Supporting Information

Bioinspired immuno-radio-enhancers toward synergistic nanomedicine through radiation-induced abscopal effects and immunocheckpoint blockade therapies

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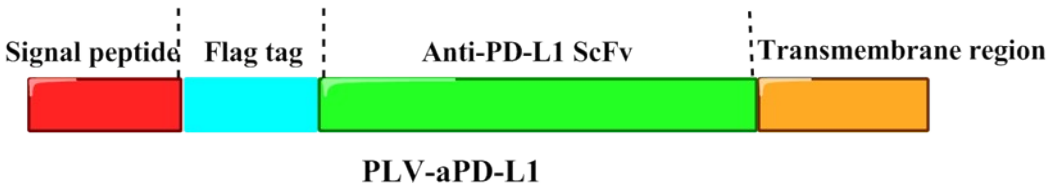

Figure S1. Schematic illustration of recombinant PLV-aPD-L1 gene fragments that were

subcloned into lentiviral PLV plasmids to express membrane-anchored anti-PD-L1 antibodies on the surface of MSCs.

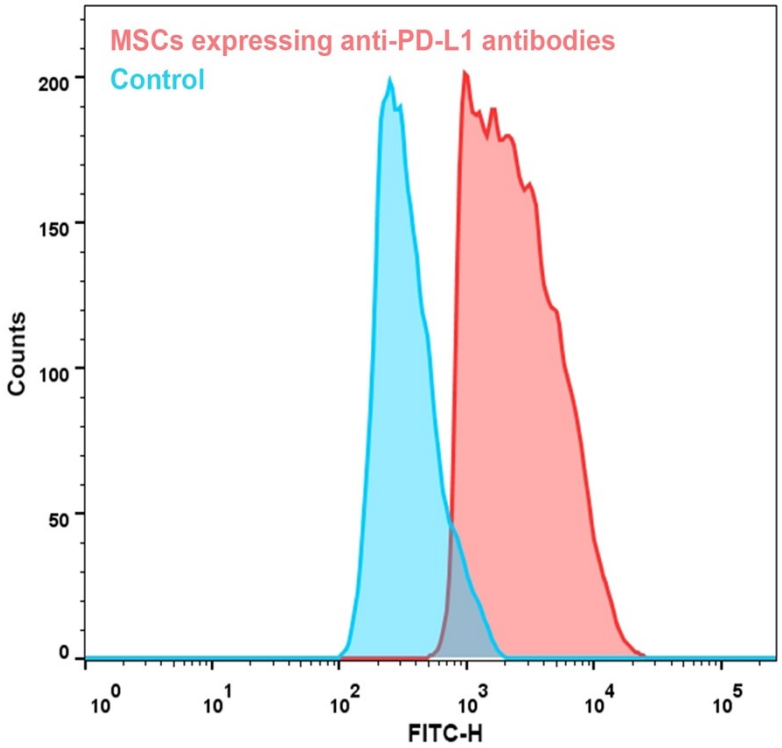

Figure S2. It was shown that about 92 % of MSCs expressed anti-PD-L1 ScFv (antibodies) on cellular surfaces using anti-flag antibodies through flow cytometry analysis.

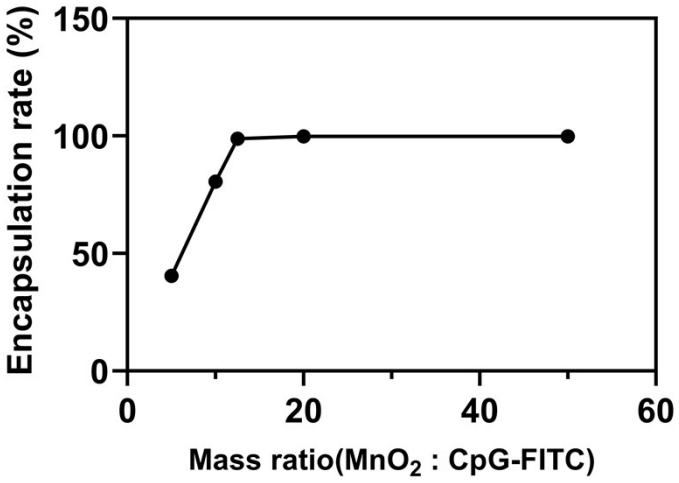

Figure S3. When mass ratios of MnO_2 NPs and CpG-FITC reached 12.5, the encapsulation rate of CpG approximated 100 %.

