Supplemental Figure Legends.

Supplemental Figure 1. Efficiency of macrophage depletion with Lip-Clod. One day prior to B16.SIY injection in WT mice, systemic depletion of macrophages was performed using Lip-Clod at 200µl/mice. At different time points post local treatment with 20 Gy, tumors and spleens were removed, single cell suspensions prepared, cells stained with anti-CD11b-PE-Cy5 and anti-F4/80-APC, then analyzed by FACS which showed 90% macrophage depletion in both spleen and tumor sites.

Supplemental Figure 2. Phenotype of TAMφ following co-injected of tumor cells with WT or TNFR1,2-/- BMDMφ. WT or TNFR1,2-/- BMDMφ were co-injected with B16.SIY cells at the ratio of 1:4 into WT mice. When mean volume reached 150-200mm^3, tumors were dissected and digested into single cell suspension. Disaggregated cells were stained with anti-CD11b, anti-F4/80 and anti-CD206 (top row). After permeabilization and fixation, cells were further stained with anti-TNFα and analyzed by FACS (bottom row). Tumor infiltration of F4/80$^+$ cells was equivalent between TNFR1,2-/- BMDMφ and WT BMDMφ. TNFR1,2-/- BMDMφ exhibited slightly reduced levels of the M2 phenotypic marker CD206. Intracellular TNFα expression was analyzed by F4/80 $^+$ gating.

Supplemental Figure 3. Validation of BMT procedures. 6 week old TNF-/- mice received 10x10^6 WT BM cells after TBI (9 Gy). 100% of the recipient mice survived BMT. 4 weeks later, BM cells and splenocytes were collected. BM cells were cultured into BMDMφ and splenocytes were stimulated using anti-CD3/anti-CD28 antibody coated beads for 5 days. Intracellular TNFα expression was analyzed by FACS (top). The same analysis was performed using TNFR1,2-/- (bottom). Blue lines represent cells from WT to TNF-/- or TNFR1,2-/- BMT mice, while red line represent cells from TNF-/- or TNFR1,2-/- to TNF-/- or TNFR1,2-/- control BMT mice. BM was reconstituted with >70% of donor cells.

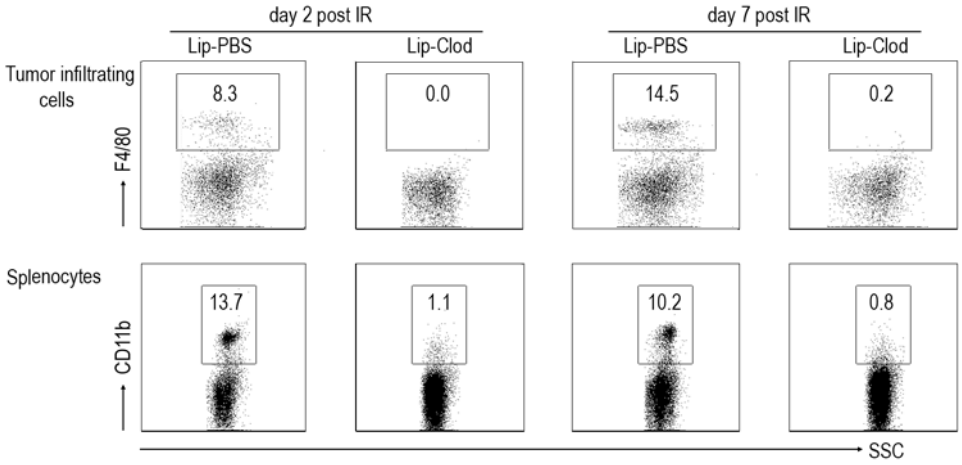
Supplemental Figure 4. **TNFα signaling in BMDMφ is sufficient and essential to promote tumor growth.** (**a**). WT BMT in TNF-/- mice promotes B16.SIY tumor growth. TNF-/- mice received BMT from WT or TNF-/- mice. 4 weeks after TBI (9 Gy) B16.SIY tumor cells were inoculated w/wo systemic macrophage depletion using Lip-Clod 1 day before tumor cell inoculation (n=11-16/group). ♦ TNF-/- to TNF-/- BMT with Lip-PBS; ◊ TNF-/- to TNF -/- with Lip-Clod; ■ WT to TNF-/- BMT with Lip-PBS; □ WT to TNF-/- BMT with Lip-Clod. (**b).** WT BMT in TNFR1,2-/- mice promotes B16.SIY tumor growth 30 days earlier than TNFR1,2_/- BMT. TNFR1,2-/- mice received BMT from WT or TNFR1,2-/- mice, and 4 weeks later B16.SIY tumor cells were inoculated w/wo systemic macrophage depletion as described (n=12-16/group). ♦ TNFR-/- to TNFR-/- BMT with Lip-PBS; ◊ TNFR-/- to TNFR -/- with Lip-Clod; ■ WT to TNFR-/- BMT with Lip-PBS; □ WT to TNFR-/- BMT with Lip-Clod.

