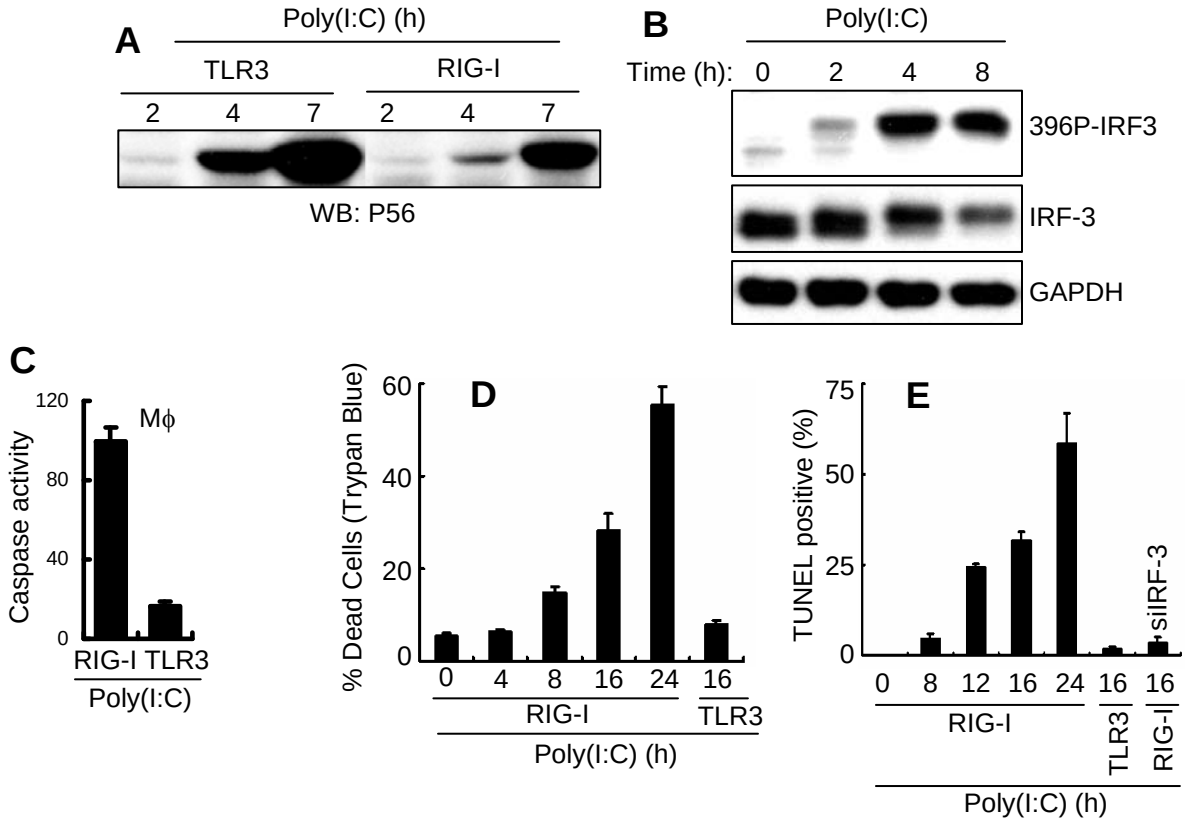

Figure S1. Both TLR3 and RIG-I signaling activate IRF-3 for gene induction pathway, but only RIG-I activation triggers apoptosis pathway. (A) HT1080 cells were treated (TLR3) or transfected (RIG-I) with poly(I:C); cell extracts were analyzed for induction of P56, a dsRNA inducible protein, by Western Blot at the indicated time after poly(I:C) treatment; **(B)** HT1080 cells were transfected with poly(I:C) for the indicated time, when the cell extracts were analyzed for phosphorylation of IRF-3 on Ser396 residue, by Western Blot; **(C)** Primary peritoneal macrophages isolated from Wt C57Bl/6 mice, were either transfected (RIG-I) or treated (TLR3) with poly(I:C); caspase activity was measured at 16 h post treatment; **(D)** HT1080 cells were either transfected (RIG-I) or treated (TLR3) with poly(I:C) for the indicated time, when the dead cells were counted using Trypan blue dye; percent dead cells, presented here, was measured by counting the Trypan Blue positive cells and total number of cells; **(E)** HT1080 cells were either transfected (RIG-I) or treated (TLR3) with poly(I:C) for 16 h, when the cells were stained with FITC-conjugated TUNEL, TUNEL positive and DAPI stained cells were counted under microscope and percent TUNEL positive cells are presented.

