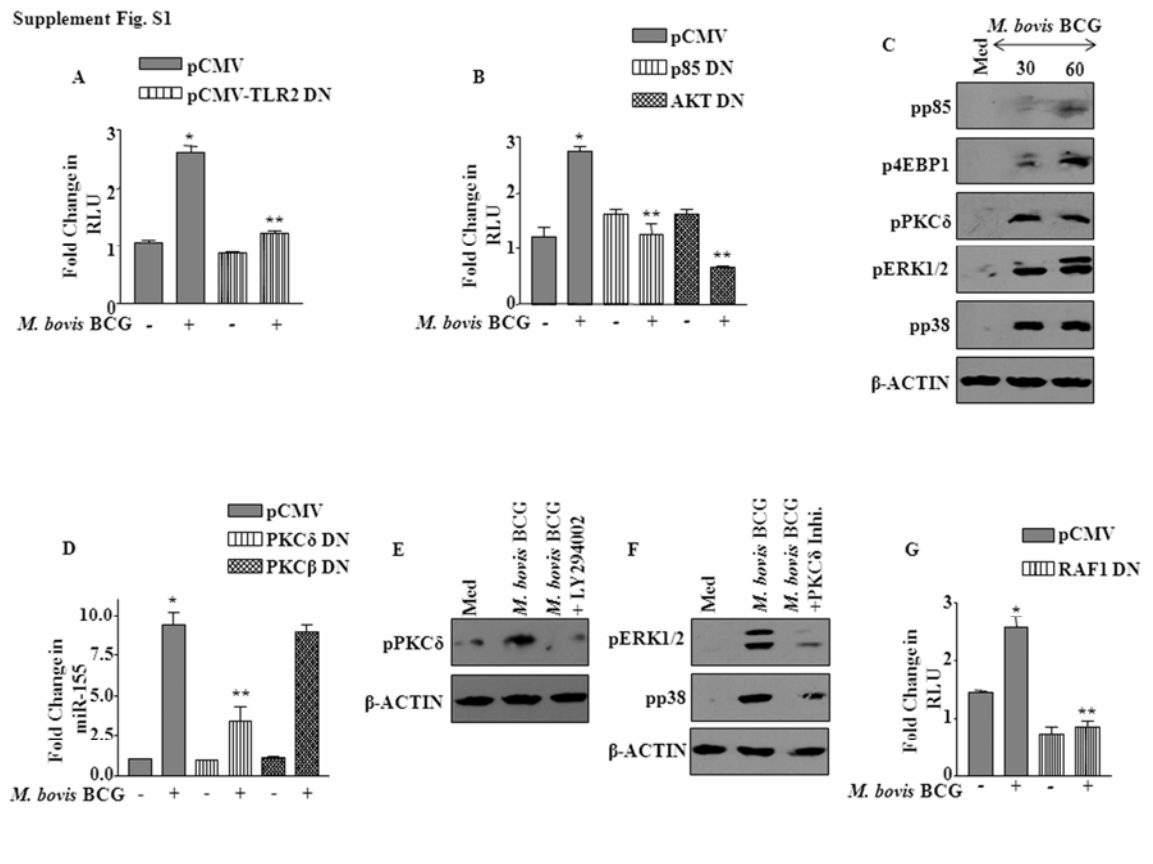
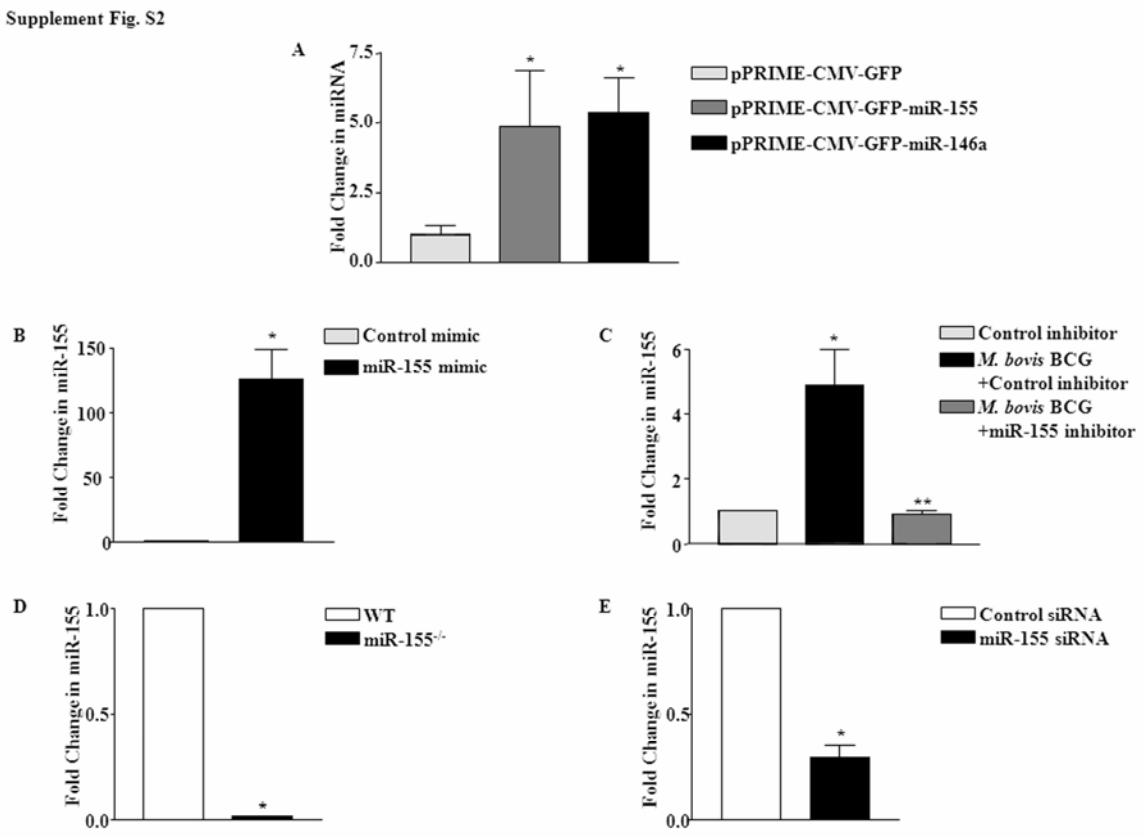


