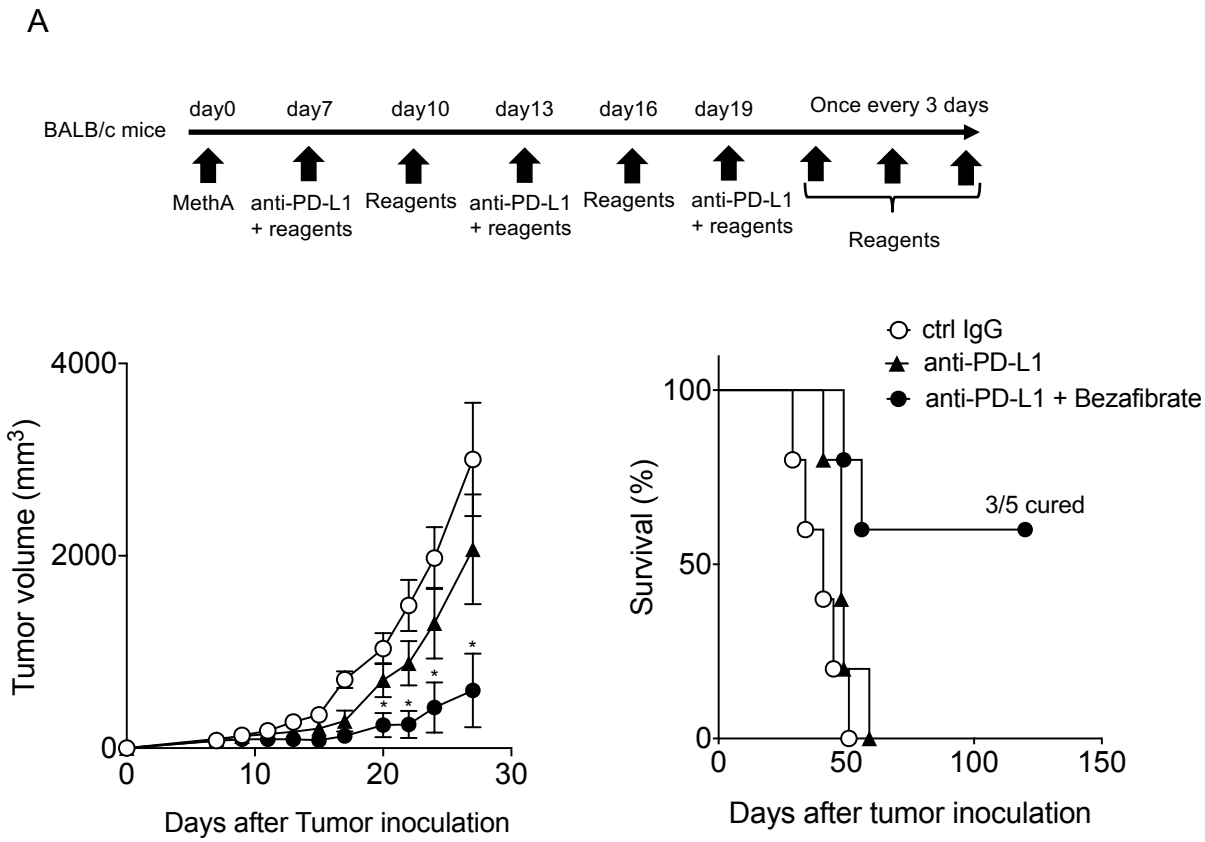
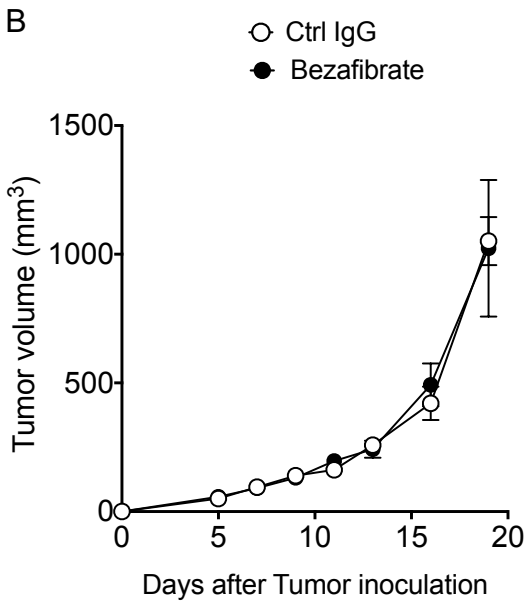
Supplementary Table S1. Primers for different transcripts.