Supplemental Figure 5. WT BMDMφ increase tumor growth. (a). Response of B16.SIY tumors co-injected with WT BMDMφ in TNFR1,2-/- mice to fractioned IR (10 x 2Gy, n=9/group). ♦ WT-Mac + B16; ◊ IR in WT-Mac + B16. (**b**). Response of B16.SIY tumors co-injected with TNFR1,2-/- BMDMφ in TNFR1,2-/- mice to fractioned IR (n=11/group). ♦ TNFR-/- Mac + B16; ◊ IR in TNFR-/- Mac + B16. Co-injection with WT BMDMφ significantly increases tumor growth compared to co-injection with TNFR1,2-/- BMDMφ (p=0.010, day 22).

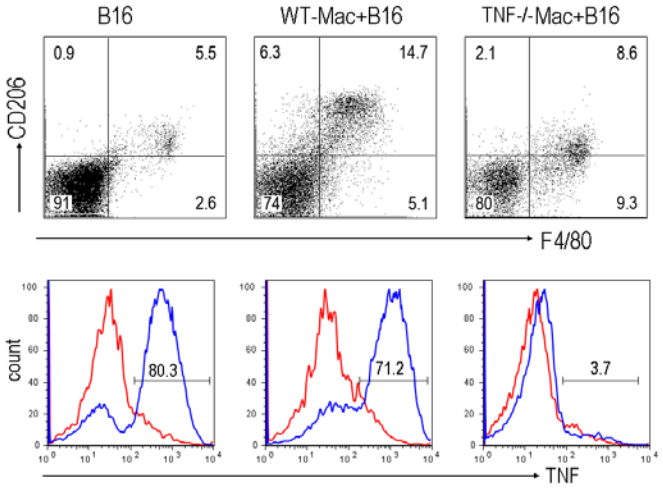
Supplemental Figure 6. **BMDMφ TNFα does not directly affect tumor cell colony formation or the radiation response of B16.SIY tumor cells.** Spent culture supernatants were collected from WT, TNF-/- or TNFR1,2-/- BMDMφ w/wo 5 Gy, and added to control or 5 Gy irradiated B16.SIY cells. After 7 days, cells were washed and stained with crystal blue. Colonies with more than 50 cells were counted. The mean of triplicates from one representative experiment is shown. The radioprotective effects of TNFα signaling in BMDMφ does not directly effect tumor cells. Open box B16; black box B16+SupTNFR1,2-/-; medium gray box B16+SupWT; light gray box B16+SupTNF-/-.

Supplemental Figure 7. **Blockade of VEGF increases radiosensitivity in B16F1 and B16.SIY tumors.** Growth of B16F1 and B16.SIY tumors in WT mice (n=6/group). Neutralizing polyclonal goat IgG against mouse VEGF-164 (R & D Systems) was suspended in PBS and administered via i.p. injection (10 µg/mouse, 3 h before each IR and 3, 8 days after IR). Control mice received goat IgG (Sigma). Blocking VEGF in WT mice led to delay of regrowth of both B16F1 and B16.SIY.

