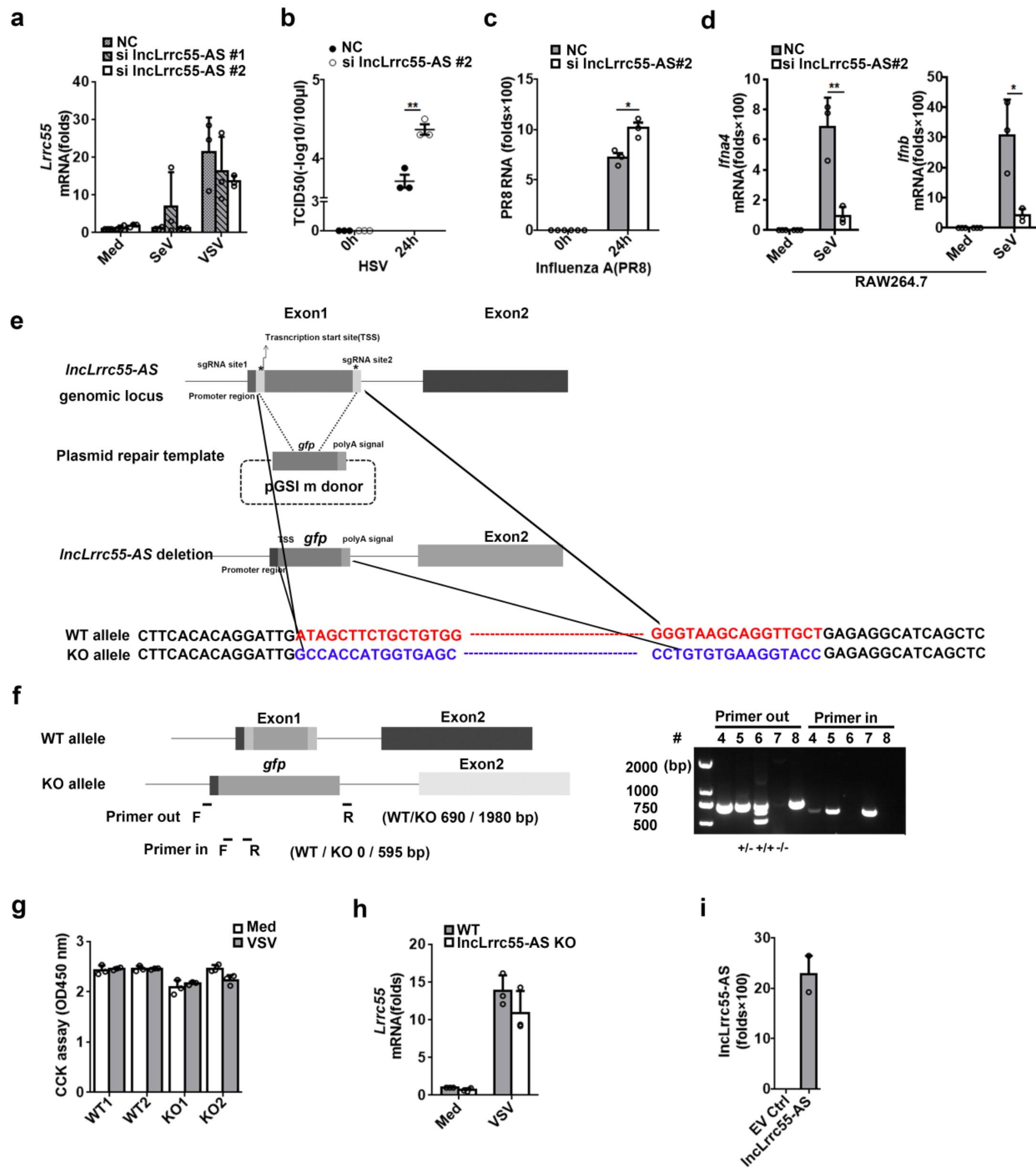

Supplementary information, Fig. S4 lncLrrc55-AS enhances IFN-I production in response to viral infection. **a** RT-qPCR analysis of *Lrrc55* mRNA expression in non-target siRNA control (NC) or lncLrrc55-AS-silenced macrophages infected with SeV or VSV for 12 hours. **b** Determination of virus loads in the supernatant from HSV infected macrophages for indicated hours by TCID50 assay. **c** Determination of Influenza A virus (PR8 strain) replication in macrophages by RT-qPCR. **d** RT-qPCR analysis of *Ifna4*, *Ifnb* mRNA expression in NC or lncLrrc55-AS-silenced RAW 264.7

cells infected with SeV for 12 hours. **e** Strategy used in generating lncLrrc55-AS KO cell or *lncLrrc55-AS*$^{-/-}$ mouse. The lncLrrc55-AS KO cell or *lncLrrc55-AS*$^{-/-}$ mouse were generated by replacing the genomic locus encoding the first exon of lncLrrc55-AS transcript with a *gfp* cassette following a poly A signal under the control of endogenous promoter of *lncLrrc55-AS*. **f** Identification of the selected cell clones. The “prime out” band was 1980bp (*lncLrrc55-AS* knock out & *gfp* knocked in) or 690bp (WT); the “primer in” band was 595bp (*lncLrrc55-AS* knock out & *gfp* knocked in) or no band (WT). **g** Cell proliferation analysis of two selected monoclonal WT or lncLrrc55-AS KO NIH/3T3 cell clones infected with VSV for 12 hours by using CCK-8. **h** RT-qPCR analysis of LRRC55 mRNA expression in selected monoclonal WT or lncLrrc55-AS KO NIH/3T3 cells infected with VSV for 12 hours. **i** RT-qPCR analysis of lncLrrc55-AS expression efficiency of plasmid. Data are from three independent experiments (**a-d, g-i**; mean ± SEM) or are representative of three independent experiments with similar results (**f**). $*P < 0.05$; $**P < 0.01$ (Student’s *t*-test or ANOVA).