Supplementary Figures

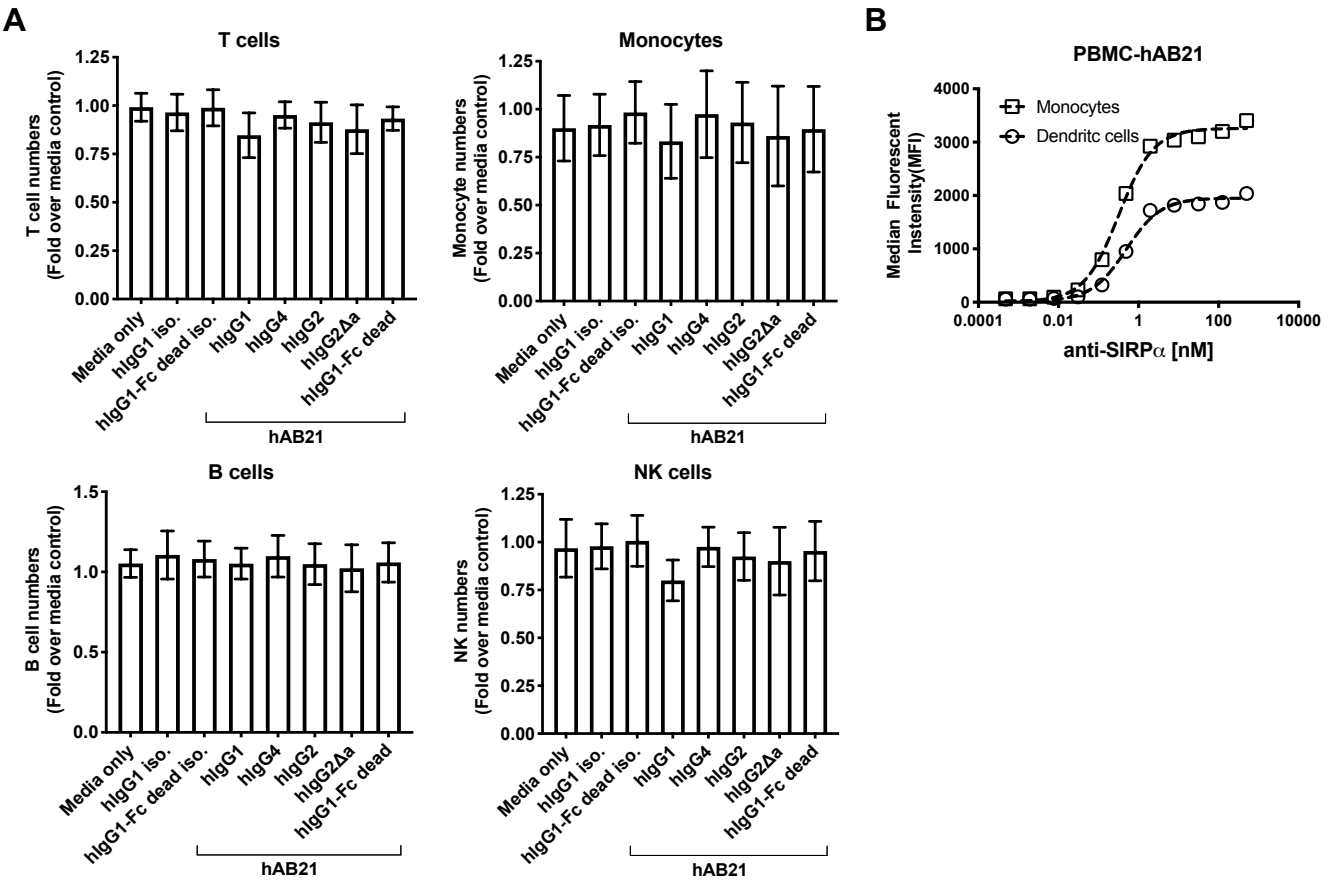

Figure S1. IgG subclasses show no effect on monocytes, B, T and NK cells. (A) Relative monocytes, B, T, and NK cell numbers in human PBMCs after 48 hour incubation with hAB21-IgG subclass variants. Each bar indicates relative cell subset number as compared to media only. IgG control is abbreviated as iso. (B) Flow cytometry analysis of hAB21 binding to human $CD14^{+}$ monocytes and $CD11c^{+}MHCII+$ DCs. Fluorescent-labeled hAB21 was incubated in increasing concentration with PBMCs at 4˚C for 60 minutes, washed and evaluated by flow cytometry. Mean fluorescent intensity is measured.

