**SUPPLEMENT FIGURE LEGENDS**

**Supplement Figure S1.** AR transcript sequencing in RAW264.7 and TRAMP-C1 cells. After isolating mRNAs from RAW264.7 and TRAMP-C1 cells, AR mRNA was amplified and sequenced from exon 1 to 9. The results demonstrate identical sequences between the macrophage cell line RAW264.7 and AR-positive TRAMP-C1.

**Supplement Figure S2.** Endotoxin test for DHT and T. Using the endotoxin assay kit (invivoGen, Sandiego, CA), alkaline phosphatase activity was measured after treating with indicated concentrations of DHT and T in RAW264.7 for 24 hours. There is no endotoxin contamination in DHT and T as alkaline phosphatase level did not change with DHT and T treatment.

**Supplement Figure S3.** Direct cell-cell contact is not required for DHT-induced cytotoxic activity of human macrophages. When the androgen-independent human prostate cancer cell lines DU145 or PC3 were co-cultured with the differentiated THP-1 in the presence of a cell culture inserts, DHT decreased the count of both DU145 and PC3. Error bars indicate average ± SE and \* p-value<0.05 compare with vehicle treated control group in all experiments.

**Supplement Figure S4.** Annexin V-FITC assay was carried out on TRAMP-C2 xenograft mice with/without castration. Castration decreased apoptosis.

**Supplement Figure S5.** Cytokine antibody arrays that include TNF-α was performed after treating RAW264.7 with 100 nM DHT for 24 hours. TNF-α protein levels increased following DHT treatment.

**Supplement Figure S6.** TRAIL siRNA decreased TRAIL protein levels in RAW264.7 and THP-1. Human and mouse TRAIL siRNAs were purchased from Qiagen (Germantown, MD).

**Supplement Figure S7.** Effect of DHT on macrophage cytotoxicity on AR-positive prostate cancer cell line, 22Rv1. THP-1 was co-cultured with 22Rv1 in the presence of cell culture inserts and 100 nM DHT for 24 hours prior to counting the number of 22Rv1 cells. Blocking of TRAIL by neutralizing antibody partially reversed the DHT-induced cytotoxic activity of THP-1. TRAIL shRNA treatment also reversed the DHT-induced cytotoxic activity. To prevent cell-cell contact, cell culture inserts were used. Error bars indicate average ± SE and \* p-value<0.05.

**Supplement Figure S8.** Secreted levels of TNF-in RAW 264.7 conditioned media following treatment with 1-100 nM DHT for 24 hours was measured with ELISA. Results demonstrate increased TNF- secretion by RAW264.7 following DHT treatment. Simultaneous treatment with 10 μM enzalutamide reversed the induction of secreted TNF-. Error bars indicate average ± SE and \* p-value<0.05 compare with vehicle treated control group in all experiments.

**Supplement Figure S9.** H&E staining of tumor xenografts. There is no significant difference in histology between vehicle treated control group and castrated group **(A)** and between castrated group and castrated with clodronate treated group **(B).**

**Supplement Figure S10.** Flow Cytometry for detection of pan macrophage population change by clodronate treatment. Macrophage population decreased following clodronate treatment. However, the absolute level was 1.2% to 0.3%. These extremely low levels suggest that alterations in the macrophage proportions do not contribute directly to the change in tumor volume.

**Supplement Figure S11. Effect of castration on neuroendocrine marker expression in TRAMP-C2 xenograft mice.** Immunofluorescence staining experiment was performed with ChgA and PTHrP antibodies. ChgA and PTHrP expression were increased by castration.

**Supplement Figure S12. Effect of castration on androgen receptor expression in TRAMP-C2 xenograft mice.** Immunofluorescence staining experiment was performed with AR antibody. AR expression was moderately decreased by castration.

**Supplement Figure S13. TNF-α antibody array list 1.**

**Supplement Figure S14. TNF-α antibody array list 2.**

**Supplement Figure S15. TNF-α antibody array list 3.**

**Supplement Figure S16. TRAIL antibody array list 1.**