Figure S1
Chattopadhyay et al

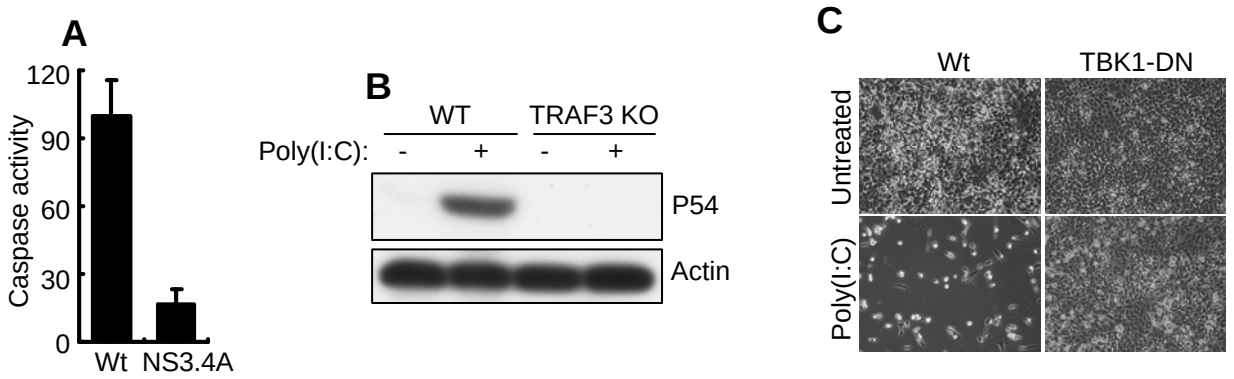

Figure S2. Components of RIG-I signaling are required for IRF-3 mediated apoptosis. (A) Human cells expressing Hepatitis C Virus NS3.4A protease (NS3.4A) were infected with SeV (at MOI:10); caspase activity was measured 48 h post infection; **(B)** TRAF3 KO MEFs and its matched Wt controls were transfected with poly(I:C); after 12 h of dsRNA treatment, cell extracts were subjected to Western Blot analysis for P54, a dsRNA-inducible protein; **(C)** HT1080 cells (Wt) expressing dominant negative mutant of TBK1 (TBK1-DN) were transfected with of poly(I:C); 24 h post transfection culture fields were photographed.