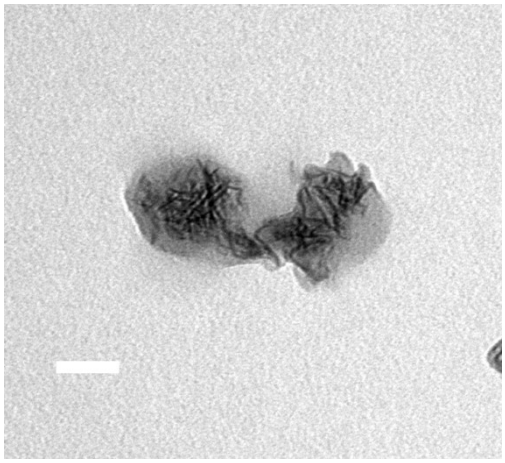

Figure S4. The enlarged TEM images of MnO_2 NP-CpG@M-aPD-L1 from Figure 1b revealed that the thickness of cell membrane coated onto the MnO_2 NPs indeed ranged from 10 to 20 nm (Scacle bar: 50 nm).

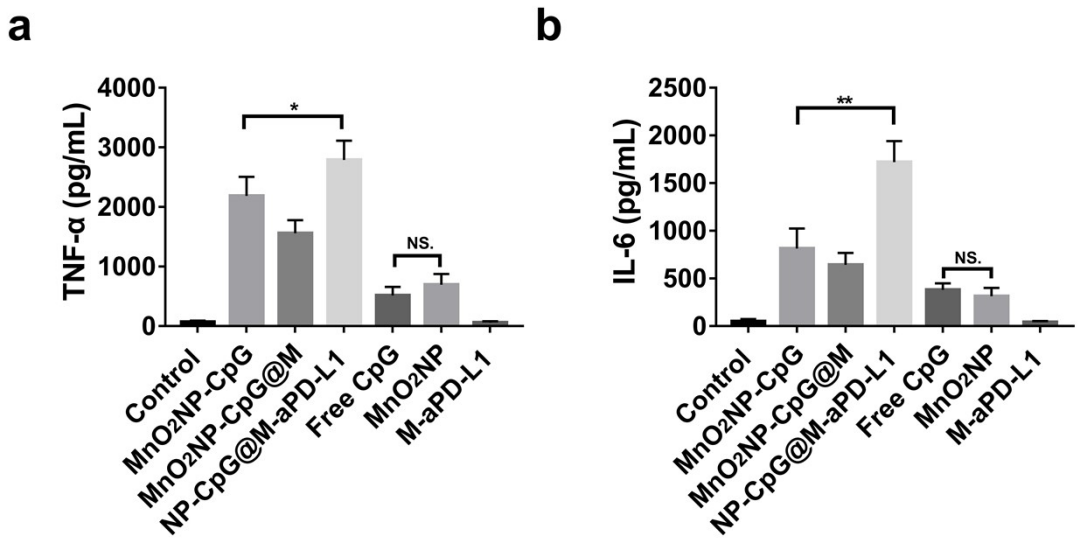

Figure S5. Targeted NPs-CpG@M-aPD-L1 (containing equivalent 1.2 μg mL^{-1}CpG adjuvants or 10 μg mL^{-1} of Mn contents) significantly increased the secretion levels of TNF-α and IL-6 cytokines from murine macrophages when compared to other control groups, as measured by ELISA kits.

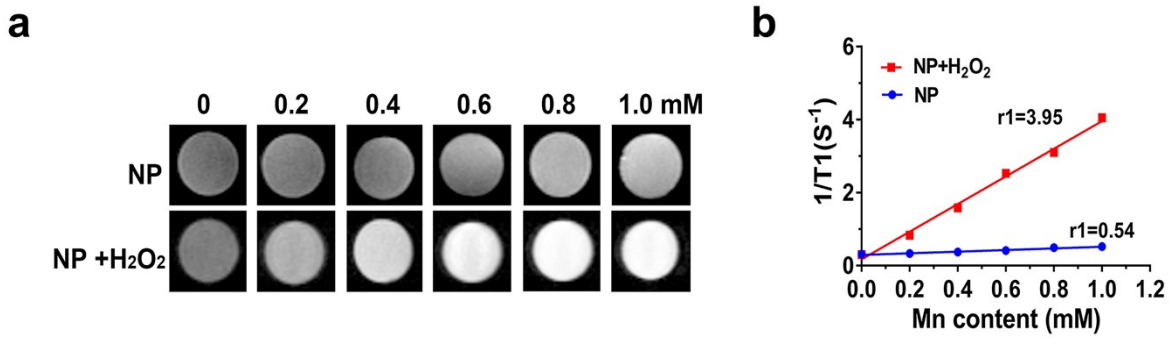

Figure S6. a) *In vitro* T_1-weighted MR imaging and b) R1 proton relaxivity ($1/T_1$) of NPs-CpG@M-aPD-L1 containing different contents of Mn element were scanned with or without H_2O_2 treatment (1.5 mM) using a micro MR imaging equipment.