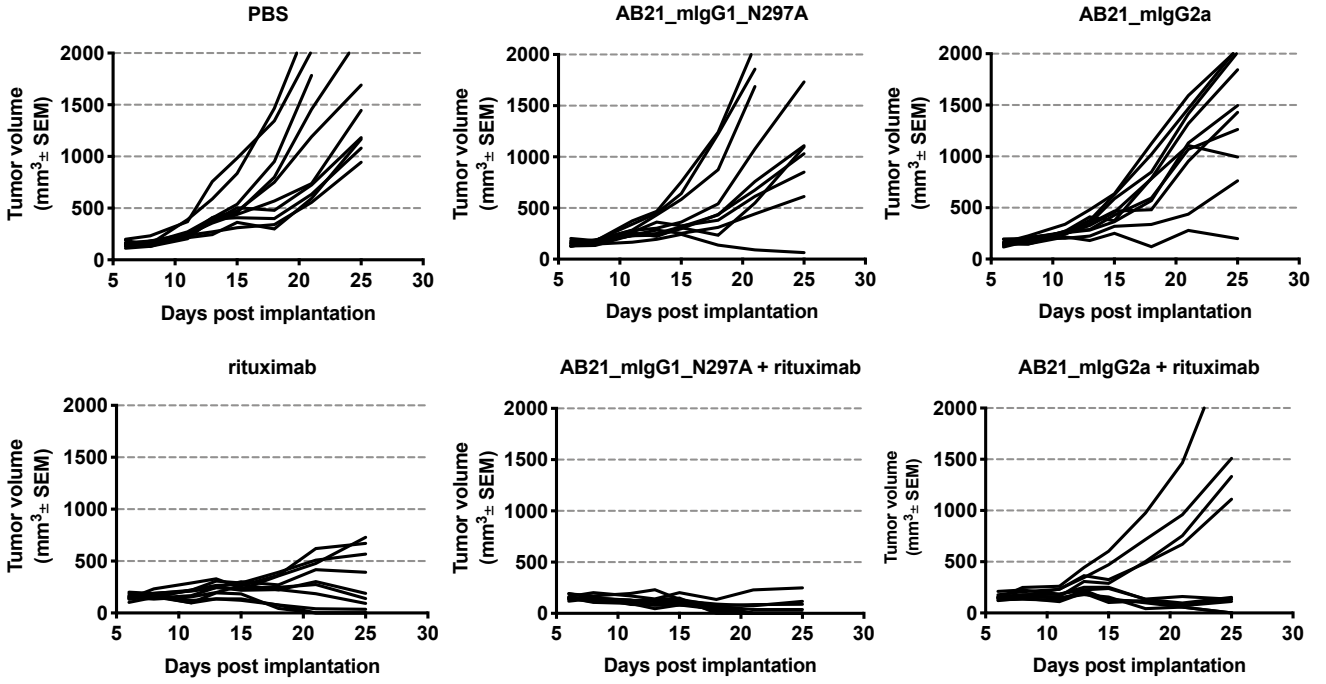

Figure S2. AB21-Fc-inactive is superior to AB21-Fc-active in combination with rituximab *in vivo.* Raji B-cell lymphoma cells were implanted subcutaneously on the right flanks of NOD-SCID mice. Mice with established tumors (average of 154 mm^3) were randomized, n=10/group, and treated intraperitoneally with vehicle, rituximab, AB21-Fc mIgG1_N297A (inactive), AB21-Fc h21_mIgG2a (active), or AB21-Fc inactive or –Fc active + rituximab. Mice were treated five doses every 3 days. Each line represents one mouse.