Figure S2
Chattopadhyay et al

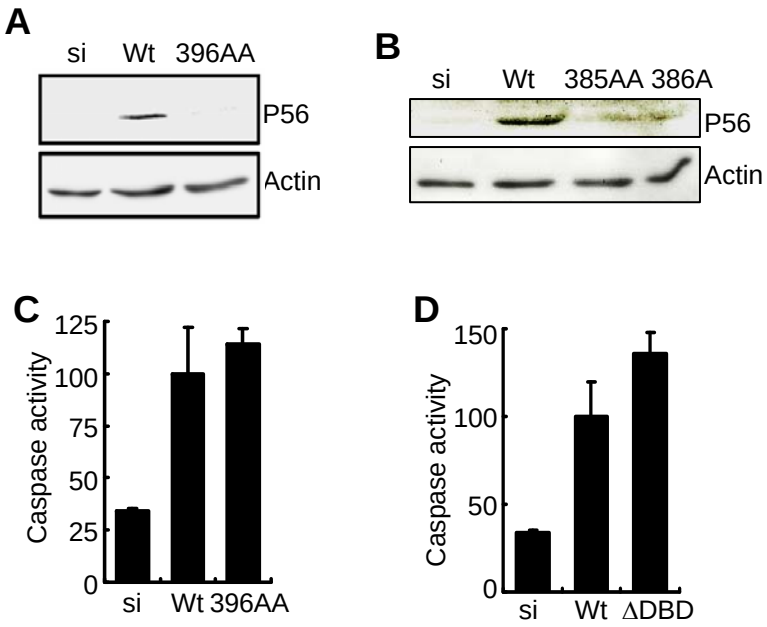

Figure S3. Transcriptionally inactive mutants of IRF-3 can trigger dsRNA induced apoptosis. HT1080-siIRF-3 (si) cells expressing Wt or mutants of IRF-3 were used for these experiments. **(A, B)** Wt IRF-3 (Wt), IRF-3 396/98AA mutant (396AA), IRF-3 385/86AA mutant (385AA) or IRF-3 386A expressing cells were transfected with poly(I:C); the cell extracts from after 6 h of poly(I:C) transfection was analyzed for P56 induction by Western Blot; **(C)** Wt and IRF-3 mutant (as indicated) expressing cells were infected with SeV for 48 h, when caspase activity was measured; **(D)** The cells expressing Wt or DNA binding domain deleted IRF-3 mutant (ΔDBD) were transfected with poly(I:C); caspase activity was measured after 16 h.

Figure S3
Chattopadhyay et al

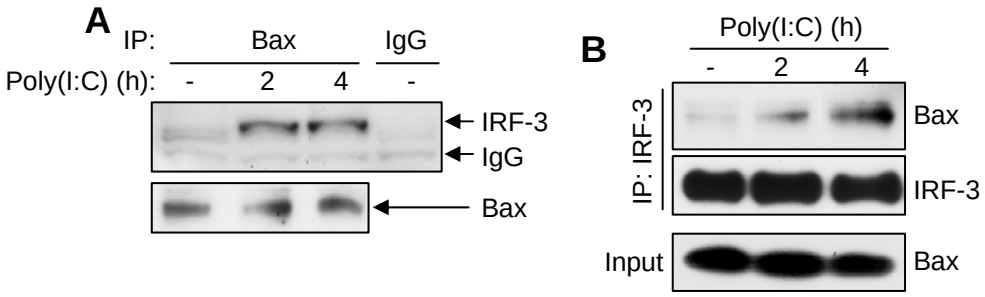

Figure S4. DsRNA signaling induces interaction of IRF-3 and Bax. A) HT1080 cells expressing Wt IRF-3 were transfected with poly(I:C) for the indicated time when the cell lysates were immunoprecipitated with Bax and analyzed for IRF-3 by Western Blot; **B)** HT1080 cells expressing Wt IRF-3 were transfected with poly(I:C) for the indicated time when the cell lysates (in CHAPS containing lysis buffer) were immunoprecipitated with IRF-3 and analyzed for Bax by Western Blot.

Figure S4
Chattopadhyay et al

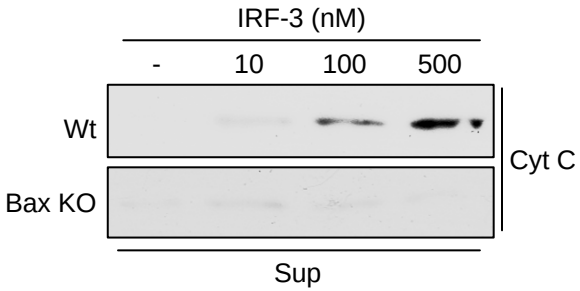

Figure S5. *In vitro* Cyt C release by IRF-3 is dependent on Bax. Human IRF-3 purified from poly(I:C) transfected cells (as described in the Materials and Methods) was used for mitochondrial activation assay, the supernatant (sup) was analyzed for Cyt C release by Western Blot.

Figure S5
Chattopadhyay et al