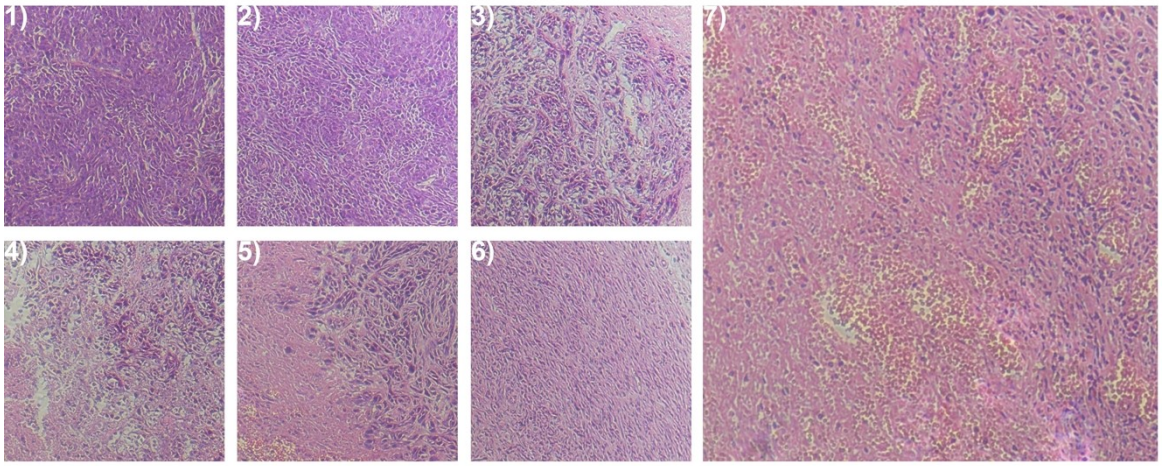

Figure S7. Hematoxylin and eosin (H&E) staining images of irradiated primary Hepa 1-6 tumors from mice with different treatments. 1) Control, 2) NP-CpG@M-aPD-L1, 3) RT, 4) RT+NP-CpG@M, 5) RT+NP@M-aPD-L1, 6) RT+M-aPD-L1 (membrane vesicles displaying aPD-L1), and 7) RT+NP-CpG@M-aPD-L1.

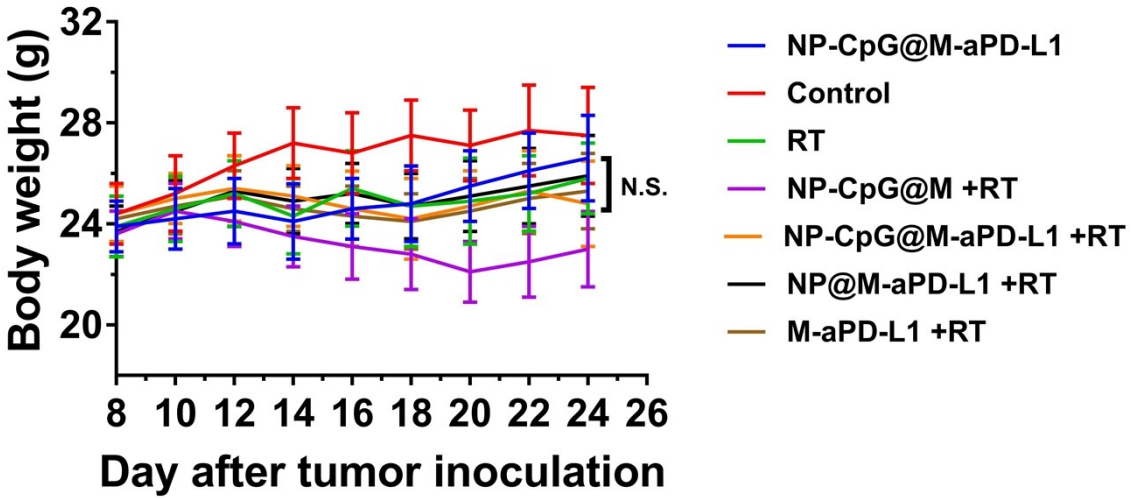

Figure S8. Body weight curves of mice with different RT treatments after intravenous injection of NP-CpG@M-aPD-L1, NP-CpG@M, NP@M-aPD-L1, or M-aPD-L1 (membrane vesicles displaying aPD-L1).