Transcript target	Forward primer (5' to 3')	Reverse primer (5' to 3')
TFAM	CACCCAGATGCAAAACTTTCAG	CTGCTCTTTATACTTGCTCACAG
Uqcrc1	ATCAAGGCACTGTCCAAGG	TCATTTTCCTGCATCTCCCG
NDUSF8	GTTCATAGGGTCAGAGGTCAAG	TCCATTAAGATGTCCTGTGCG
ATP5a1	CATTGGTGATGGTATTGCGC	TCCCAAACACGACAACTCC
Cpt1b	CCTCCGAAAAGCACCAAAAC	GCTCCAGGGTTCAGAAAGTAC
LCAD	GGTGGAAAACGGAATGAAAGG	GGCAATCGGACATCTTCAAAG
MCAD	TGTTAATCGGTGAAGGAGCAG	CTATCCAGGGCATACTTCGTG
Cpt1a	CCATCCTGTCCTGACAAGGTTTAG	CCTCACTTCTGTTACAGCTAGCAC
Birc3	ACGCAGCAATCGTGCATTTTG	CCTATAACGAGGTCACTGACG
CREB1	GGAATCTGGAGCAGACAACC	ATAACGCCATGGACCTGGAC
Bcl2	GGACTTGAAGTGCCATTG GT	AGCCCCTCTGTGACAGCTTA
API5	TCCAGGGTAAAACGGGTGAG	CAACGACTTTAATCTTGTTCTCTTCTGT

PGC-1α : QuantiTect Primer Assay, Mm_Ppargc1a_1_SG (QT00156303), Qiagen

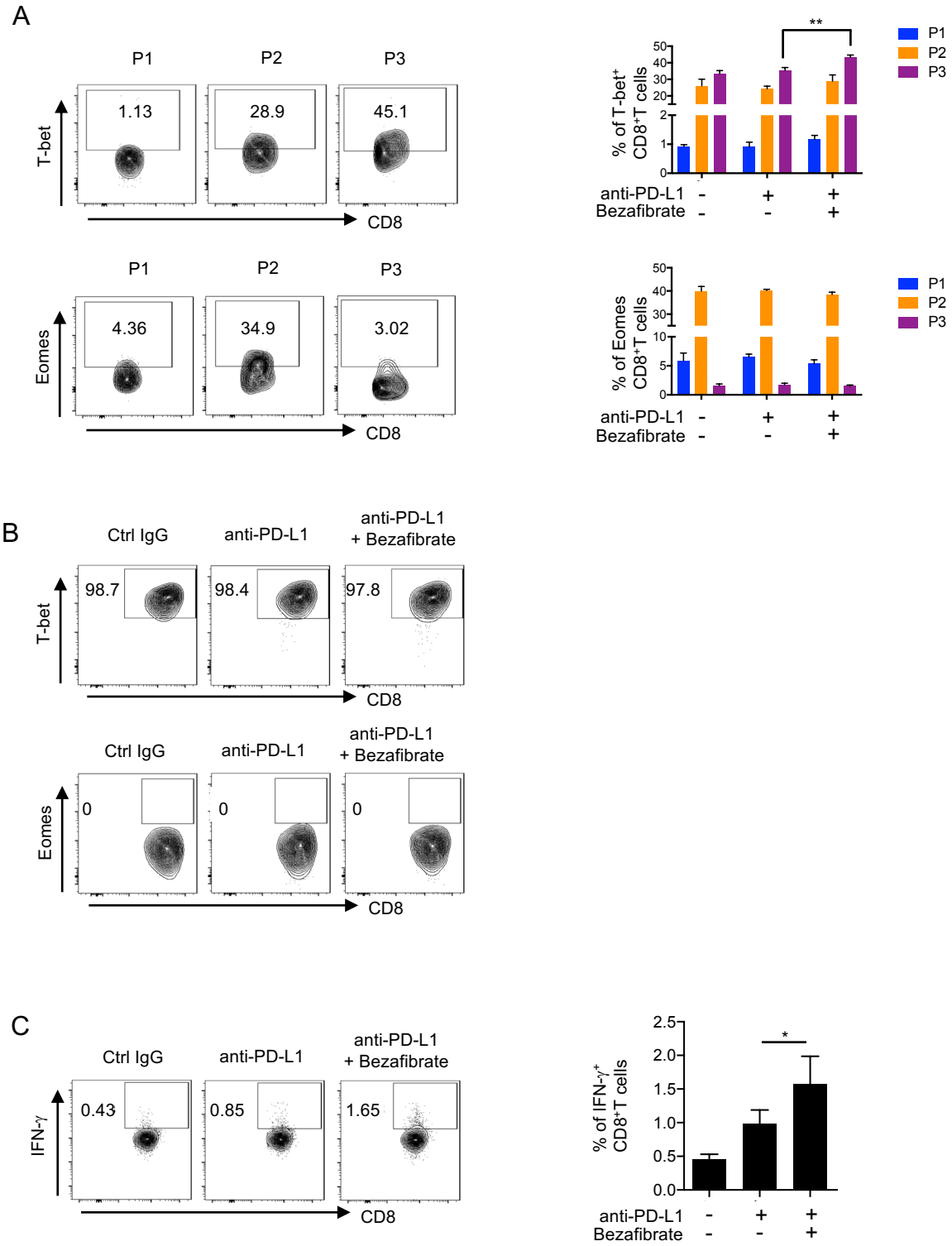
Supplementary Fig. S1.