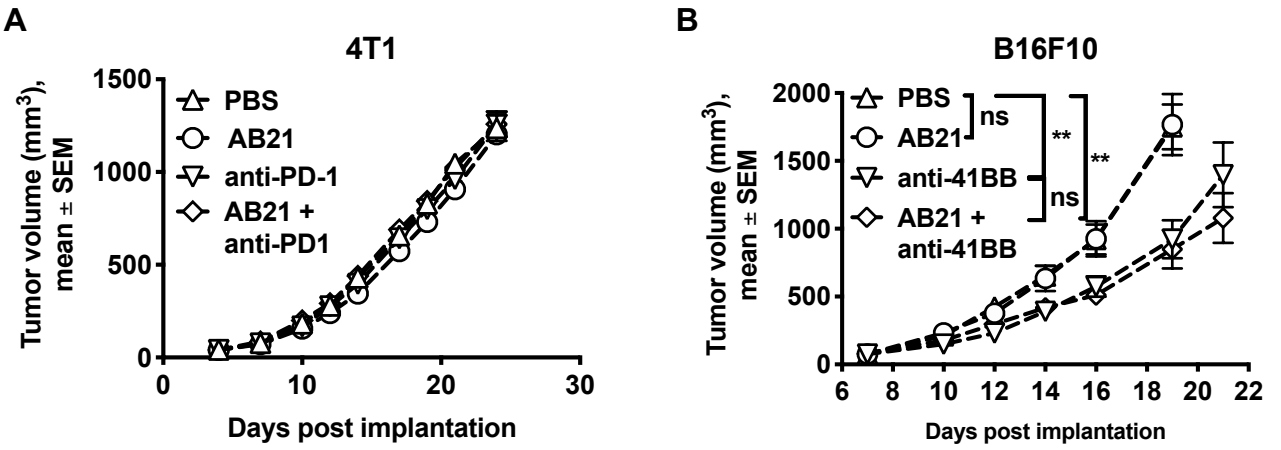

Figure S3. Single and combination efficacy in less immunogenic models, B16F10 and 4T1. (A) 4T1 cells were implanted subcutaneously in Bab/c mice Mice with established tumors were randomized, n=10 mice/group, and treated intraperitoneally with PBS, AB21, anti-PD-1, or AB21 + anti-PD-1. Mice were treated four times every three days for anti-PD-1 and five times every three days for AB21. **(B**) B16F10 melanoma cells were implanted subcutaneously in C57BL/6 mice. Mice with established tumors were randomized, n=10 mice/group, and treated intraperitoneally with PBS, AB21, anti-41BB, or AB21 + anti-41BB. Mice were treated three times every three days. One-Way ANOVA Tukey's multiple comparisons test on D19 was performed. **p<0.01 and ns is not significant

