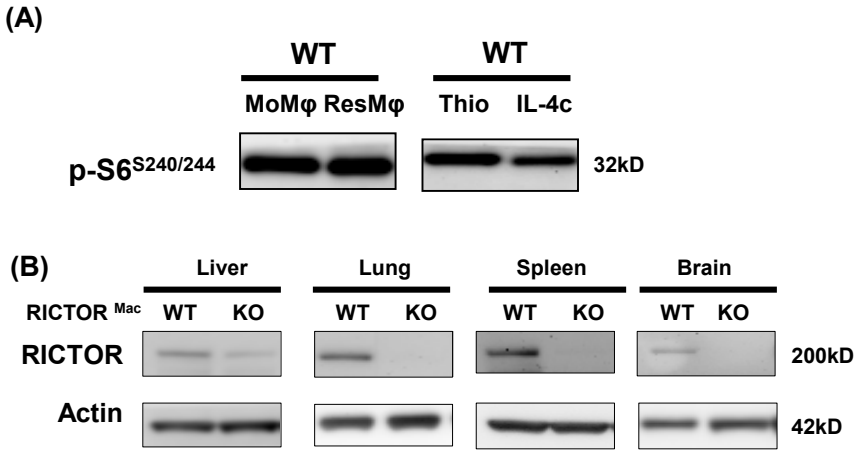
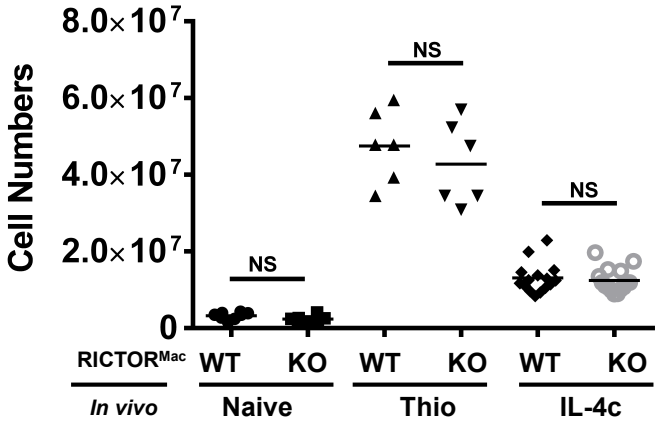
Figure S1