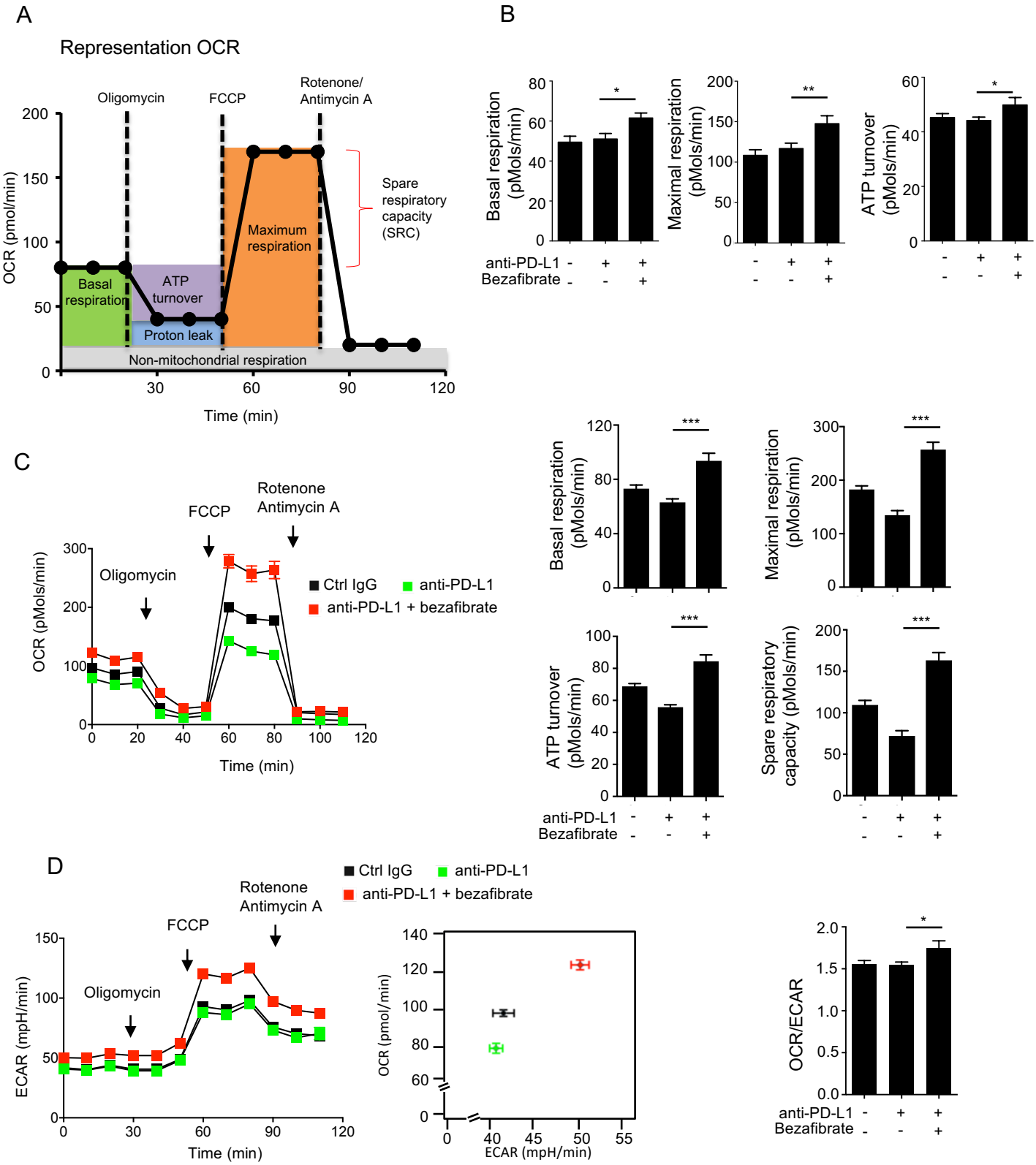
Supplementary Fig. S1. Synergistic effect of bezafibrate with PD-1 blockade *in vivo*: (**A**) Schematic diagram of the combination therapy schedule (upper). Following this schedule, MethA-bearing BALB/c mice were treated with anti-PD-L1 mAb along with bezafibrate. Tumor sizes and/or survival rates are shown (lower). (**B**) MethA-bearing BALB/c mice were treated with bezafibrate alone on the same schedule as in **A**. Tumor sizes are shown. (**A**–**B**) Data represent the means ± SEM of five mice. *$p < 0.05$, one-way ANOVA analysis (anti–PD-L1 mAb vs. anti–PD-L1 mAb + bezafibrate).

Supplementary Fig. S2.



