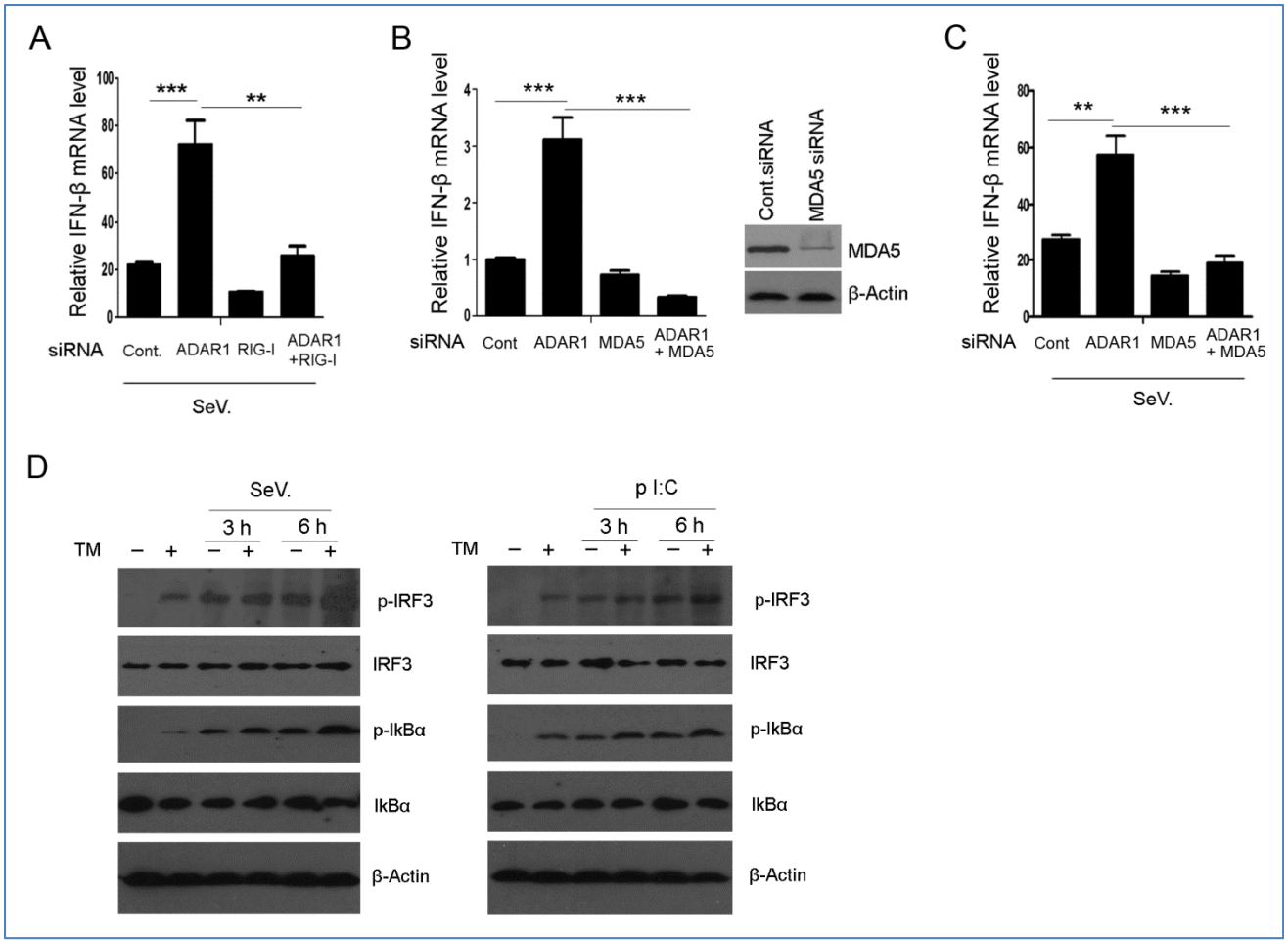
Supplementary Data

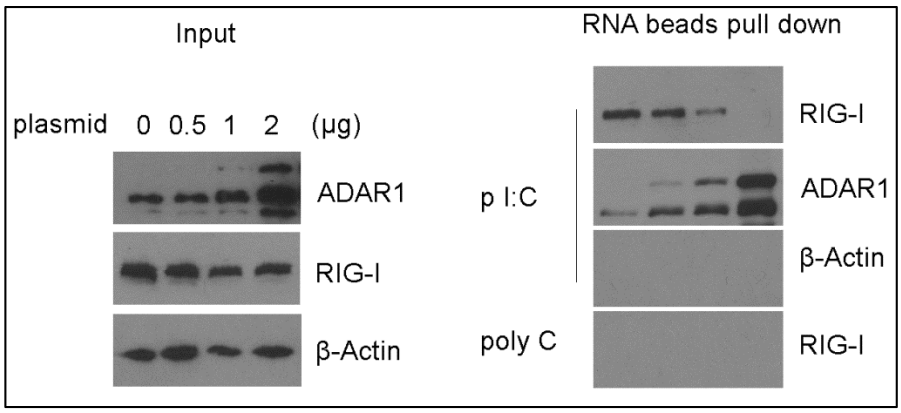
Supplementary Figure 1



Supplementary Figure 1. ADAR1 interferes with cytosolic RLR pathways.