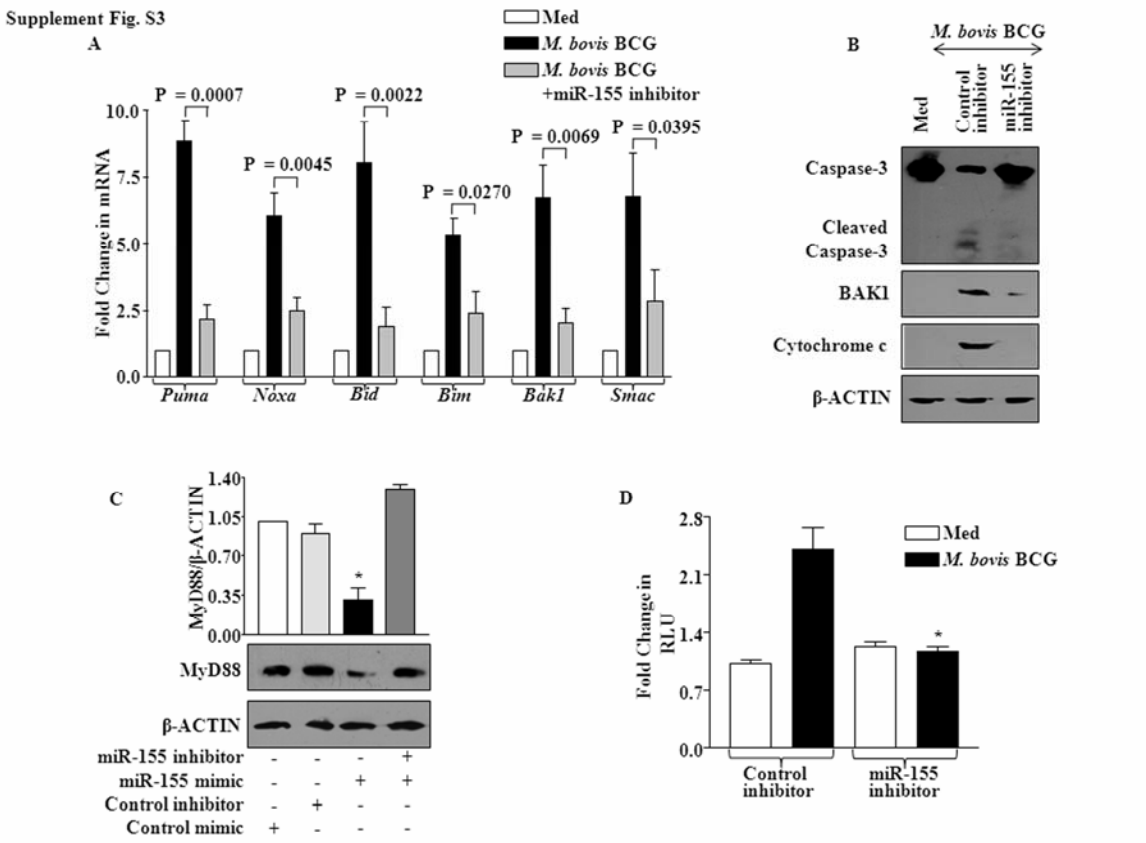
Supplemental Figure S1. *M. bovis* BCG triggers activation of TLR2/PI3K/PKCδ/MAPK signaling axis. (A) RAW 264.7 macrophages were transfected with TLR2 DN or vector control and *M. bovis* BCG induced up-regulation of miR-155 was monitored using real time quantitative RT-PCR. Data are mean ± SE, n = 3. (B) Dominant negative mutants of p85 and AKT kinases were over-expressed in macrophages and change in miR-155 promoter luciferase activity was monitored after *M. bovis* BCG infection. Control macrophages were transfected with pCMV vector alone. (mean ± SE, n = 3). (C) The kinetics of PI3K/PKCδ/MAPK signaling dynamics upon *M. bovis* BCG infection of macrophages is shown. Western blots are representative of 3 separate experiments. (D) Upon transfection of macrophages with dominant negative mutants of PKCδ and PKCβ kinases, cells were infected with *M. bovis* BCG and change in expression levels