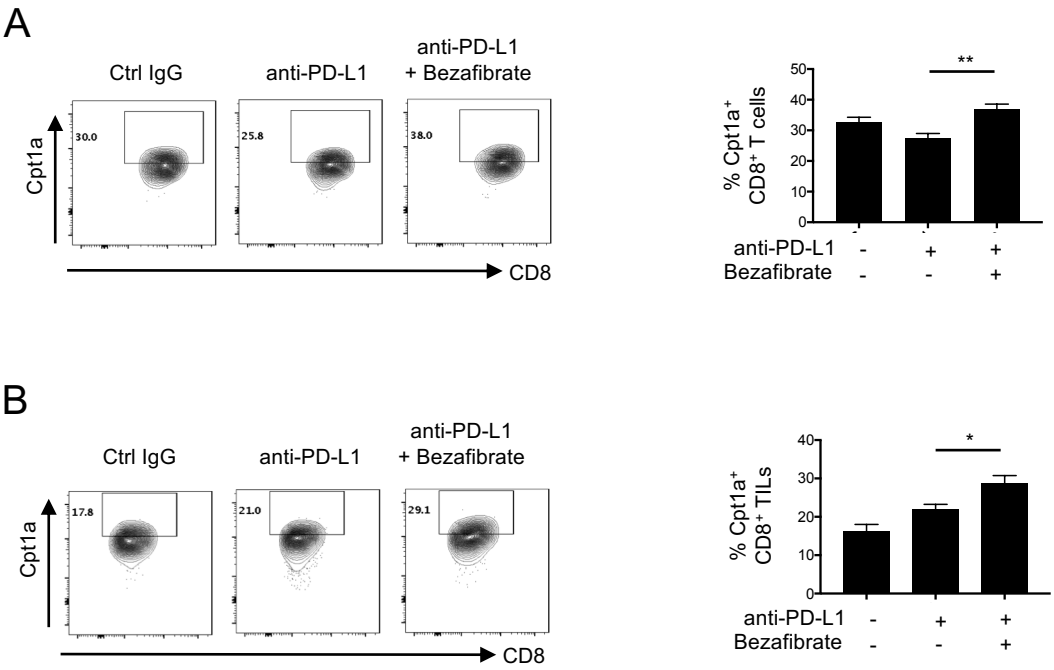
Supplementary Fig. S2. Bezafibrate combination enhances the effector function of CD8⁺ T cells *in vivo*: MC38-bearing mice were treated with anti-PD-L1 mAb and bezafibrate on the same schedule as shown in Supplemental figure S1A. Mice were sacrificed and CD8⁺ T cells in DLN and tumor sites were analyzed on the indicated day. (**A**) DLN cells on day 15 were stained with anti-CD8, CD62L, CD44, T-bet and Eomes mAb. Representative FACS profiles of P1–P3 stained with the T-bet and Eomes in the mice treated with anti-PD-L1 mAb and bezafibrate are shown (left). Frequency of P1–P3 stained with T-bet and Eomes were compared between treated groups (lright). Colors correspond to those of the P1–P3 populations. (**B**) Cells isolated from the tumor mass on day 11 were stained with anti-CD8, and CD45.1, T-bet and Eomes mAb. Representative FACS profiles of CD8⁺ TILs stained with the T-bet and Eomes in the treated groups are shown. (**C**) DLN cells in day 15 were stimulated with anti-(CD3+CD28) antibodies, and IFN-γ was intracellularly stained in CD8+ T cells from treated mice. Representative FACS data of CD8⁺ T cells gated (left), frequency (right) of IFN-γ+ T cells among CD8⁺ T cells are shown. (**A**, **C**) Data represent the means ± SEM of four to five mice.

Supplementary Fig. S3.



