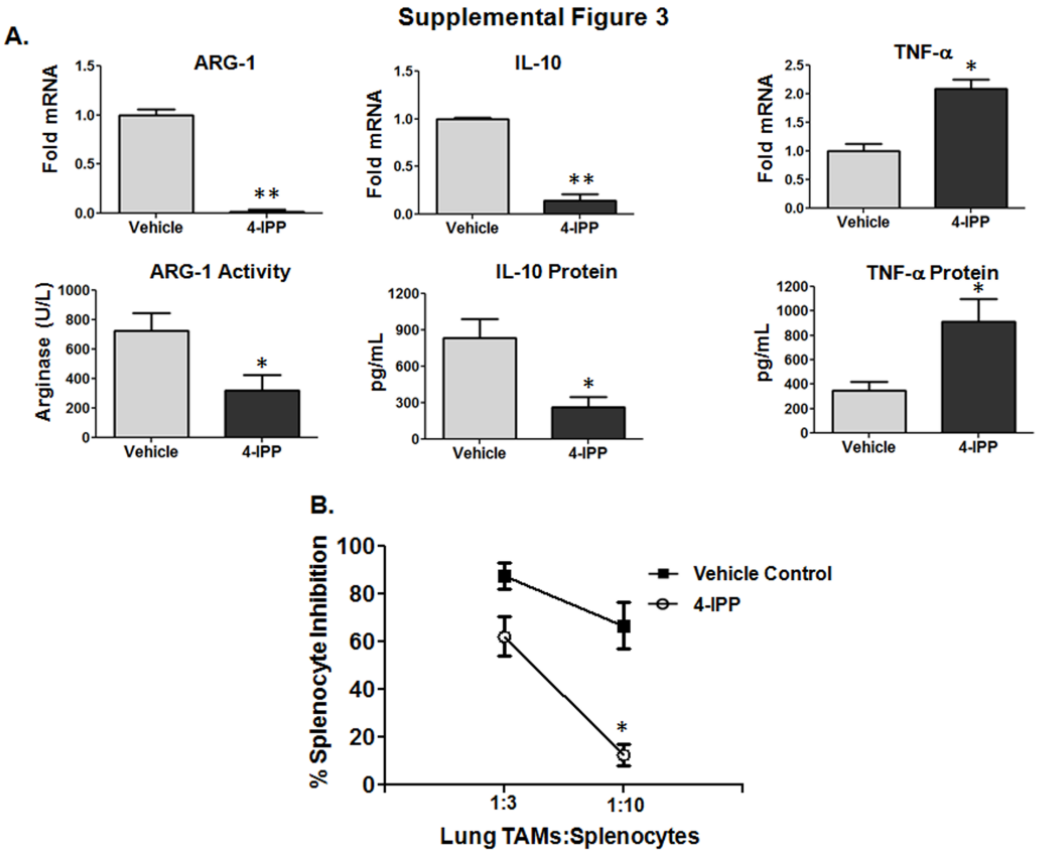


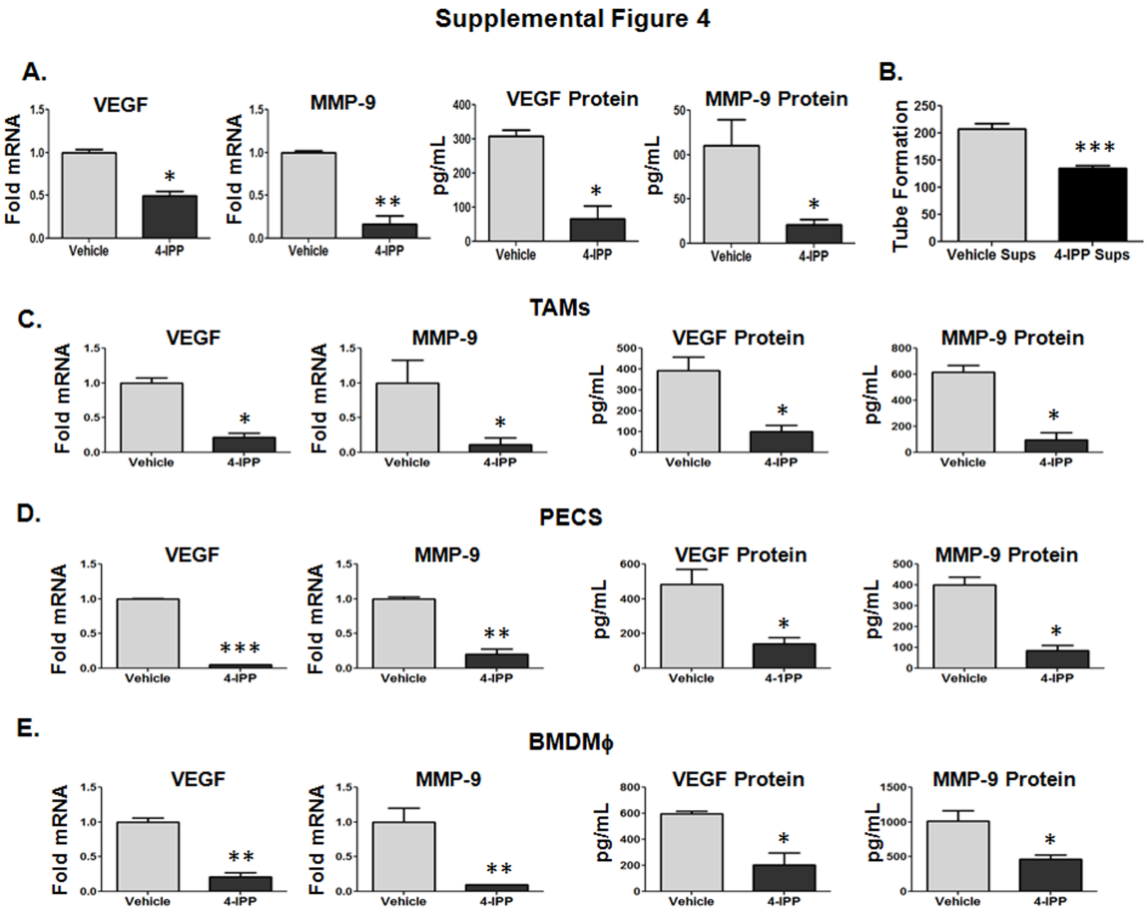
Supplemental Figure 1. 4-IPP treatment in MIF-deficient mice has negligible effect on tumor growth and on the peripheral macrophage pro-inflammatory profiles. (A) C57BL/6 $MIF^{+/+}$ and $MIF^{-/-}$ mice were injected with B16 cells (s.c.). 7 days post tumor inoculation, mice were treated i.p. with 4-IPP (80 mg/kg in corn oil; injected into $MIF^{-/-}$ mice) or vehicle control (corn oil; injected into $MIF^{+/+}$ and $MIF^{-/-}$) for 14 days and tumor volumes were plotted. Data represents the average tumor volumes of 10 mice/group ± SEM and are representative two independent experiments. **(B)** Tumor growth was monitored daily in all animals until sacrifice due to tumors exceeding 5% of body weight. **(C)** Resident PECs from C57BL/6 mice bearing a s.c. melanoma tumor (n = 10) were pooled and activated *in vitro* with LPS for 24 hours. mRNA levels were analyzed from indicated cells. Data represents the average of ± SEM of duplicate samples representative of three independent experiments. *P* values = *, p≤0.05; **, p≤0.005; ***, p≤0.0005.