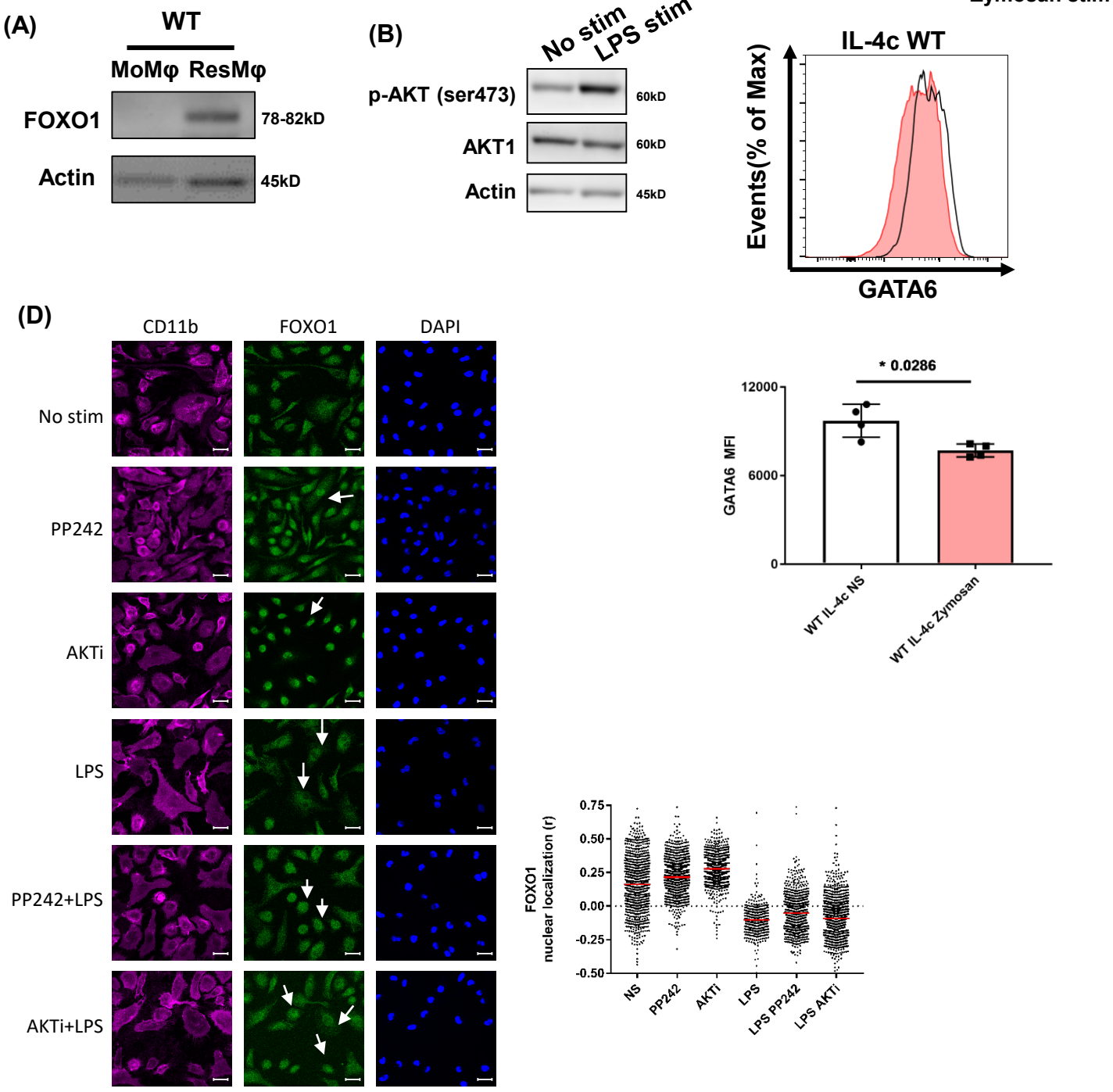
FigS1, related to Figure 1. (A) Tissue-resident peritoneal macrophages have similar mTORC1 activity compared with monocyte-derived peritoneal macrophages. Peritoneal exudates cells from Figure 1A were subjected to immunoblotting to measure mTORC1 activity, as indicated by p-S6. (B) Sorted tissue resident macrophages from liver, lung, spleen, and brain were subjected to immunoblotting to confirm RICTOR deletion.