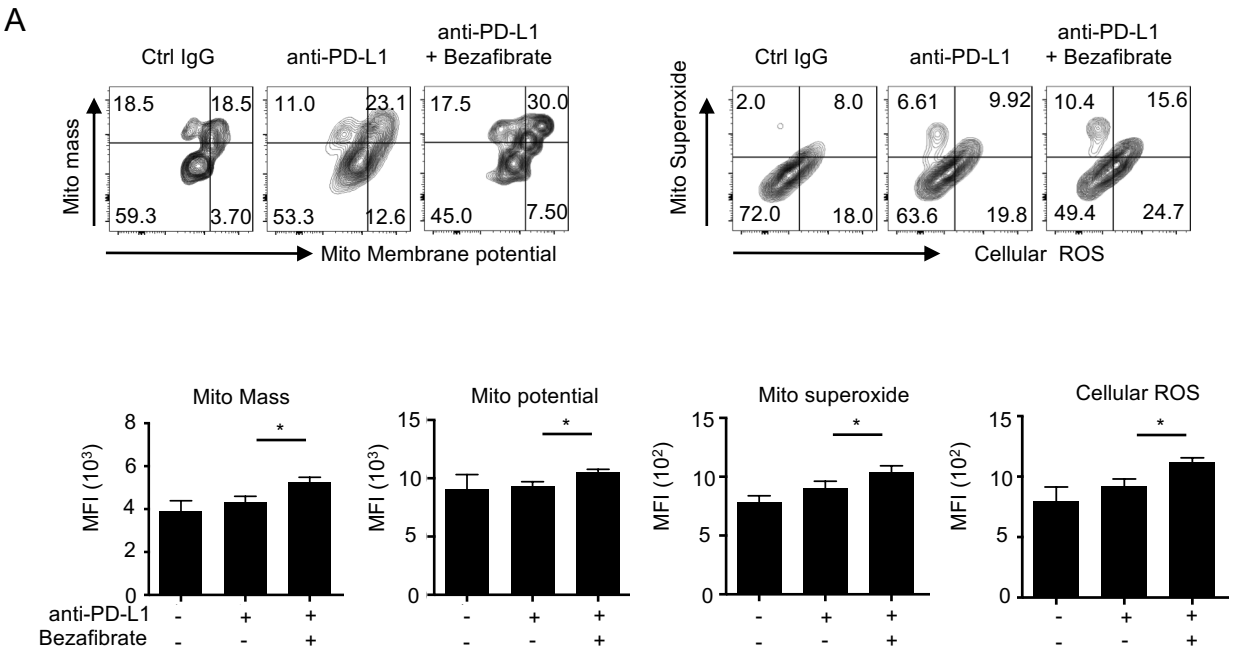
Supplementary Fig. S3. Bezafibrate combination boosts energy metabolism in CTLs *in vivo*: (**A**) For simplicity, a representative OCR plot is drawn, where basal respiration, ATP turnover, maximum respiration, spare respiratory capacity, proton leak, and non-mitochondrial respiration are shown (Seahorse Bioscience). (**B**) MC38-bearing mice were treated with anti-PD-L1 mAb and bezafibrate on the same schedule as shown in Supplementary figure 1A. On day 9, the mice were sacrificed and $CD8^+$ T cells in DLN were analyzed. OCR was measured using DLN $CD8^+$ T cells isolated from treated mice. Cells were mixed from five mice. Basal respiration, maximal respiration, and ATP turnover were calculated. (**C**) According to the therapy schedule shown in Supplementary figure S1A, MC38-bearing mice were sacrificed on day 13. OCR was measured using DLN $CD8^+$ T cells isolated from treated mice. Cells were mixed from five mice. Basal respiration, maximal respiration, ATP turnover, and SRC were calculated. (**D**) In the same experiment as shown in (**C**), ECAR of DLN $CD8^+$ T cells were measured (left). Basal OCR and ECAR values are plotted (middle). OCR/ECAR ratio was measured (right). (**B**–**D**) Data represent the means ± SEM of 6 wells. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, one-way ANOVA analysis. Data are representative of two independent experiments.

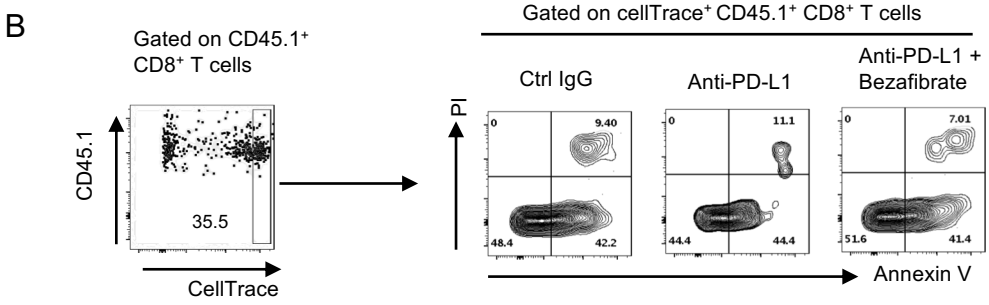
Supplementary Fig. S4.



Supplementary Fig. S4. Bezafibrate upregulates Cpt1a expression CD8⁺ T cells *in vivo* : MC38-bearing mice were treated with anti-PD-L1 mAb and bezafibrate on the same schedule as shown in Supplemental figure S1A. Mice were sacrificed and CD8⁺ T cells in DLN and tumor sites were analyzed on the indicated day. (**A**) DLN cells on day 15 were stained with anti-CD8, CD62L, CD44 and Cpt1a mAbs. Representative FACS patterns of P3 stained with Cpt1a are shown (left). The frequency of Cpt1a⁺ CD8⁺ T cells were calculated in P3 population from treated mice (right). (**B**) Cells isolated from the tumor mass on day 15 were stained with anti-CD8, CD45.2 and Cpt1a mAb. Representative FACS data of CD8⁺ TIL (left) and the frequency (right) of Cpt1a⁺ T cells among CD8⁺ T cells are shown. (**A, B**) Data represent the means ± SEM of five mice. *$p < 0.05$, **$p < 0.01$, one-way ANOVA analysis.

