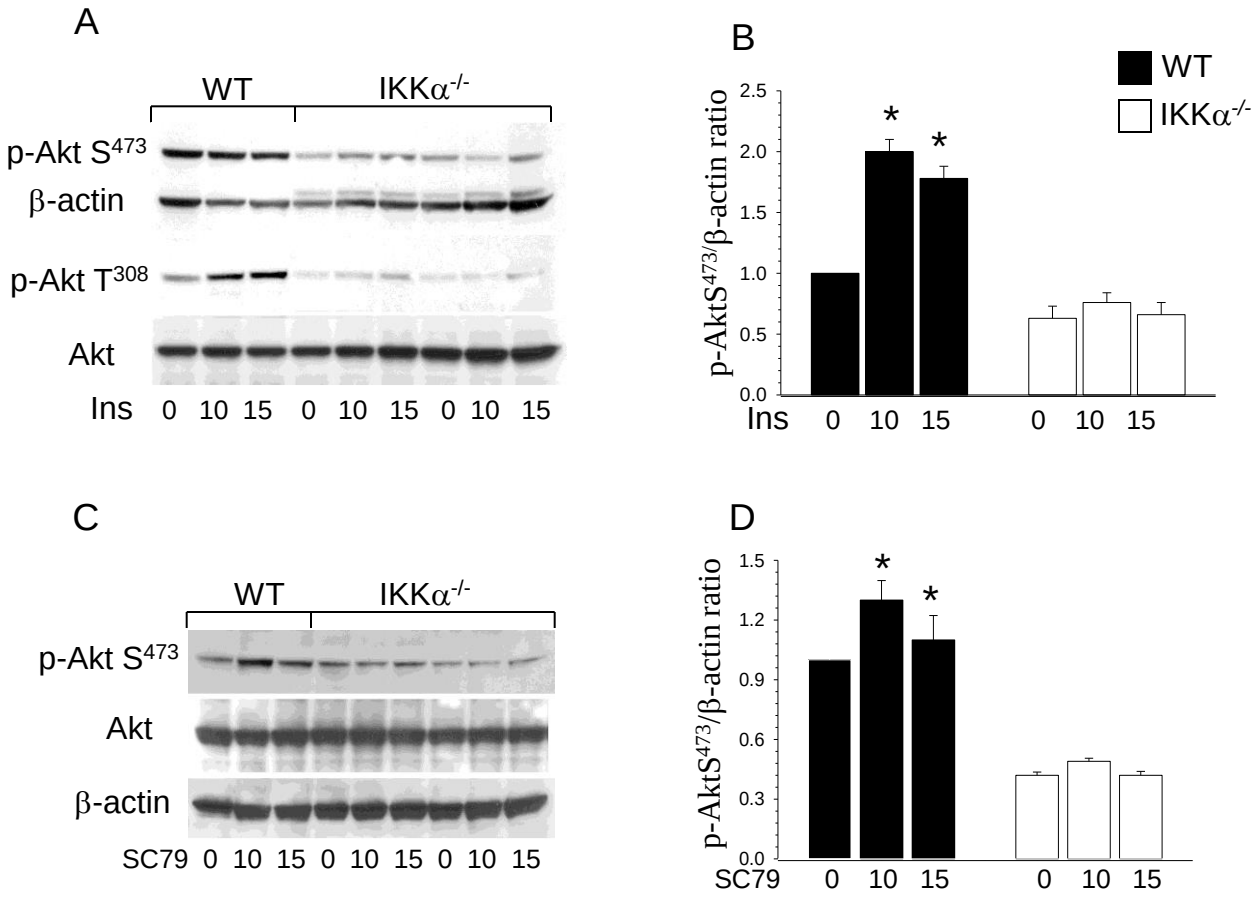
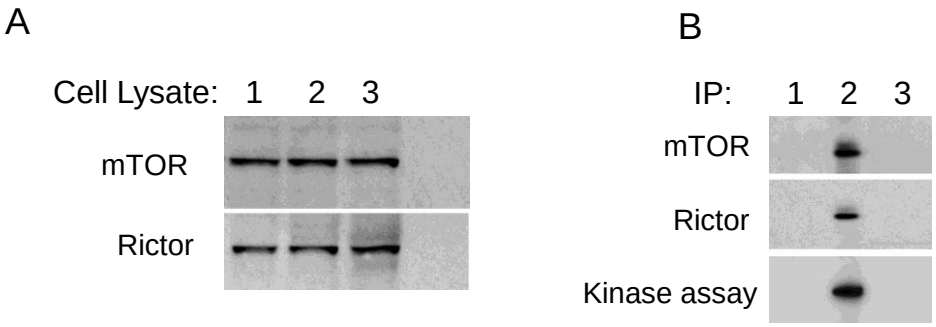