Figure S2



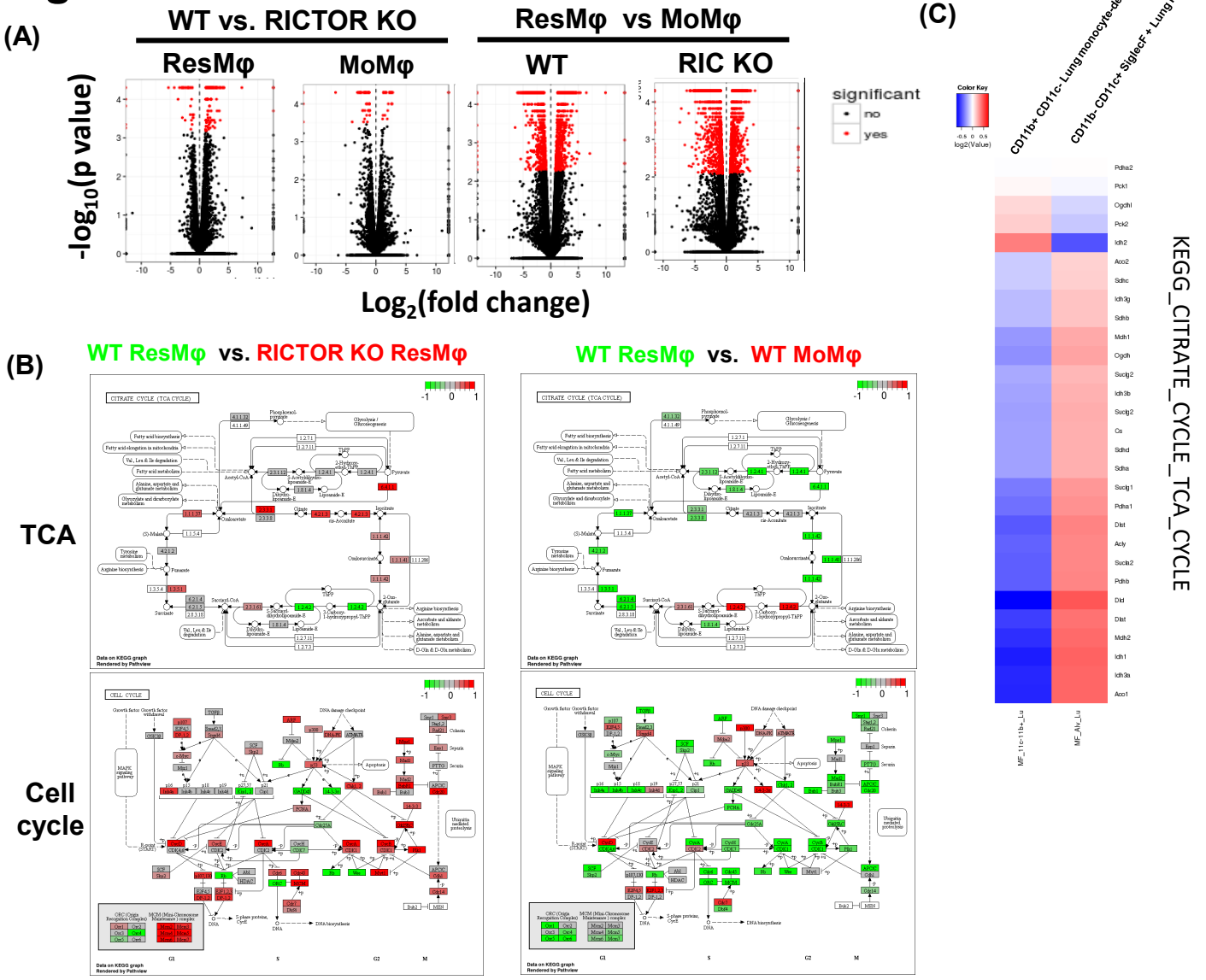
FigS2, related to Figure 2. RICTOR-WT and RICTOR-KO^{Mac} mice have similar numbers of thioglycollate or IL-4c induced macrophages. RICTOR-WT and RICTOR-KO^{Mac} mice were injected with of thioglycollate on day 0 or IL-4c on day 0 and 2. On day 4, total peritoneal exudates cells were counted.