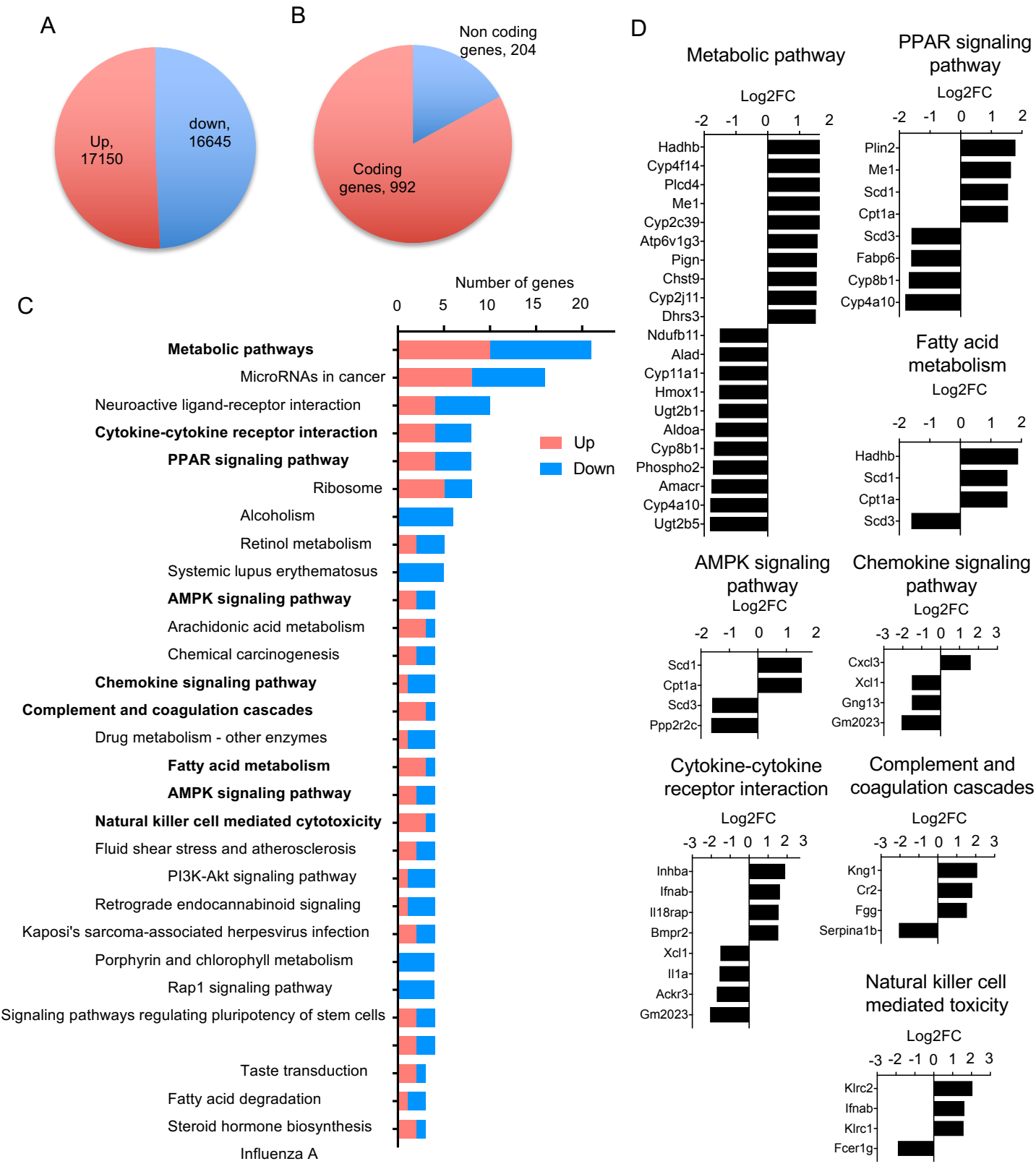
Supplementary Fig. S5.