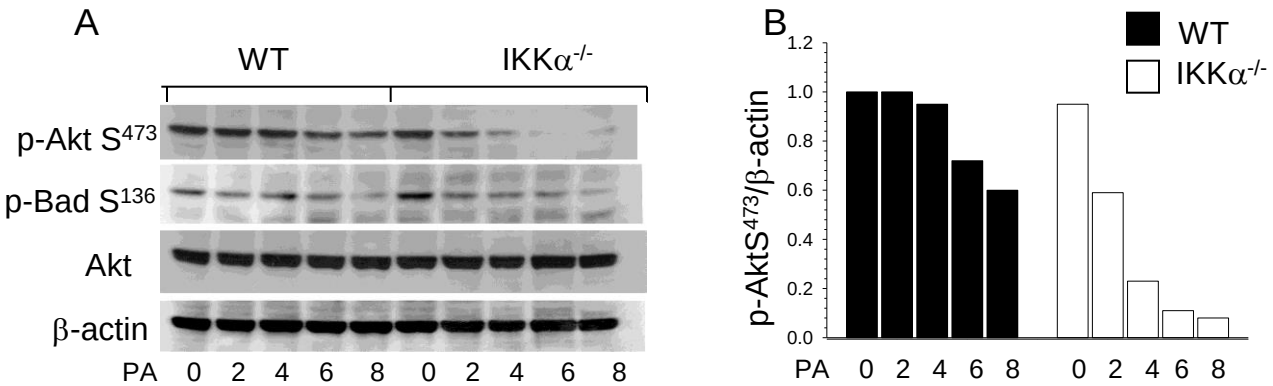