of miR-155 was assayed using real time quantitative RT-PCR. (mean ± SE, n = 3). (E) Pretreatment of macrophages with LY294002 (PI3K inhibitor) significantly reduced *M. bovis* BCG induced activation of PKCδ. (F) Abrogation of PKCδ activity by PKCδ inhibitor, suppressed *M. bovis* BCG triggered activation of ERK1/2 and p38 MAPKs. Blots represent 2 independent experiments. (G) RAF1 dominant negative mutant was over-expressed in macrophages. Upon infection with *M. bovis* BCG, miR-155 promoter luciferase activity was assayed. Data represents a mean of 3 independent experiments. RLU, Relative luciferase units; Med, Medium; *, $P < 0.05$ versus control, **, $P < 0.05$ versus *M. bovis* BCG infected macrophages.



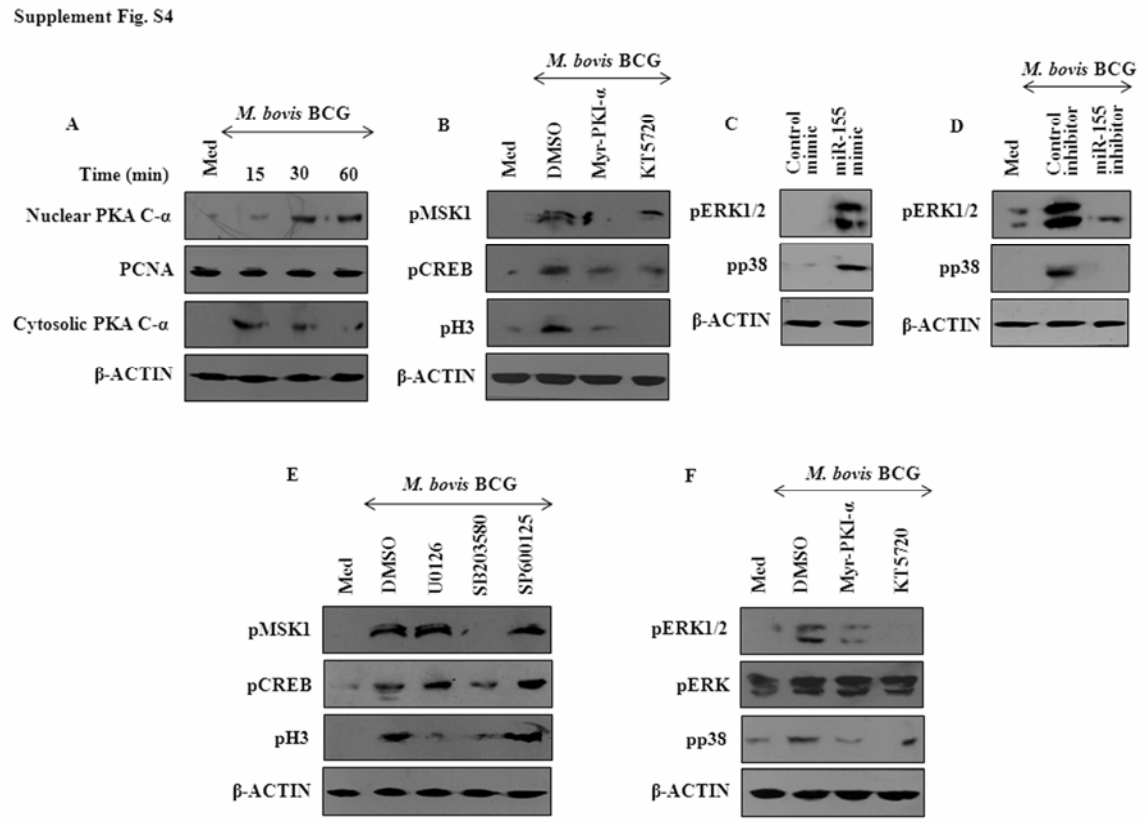
Supplemental Figure S2. Validation of miR-155 over-expression/silencing. (A and B) Macrophages were transfected with miR-155 over-expressing plasmid (pPRIM-CMV-GFP-miR-155) or miR-146a over-expressing plasmid (pPRIM-CMV-GFP-miR-146a) or control vector (A) or miR-155 mimic and corresponding control mimic (B). The over-expression levels of miR-155 and miR-146a were assayed by real time quantitative RT-PCR analysis (mean ± SE, n = 3). (C) Macrophages were transfected with control inhibitor or anti-miR-155 (miR-155 inhibitor) prior to *M. bovis* BCG infection. Expression of miR-155 was assayed by real time quantitative RT-PCR. Data represent mean ± SE of 3 different set of experiments. (D) Expression levels of miR-155 in WT and miR-155$^{-/-}$ BMDM was assayed by real time quantitative RT-PCR. (mean ± SE, n = 5). (E) Silencing of miR-155 in miR-155 siRNA transfected macrophages was validated by