The dependence of RIG-I and MDA5 in ADAR1 modulated type I IFN inductions and the activation of downstream signaling were tested in HEK293 and iKO-MEFs. (**A**). IFN-β expression was measured by real-time PCR in HEK293 cells transfected with ADAR1 siRNA or RIG-I siRNA or both in response to SeV infection. The elevated level of IFN-β expression induced by ADAR1 knockdown is decreased in cells when RIG-I was simultaneously knocked down. (**B**) Knockdown of MDA5 in HEK293 cells shows the similar effect as knockdown RIG-I without SeV infection and (**C**) under SeV infection. Data shown is the mean ± S.D. ** $p<0.01$; *** $p<0.001$. (**D**) RIG-I and MDA5's downstream biochemistry modifications on IRF3 and IkB-α were monitored by western blot with specific antibodies against the phosphorylated proteins after SeV infection or poly I:C transfected into the iKO-MEFs. Tamoxifen (TM) induces ADAR1 deletion in these iKO-MEFs. Non-TM treated cells were used as control for each condition and time points.

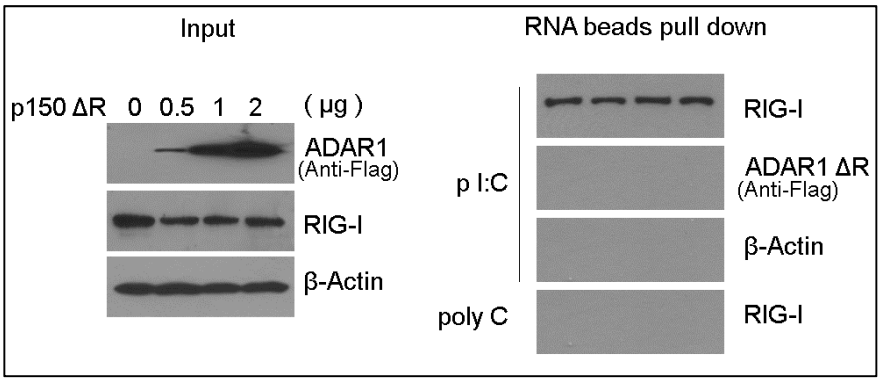
Supplementary Figure 2



Supplementary Figure 2. Over expression of ADAR1 in HEK293 cells inhibits cellular RIG-I bound to poly I:C.

The protein extracts from HEK293 cells transfected with increasing amounts of ADAR1 plasmid for 48 hours were incubated with poly I:C conjugated agarose beads. The proteins pulled down by the poly I:C beads were analyzed on Western blot with ADAR1 and RIG-I antibodies. Poly C beads were used as a control for binding specificity.

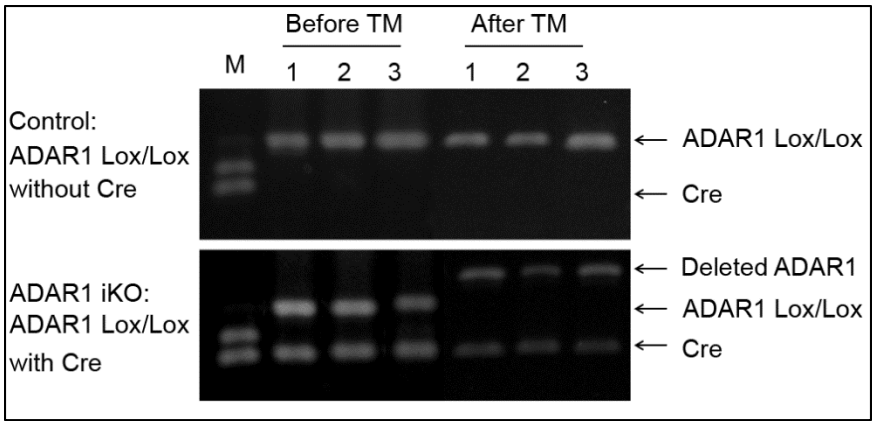
Supplementary Figure 3



Supplementary Figure 3. ADAR1 lacking RNA binding domain does not affect cellular RIG-I binding with poly I:C

The protein extracts were prepared from HEK293 cells transfected with p150 ΔR plasmid expressing ADAR1 protein lacking RNA binding domain. RIG-I binding with poly I:C beads was tested by western blot. Poly C beads were used as a control for binding specificity.

Supplementary Figure 4



Supplementary Figure 4. Efficient ADAR1 gene deletion *in vivo* after tamoxifen administration into iKO mice

Genotype analysis of three mice from control and ADAR1 iKO groups is shown. Tamoxifen was administrated into the mice at the dosage of 0.1mg/g body weight and PCR genotype analysis was performed five days after the induction. Control mice carry floxed ADAR1 gene without Cre-ER transgene. The PCR products of the floxed ADAR1, deleted ADAR1, and Cre gene are indicated by the arrows. M: DNA size marker.