Supplemental Figure I. **Akt S^{473} phosphorylation is suppressed in IKK$\alpha^{-/-}$ macrophages compared to WT cells in response to insulin (A,B) or Akt activator, SC79 (C,D).**

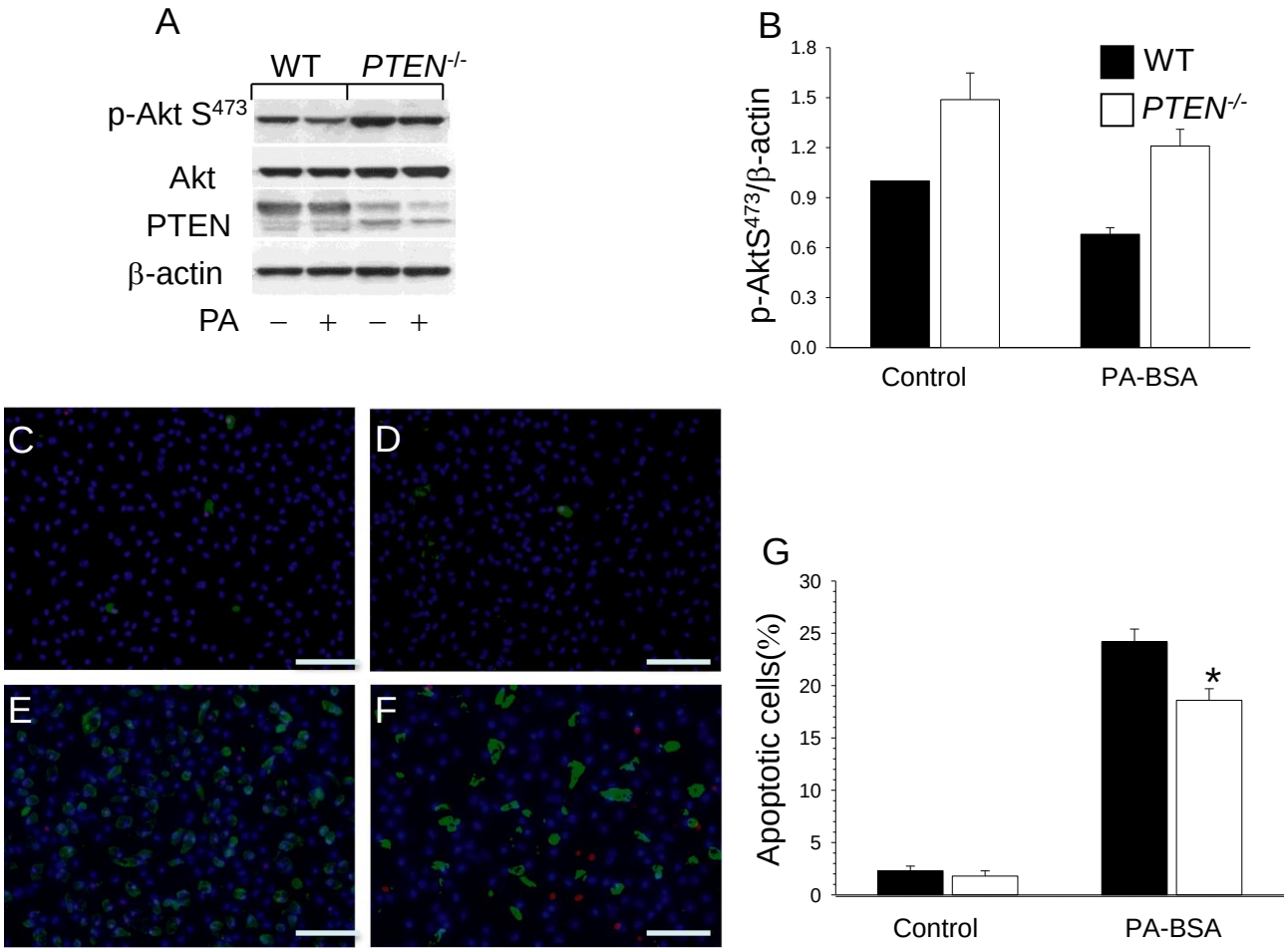
Peritoneal macrophages were incubated in serum free media for 16 hours and then treated with insulin (100 nM ; A,B) or Akt activator, SC79 (4 μg/mL; C,D) for the indicated time. Cell protein extract (60 mg/well) was resolved and analyzed by Western blot using indicated antibodies. Graphs represent data (mean ± SEM) of three (A,B) and two (C,D) experiments (*$p < 0.05$ compared to control untreated group).