real time quantitative RT-PCR. The expression levels were compared with control siRNA transfected cells. (mean ± SE, n = 3). Med, Medium; *, $P < 0.05$ versus control; **, $P < 0.05$ versus *M. bovis* BCG stimulation.



Supplemental Figure S3. miR-155 is a inducer of apoptosis. (A) A set of macrophages were transfected with control inhibitor oligonucleotides or with miR-155 inhibitor oligonucleotide. Upon infection of macrophages with *M. bovis* BCG, change in the expression levels of pro-apoptotic genes were monitored using real time quantitative RT-PCR analysis (mean ± SE, n = 3). (B) Macrophages were treated as explained in panel A and activation of apoptosis was assayed using western blot analysis. Blots are representative of 3 independent experiments. (C) The inhibitory role of miR-155 inhibitor oligonucleotides was validated by co-transfection of miR-155 mimics and miR-155 inhibitor oligonucleotides. Total cell protein was harvested and expression levels of MyD88, a well characterized target of miR-155 were assayed using western blot analysis. Representative blots along with quantification of 3 independent experiments are

47 shown. *, P < 0.05 versus control. (D) Macrophages were co-transfected with miR-155 promoter
48 luciferase constructs and miR-155 inhibitor oligonucleotides or contol inhibitor. Upon infection
49 with *M. bovis* BCG, miR-155 promoter luciferase activity was assayed. (mean ± SE, n = 4). *, P
50 < 0.05 versus *M. bovis* BCG infected macrophages.



Supplemental Figure S4. miR-155 plays a vital role in regulating *M. bovis* BCG activated PKA pathway. (A) *M. bovis* BCG infection activates the PKA signaling as monitored by nuclear translocation of PKA catalytic subunit (PKA C-α) into the nucleus. (B) Abrogation of PKA activity by pharmacological reagents regulates MSK1, CREB and H3 phosphorylation. (C and D) Over-expression of miR-155 or silencing of miR-155 by transfecting macrophages with miR-155 mimic (C) and miR-155 inhibitor (D) respectively modulates ERK1/2 and p38 activation. Blots show phosphorylation of ERK1/2 and p38 protein levels. (E) Pretreatment of macrophages with a series of MAPK specific inhibitor prior to *M. bovis* BCG infection abrogates MSK1, CREB and H3 activation. (F) PKA activity modulates ERK1/2 and p38 activation as treatment of PKA inhibitors abrogates ERK1/2 and p38 phosphorylation. Western blots are representative of

3 independent experiments. DMSO serves a vehicle control and β-ACTIN as loading control. Med, Medium.