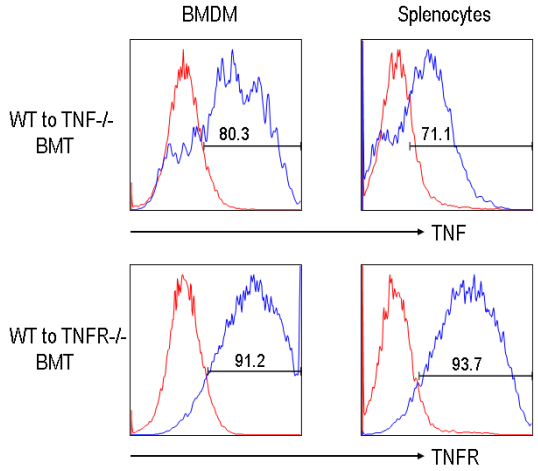
Meng Supplemental Figure 1



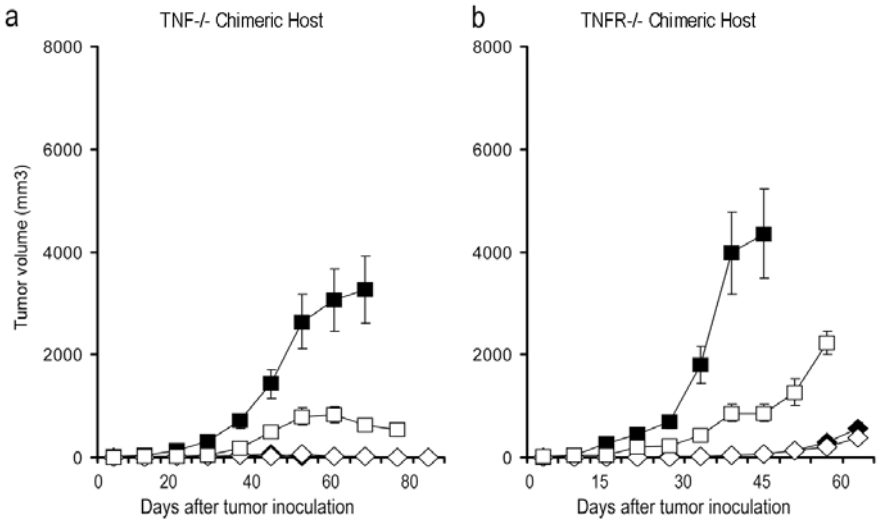
Meng Supplemental Figure 2



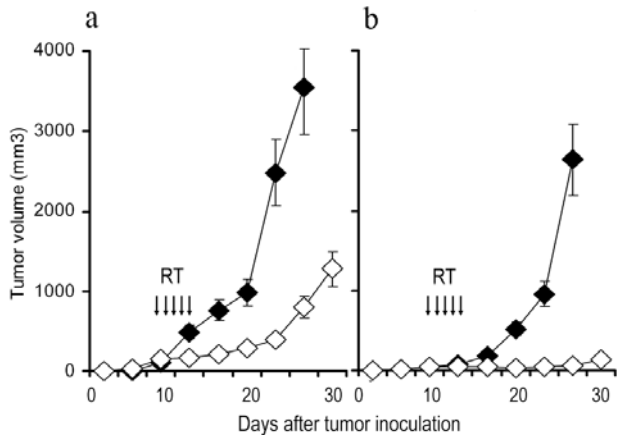
Meng Supplemental Figure 3.



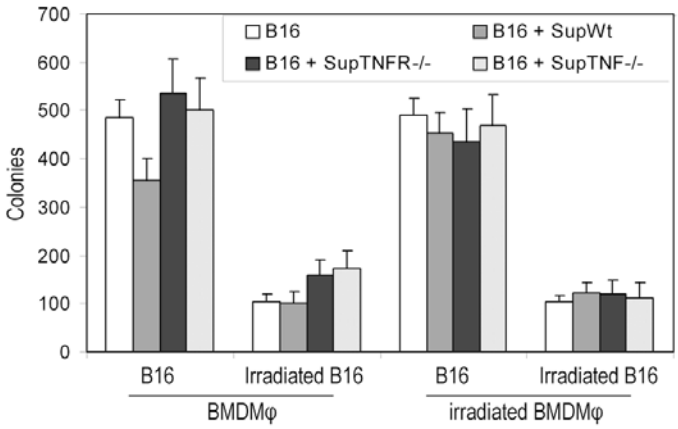
Meng Supplemental Figure 4



Meng Supplemental Figure 5



Meng Supplemental Figure 6



Meng Supplemental Figure 7