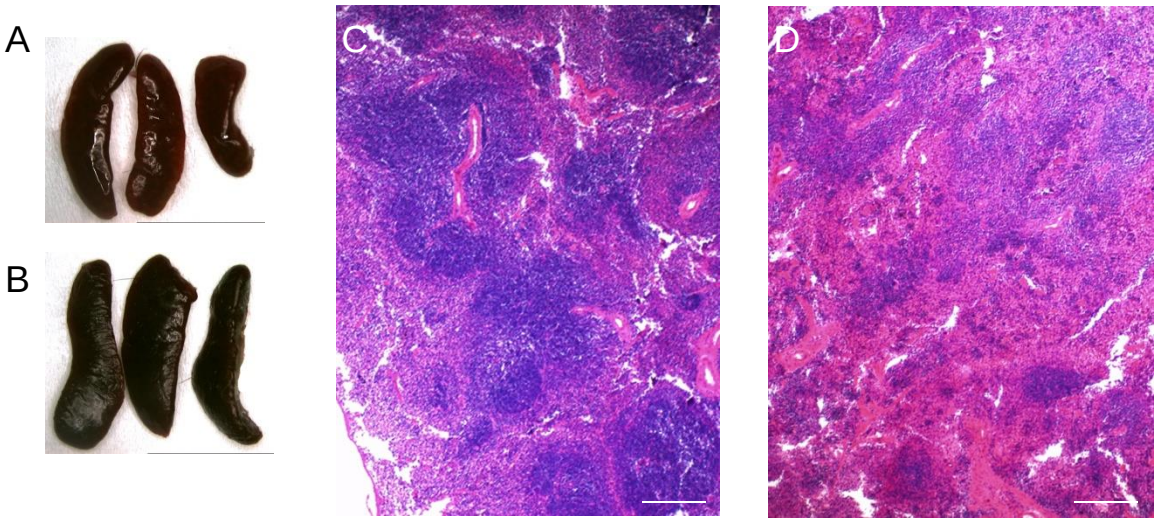
Supplemental Figure II. **Loss of IKKα in macrophages prevents the precipitation of mTOR complex by antibody to IKKalpha**
Cell lysate (A) and precipitates isolated from IKK$\alpha^{-/-}$ peritoneal macrophages were resolved by electrophoresis and incubated with isotype control (1), antibody to Rictor (2), or antibody to IKKα (3); kinase activity detected by antibodies to p-Akt (S^{473}) and in the presence of full-length Akt1 protein as the substrate.



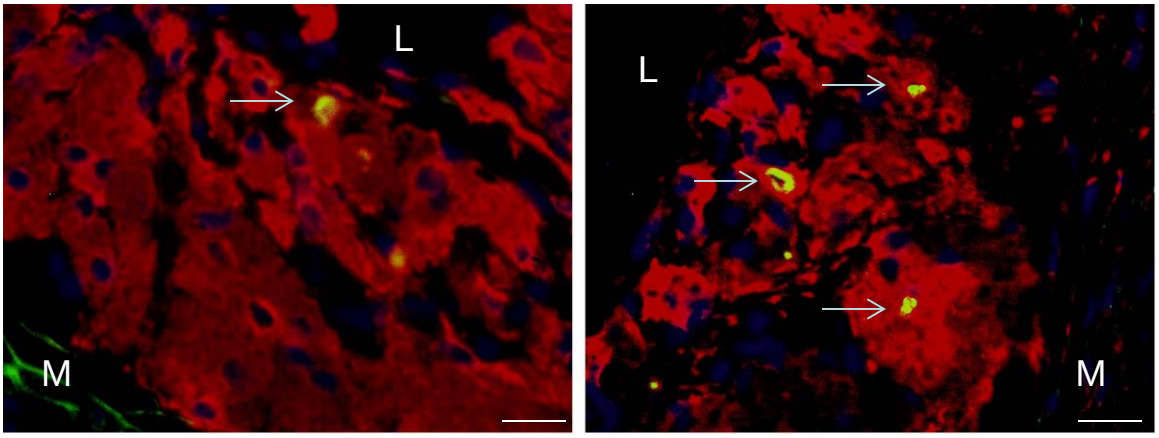
Supplemental Figure III. **IKK$\alpha^{-/-}$ macrophages are more sensitive to lipotoxic treatment with PA-BSA, which induces ER stress resulting in suppression of Akt and Bad signaling more than in WT cells.**
Peritoneal macrophages were treated with 0.5mM PA-BSA for 0 (control), 1, 3, 6 and 8 hours. Cell protein extract (60μg/well) was resolved and analyzed by Western blot using indicated antibodies (A). B. Ratio of p-Akt S^{473}/β-actin in WT and IKK$\alpha^{-/-}$ macrophages.