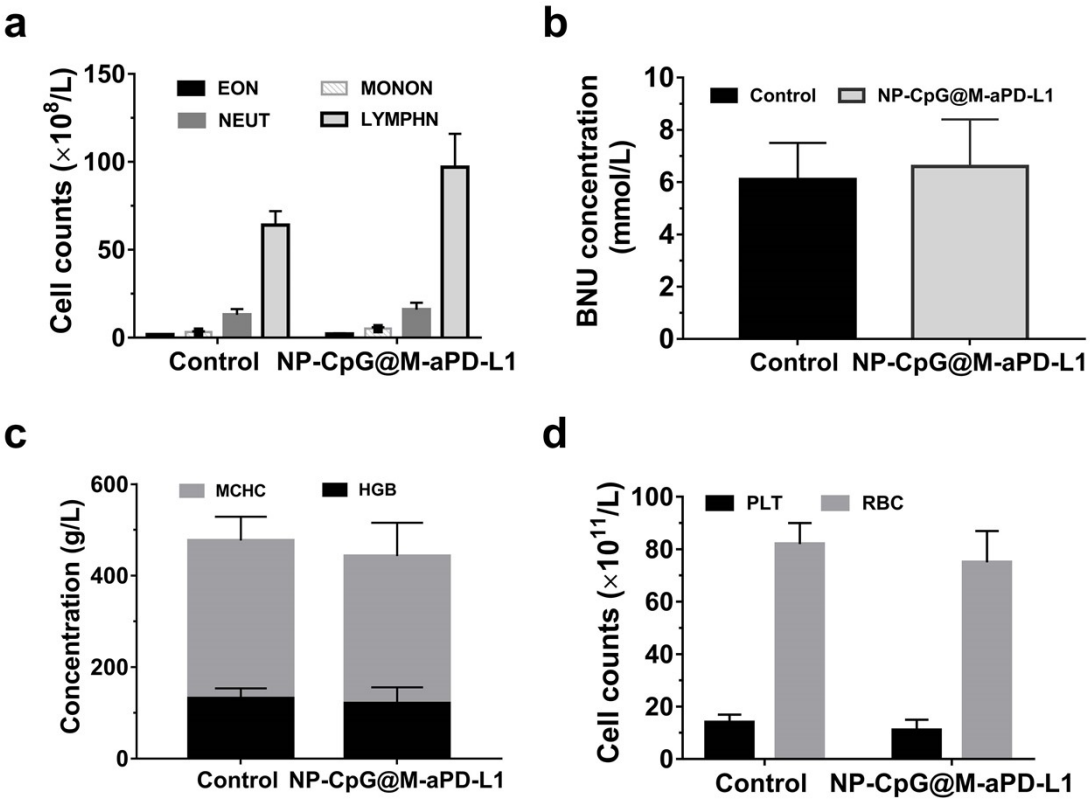

Figure S9. Blood biochemical tests of the mice 7 day after the last treatment with PBS or NP-CpG@M-aPD-L1 plus RT. (MONON: Mononuclear macrophages, EON: Eosinophils, NEUT: Neutrophile granulocyte, LYMPHN: Lymphocyte, BNU: Urine nitrogen content, MCHC: Mean corpuscular haemoglobin concentration, PLT: blood platelet, HGB: Hemoglobin, RBC red blood cell)

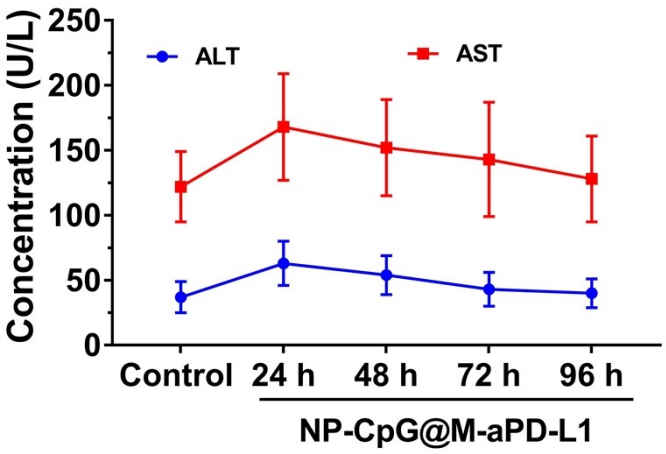

Figure S10. Liver functions after a single *i.v.* injection of NP-CpG@M-aPD-L1 were further examined by measuring the activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) from mouse serum at predetermined time.