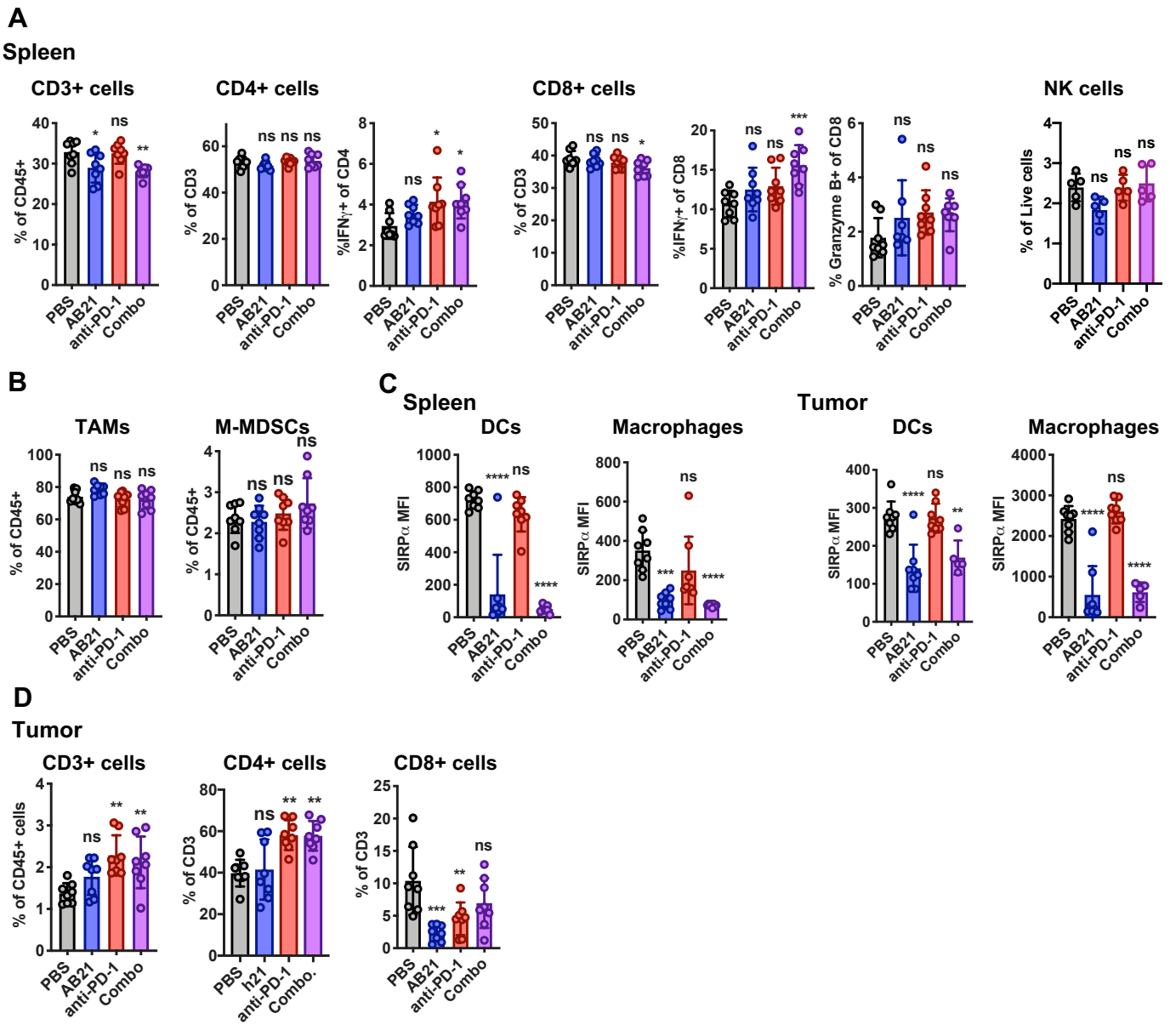

Figure S4. Characterization of the lymphoid and myeloid compartments of tumors and spleen. MC38 colon carcinoma cells were implanted subcutaneously in C57BL/6 mice. Mice with established tumors were randomized and treated intraperitoneally with PBS, AB21, anti-PD-1 or combo (AB21 + anti-PD-1). (A) Quantifications of splenic CD3, CD4, CD8 and NK cells as a proportion of CD45 or CD3 and IFNγ and granzyme B expressing T cells. (B) Quantifications of tumor associated macrophages (TAMs) and M-MDSCs in tumors. (C) Quantification of SIRPα expression on monocytes ($Gr1^{hi}CD11b^{+}$) and DCs ($CD11c^{+}MHC\text{-}II^{+}$) in spleen and tumor. (D) Quantification of CD3, CD4 and CD8 as a proportion of live $CD45^{+}$ or $CD3^{+}$ cells in the tumor. Plotted as mean +/- SD and analyzed by Ordinary one-way ANOVA, Tukey's multiple comparisons test. *p < 0.05, **p < 0.01, ****p < 0.0001, n.s. is not significant.

Table S1

Data Collection	
Space group	P6122
Cell dimensions	
a, b, c (Å)	189.1, 189.1, 78.4
α, β, γ (Å)	90.00, 90.00, 120.00
Resolution	61.92 – 2.27 (2.32 – 2.27)
Unique Reflections	38395 (2803)
I/σI	10.9 (1.6)
Completeness (%)	99.6 (99.9)
Redundancy	13.5 (13.8)
R_{sym}	17.6 (173.1)
Refinement	
Resolution (Å)	61.92 – 2.27 (2.32 – 2.27)
No. reflections	
Used for refinement	36422
Used for Rfree calculation	1972
R_{factor} (%)	23.6 (32.7)
R_{free} (%)	28.1 (36.7)
No. atoms	
Protein	4050
Water molecules	166
Sulfates	5
B-factors (Å2, average)	
Protein	40.51
Water molecules	36.28
r.m.s. deviations	
Bond lengths (Å)	0.0097
Bond angles (°)	1.4812
Ramachandran Favored (%)	95.67
Ramachandran Allowed (%)	5.16
Ramachandran Outliers (%)	0.94

*Values in parentheses are for the highest resolution shell.