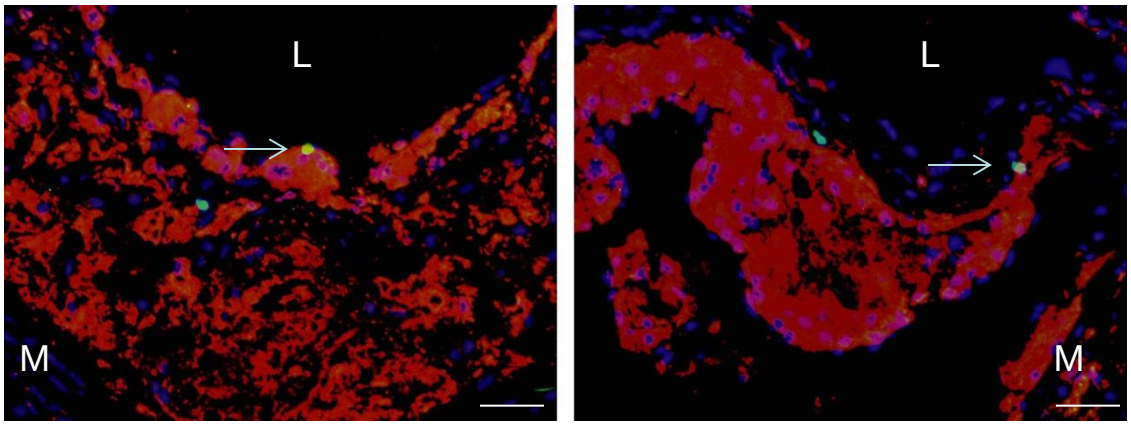
Supplemental Figure IV. **Akt signaling and apoptosis in WT and *PTEN*$^{-/-}$ peritoneal macrophages treated with BSA and PA-BSA.**
WT and *PTEN*$^{-/-}$ peritoneal macrophages were treated with BSA (control) or 0.5M PA-BSA for 3 (A,B) or 24 hours (C-G); WT and *PTEN*$^{-/-}$ macrophage proteins were analyzed by Western blot (A) and the ratio of p-AktS^{473}/β-actin was measured (B) or cells were stained by the Alexa Flour 488 Annexin V/Dead cell apoptosis kit (C-F); Note Annexin V revealed apoptotic cells (green), propidium iodide detected dead cells (red) and DAPI stained nuclei (blue) in WT and *PTEN*$^{-/-}$ macrophages treated with BSA (C,D) and PA-BSA (E,F, respectively); scale bar represents 50μm. G. Percent of apoptotic cells in WT and *PTEN*$^{-/-}$ macrophages (*p <0.05 vs. WT cell by Mann-Whitney Rank Sum Test).



Supplemental Figure V. **Spleen enlargement (B) and altered spleen histology (D) in *LDLR*$^{-/-}$ mice transplanted with IKK$\alpha^{-/-}$ (B,D) marrow compared to control mice with WT marrow (A,C).** Paraffin sections (C,D) stained with hematoxylin-eosin. Scale bar indicates 200 μm.