Figure S3



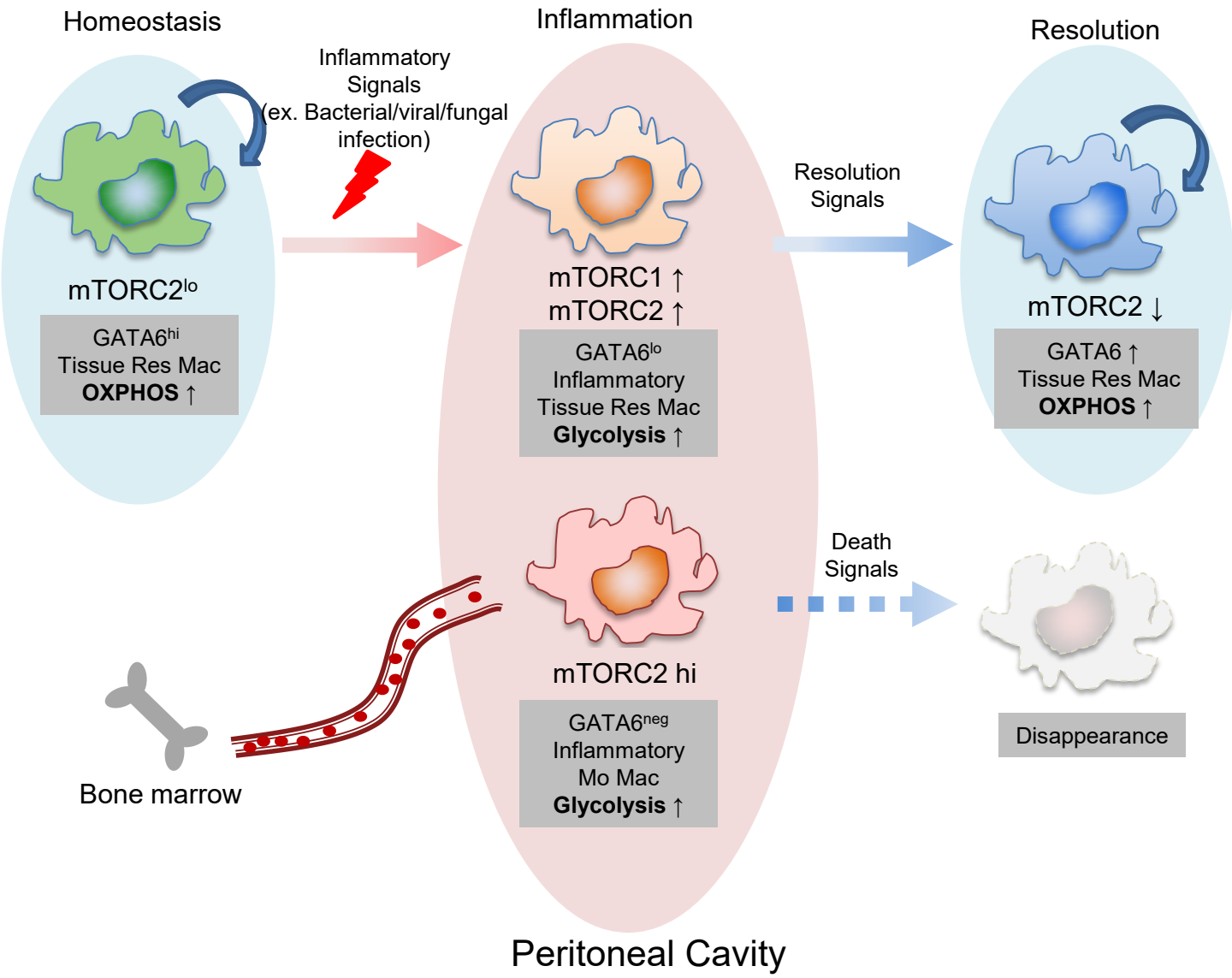
FigS3, related to Figure 6. Inflammation reduced GATA6 expression in tissue-resident macrophages in mTORC2-FOXO1 dependent manner. (A) Foxo1 expression level were measured in sorted $CD11b^{+}F4/80^{lo}$ monocyte-derived macrophages and $CD11b^{+}F4/80^{hi}$ tissue-resident macrophages from naïve mice. Higher FOXO1 expression was observed in tissue resident macrophages. (B) IL-4c elicited macrophages were treated with PP242 (inhibitor of mTOR activity), AKT inhibitor VIII, LPS, PP242+LPS or AKT inhibitor+LPS for 2hrs. PP242 and AKT inhibitor increased FOXO1 nuclear localization even with LPS treatment which reduced FOXO1 nuclear localization. (C) Attached peritoneal macrophages from IL-4c treated mice were stimulated with 100ng/mL LPS, and mTORC2 activity was measured by immunoblot. (D) Attached peritoneal macrophages from IL-4c treated mice were stimulated with 50ug/mL zymosan for 18hrs, and GATA6 expression were assessed by flow cytometry with statistical analysis.

Figure S4



FigS4 related to Figure 7. Tissue resident macrophages display increased oxidative phosphorylation compared to monocytic macrophages. (A) Volcano plot showing changes in gene expression in WT vs RICTOR KO in tissue resident macrophages or monocytic macrophages (Left panel) and Tissue resident macrophages vs. monocytic macrophages in WT or RICTOR KO (Right panel). (B) Gene Set Enrichment Analysis of TCA cycle (Upper) and cell cycle (bottom) related genes in WT vs RICTOR KO tissue resident macrophages (Left) or tissue resident macrophages vs monocytic macrophages in WT (right) (C) TCA cycle related gene sets (KEGG_CITRATE_CYCLE_TCA_CYCLE) to identify transcriptional characteristic of lung monocyte-derived cells (MF_CD11c-CD11b+Lu) vs. resident macrophages (Lung Alveolar mac CD11b- CD11c+ SiglecF +) from The Immunological Genome Project

Figure S5



FigS5 related Figure 1-7 Proposed model: Under homeostatic condition in the peritoneal cavity, tissue-resident macrophages maintain high GATA6, lower mTORC2 activity and increased oxidative phosphorylation compared to monocyte-derived macrophages. In response to inflammatory signals, tissue-resident macrophages undergo emergent increase of mTORC1 and mTORC2 activity and glycolysis, and recruit GATA6^{neg} inflammatory macrophages from blood. After the clearance of stimuli, tissue-resident macrophages restore higher GATA6 by decreasing mTORC2 activity to reestablish homeostasis.