Supplemental Figure 2. Alternative activation of peritoneal macrophages and TAMs from tumor-bearing mice is altered by MIF-deficiency or small molecule inhibition. (A, B) PECs **(A)** and TAMs **(B)** from $MIF^{+/+}$ and $MIF^{-/-}$ C57BL/6 mice (10/group) bearing a s.c. melanoma tumor were pooled and activated *in vitro* with LPS for 16 hours. RNA isolated was analyzed for mRNA expression by qPCR. Data represents the average ± SEM of duplicate samples. *P* values = *, p≤0.05; **, p≤0.005; ***, p≤0.0005; relative to control group by two tailed Student's *t* test. **(C)** MIF-deficiency alters the cell surface phenotype of alternative activated TAMs in tumor-bearing mice. Single-cell suspension of tumor-infiltrating cells from $MIF^{+/+}$ and $MIF^{-/-}$ melanoma-bearing mice were analyzed by flow cytometry. Histograms showing the cell surface expression of CD206, CD23, CD11c, CD80, MHC-II and CD86 markers in gated $F4/80^{+}$ cells. Numbers in gates represent the percentages of positive cells in the F4/80 cell subpopulations.



Supplemental Figure 3. TAM alternative activation profile and phenotype is attenuated by *ex vivo* 4-IPP treatment. (A) TAM polarization profiles. F4/80^{+} TAMs were isolated from the lungs of B16-F10-bearing MIF$^{+/+}$ C57BL/6 mice (n = 10). Cells were activated *in vitro* with LPS in the presence of either DMSO (vehicle control) or 4-IPP (50 μM) for 24 hours. mRNA expression was analyzed by qPCR. Arginase activity was quantified using the arginase assay Kit and protein expression were analyzed in supernatants by ELISA. **(B)** TAMs from B16-F10-bearing mice were pre-treated with 4-IPP (50 μm) or DMSO. Cells were cultured in triplicates for 16 hours. Splenocytes from OT-1 mice were then added to wells containing TAMs in presence of the ovalbumin (200 μg/ml) and cultured for additional 72 hours. Eighteen hours before harvesting, co-cultures were pulsed with [^{3}H]-thymidine. Each set of data represents the average ± SEM of duplicate samples and are representative of three independent experiments. *P* values = *, p≤0.05; **, p≤0.005 relative to control group by two tailed Student's *t* test.



Supplemental Figure 4. Lung TAM angiogenic potential is attenuated with *in vitro* 4-IPP treatment. (A) F4/80^{+} TAMs were isolated from the lungs of B16-F10-bearing MIF$^{+/+}$ C57BL/6 mice (n = 10). Cells activated *in vitro* with LPS in the presence of either DMSO (vehicle control) or 4-IPP (50 μM) for 24 hours. RNA from indicated cells was analyzed by qPCR. Protein expression was analyzed in supernatants by ELISA. **(B)** Supernatants from F4/80^{+} TAMs **(A)** were used to re-suspend HUVECs and then plated on GF-depleted Matrigel plugs for 16 hours. Tubes were quantified by counting the number of connecting branches between discrete endothelial cells. **(C, D, E**) VEGF and MMP-9 expression in s.c. TAMs **(C)**, PECs **(D)** and BMDMϕ **(E)** from B16-F0-bearing MIF$^{+/+}$ mice is decreased with *in vitro* 4-IPP treatment. Each set of data represents the average ± SEM of duplicate samples and are representative of two independent experiments. *P* values = *, p≤0.05; **, p≤0.005; ***, p≤0.0005 relative to control group by two tailed Student's *t* test.