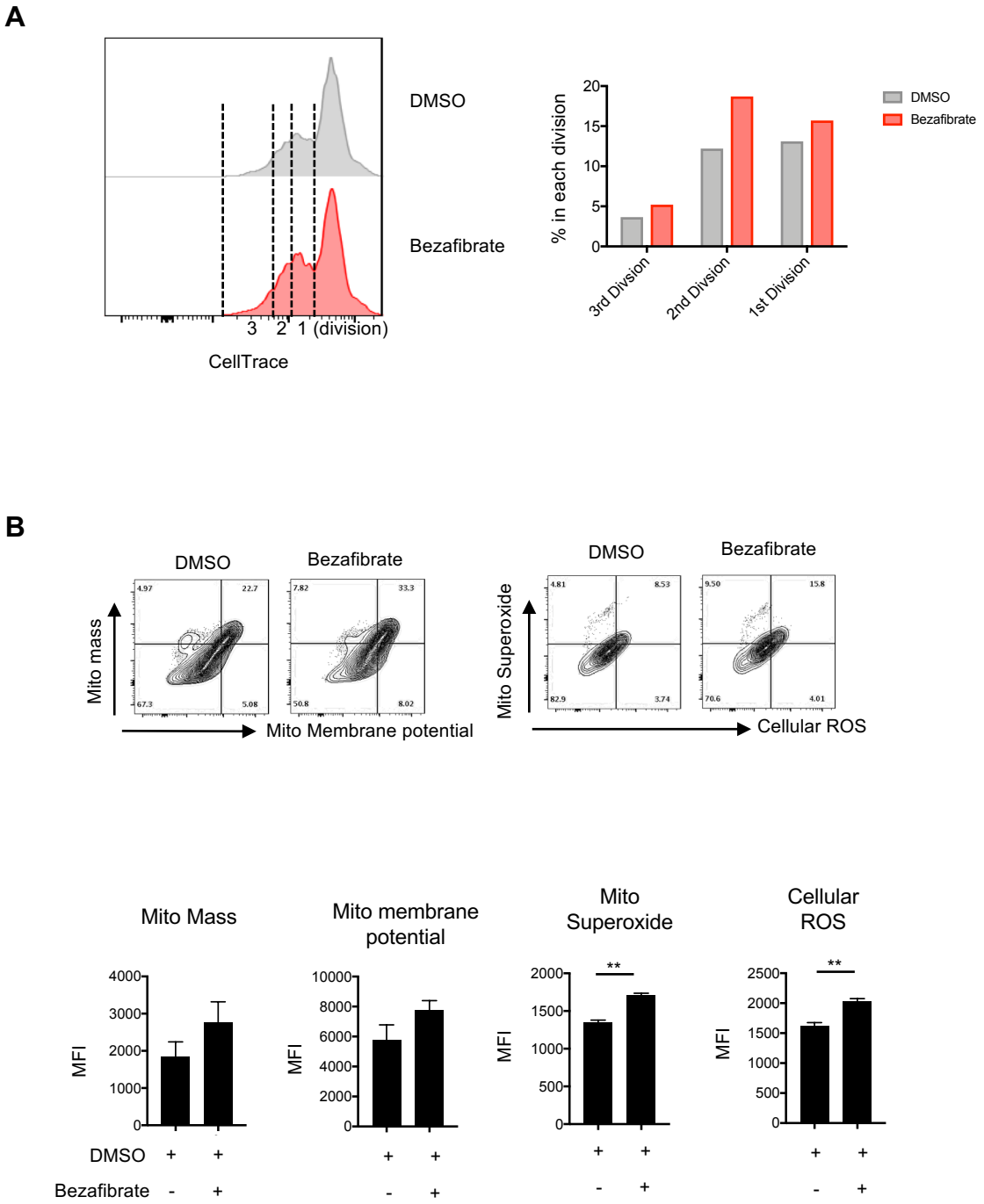
Supplementary Fig. S5. Mitochondrial activity and number of tumor-infiltrated TR CTLs increase by bezafibrate combination: (**A**) DLN cells used in Figure 4A were stained with anti-CD8, CD45.1 mAb, and mitochondrial dyes. Representative FACS profile of each mitochondrial dye staining in each group after gating at $CD8^+$ $CD45.1^+$ T cells was shown (upper). MFI of $CD8^+$ $CD45.1^+$ T cells with each dye staining were compared between treated groups (lower). (**B**) DLN cells used in Figure 4A were stained with Annexin V and propidium iodide (PI). Representative FACS profiles of Annexin V and PI staining after gating on $CellTrace^+$ $CD45.1^+$ $CD8^+$ T cells are shown. (**A**) The data represent the means ± SEM of four or five mice. *$p < 0.05$, one-way ANOVA analysis.

Supplementary Fig. S6.