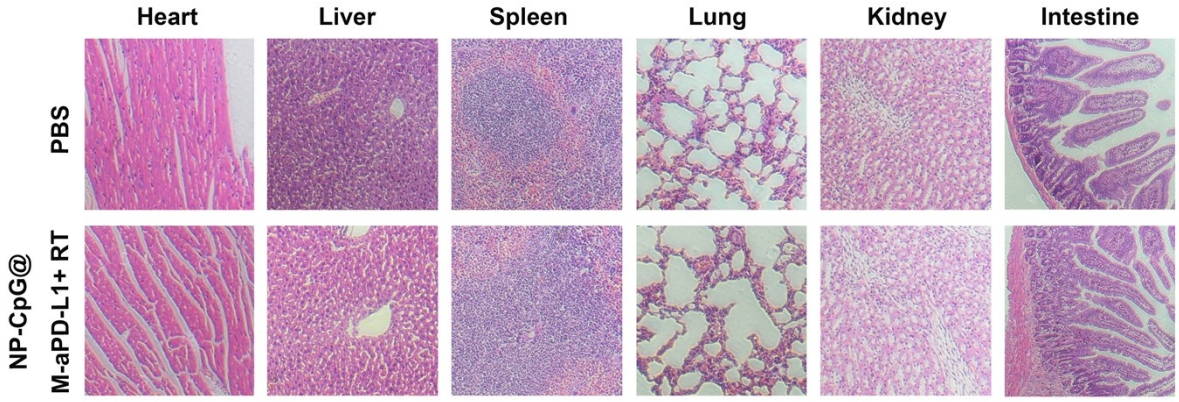

Figure S11. Hematoxylin and eosin (H&E) staining images of major organs from the mice after the last treatment with PBS or NP-CpG@M-aPD-L1 plus RT. There was no significant damage seen in these H&E images.

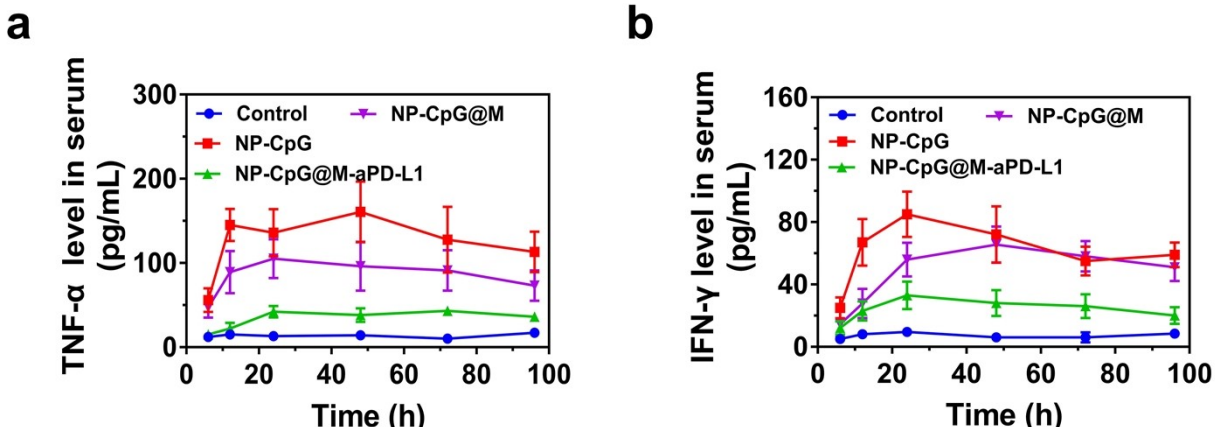

Figure S12. Serum TNF-α and IFN cytokine profiles at different time points after a single *i.v.* injection of NP-CpG@M-aPD-L1, NP-CpG, NP-CpG@M, or PBS. These results showed that tumor-targeting NP-CpG@M-aPD-L1 increased fewest levels of serum cytokines, when compared to other treatment groups.