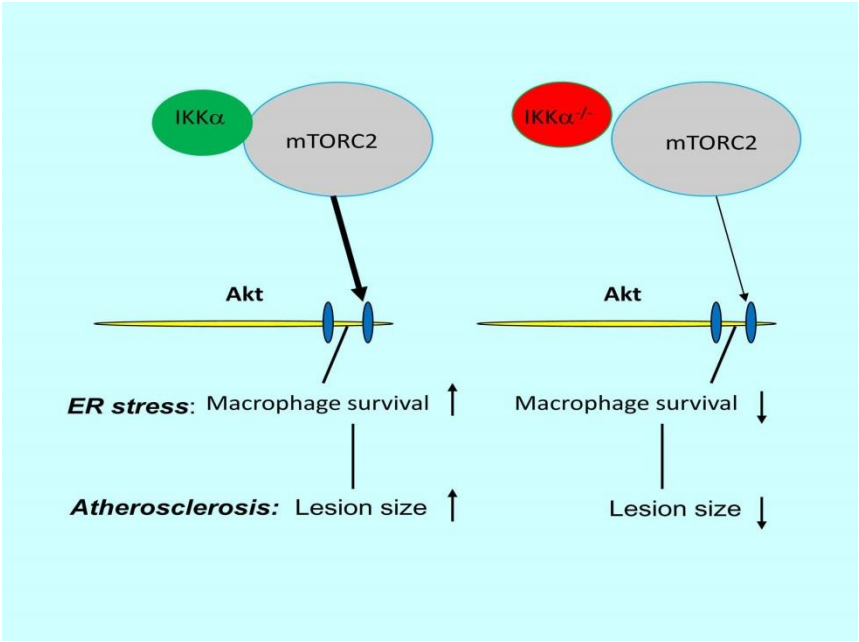


Supplemental Figure VI. A**poptotic cells in atherosclerotic lesions of *LDLR*$^{-/-}$ mice transplanted with WT or IKK$\alpha^{-/-}$ FLC after 8 weeks of the Western diet.**
Double staining of sections from aortic sinus with rat antibody to macrophage, MOMA-2 (red) and rabbit anti-cleaved caspase 3 (green) counterstaining with nuclear stain DAPI (blue) in atherosclerotic lesions of WT→*LDLR*$^{-/-}$ and IKK$\alpha^{-/-}$→*LDLR*$^{-/-}$ mice. Note co-localization of cleaved caspase 3 and MOMA-2 (yellow); Abbreviations: L- lumen, M – media; Scale bar indicates 50 μm.



WT→LDLR$^{-/-}$ IKKα$^{-/-}$→LDLR$^{-/-}$

Supplemental Figure VII. **Detection of Ki-67 marker in atherosclerotic lesions of *LDLR*$^{-/-}$ mice reconstituted with WT or IKKα$^{-/-}$ FLC FLC after 8 weeks of the Western diet.**
Double staining of sections from aortic sinus with rat antibody to macrophages, MOMA-2 (red) and rabbit antibody to proliferative marker, Ki-67 (green), counterstaining with nuclear stain DAPI (blue) in atherosclerotic lesions of WT→*LDLR*$^{-/-}$ and IKKa$^{-/-}$→*LDLR*$^{-/-}$ mice. Note co-localization of Ki-67 and MOMA-2 (yellow); Abbreviations: L- lumen, M – media; Scale bar indicates 50 μm.



Supplemental Figure VIII. **A schematic presentation of the role of IKKα in mTORC2-mediated Akt signaling in mouse macrophage survival and atherosclerosis**

Supplemental Table I. **Body weight, total serum cholesterol and triglyceride levels in female and male *LDLR*$^{-/-}$ mice reconstituted with wild type or IKK$\alpha^{-/-}$ fetal liver cells**

Type of FLC reconstituted	Body weight (grams)	Cholesterol mg/dL	Triglycerides mg/dL
Females			
WT→*LDLR*$^{-/-}$ (n=11)	25.2 ± 0.5	769 ± 22	258 ± 31
IKK$\alpha^{-/-}$→*LDLR*$^{-/-}$ (n=10)	24.9 ± 0.4 *p=0.67*	779 ± 64 *p=0.59*	248 ± 32 *p=0.80*
Males			
WT→*LDLR*$^{-/-}$ (n=9)	23.6 ± 0.5	701 ± 34	176 ± 16
IKK$\alpha^{-/-}$→*LDLR*$^{-/-}$ (n=7)	24.7 ± 0.5 *p=0.46*	637 ± 41 *p=0.26*	167 ± 16 *p=0.32*

Values are in mg/dl (mean ± SEM). The number of recipient mice in each group is indicated by *n*. The differences are not statistically significant between the groups.