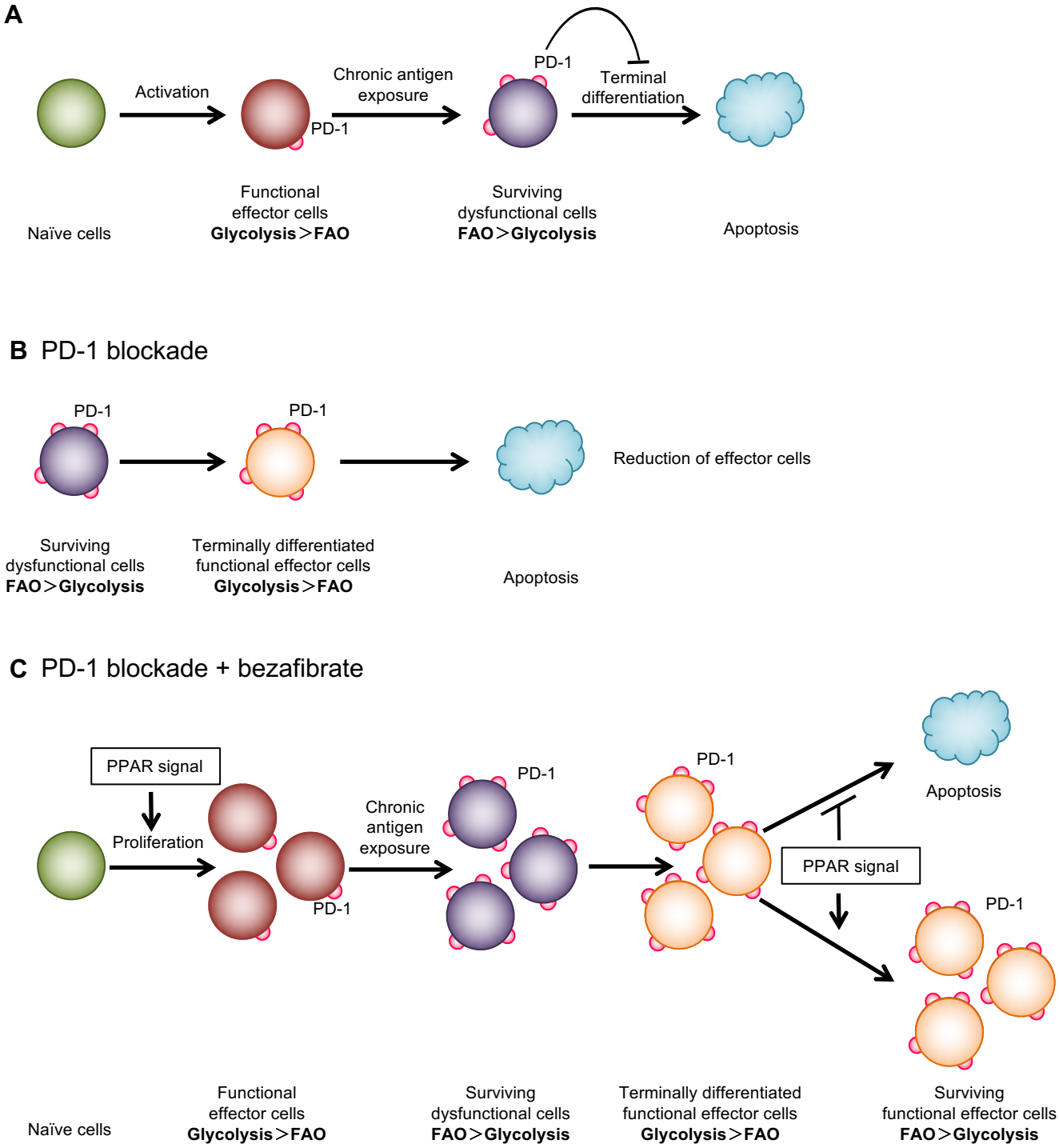
Supplementary Fig. S6. Genes regulated by bezafibrate in killer T cells *in vitro*: (**A**–**D**) Following the schedule shown in Figure 5A, total RNA of cultured CD8$^+$ T cells on day 13 was extracted and subjected to microarray assay to compare gene expression levels. (**A**) Distribution of all up- and down-regulated genes. (**B**) Distribution of genes showing a more than 1.5-fold change according to their coding and non-coding nature. (**C**) Bar chart showing the number of genes differentially expressed by bezafibrate treatment, with increased expression in *red* and decreased expression in *blue* based on KEGG pathway analysis. The pathways were sorted by the number of genes with three or more and p value < 0.05. (**D**) Genes with 1.5-fold change among the indicated pathways defined by KEGG.

Supplementary Fig. S7.



Supplementary Fig. S7. Bezafibrate activates mitochondria of naïve CD8⁺ T cells in the priming phase *in vitro* : (**A**) Naïve CD8⁺ T cells were isolated from the spleen of C57BL/6 mice, labeled with CellTrace dye, stimulated with anti-CD3 and CD28 mAb-coated beads with bezafibrate for 2 days as treated in Fig. 6A. T cell proliferation was measured by dye dilution method. Histogram of CellTrace intensity (left) and % of each division (right) were compared between treated groups. (**B**) Naïve CD8⁺ T cells were isolated from the spleen of C57BL/6 mice, stimulated with anti-CD3 and CD28 mAb-coated beads with bezafibrate for 2 days as treated in Fig. 6A. Representative FACS profiles of staining of mitochondrial dyes are shown (upper). MFI of each dye was compared between treated groups (lower). MFI of each dye was compared between treated groups (lower). (**B**) Data represent the means ± SEM of 3 wells. $^{**}p < 0.01$, two-tailed student *t*-test.

Supplementary Fig. S8.



Supplementary Fig. S8. Scheme for bezafibrate-induced antitumor immunity in PD-1 blockade: (**A**) PD-1 signaling prevents the terminal differentiation of effector T cells but promotes dysfunction. (**B**) PD-1 blockade rescues effector function while enhancing terminal differentiation and decreasing the number of effector T cells. (**C**) Bezafibrate activates PPARs, which induces FAO and Bcl2, leading to inhibition of apoptosis and terminal differentiation in T cells. PPARs activation can also lead to mitochondrial activation, which promotes proliferation of effector CTLs. These pathways help to increase the number of effector CTLs.