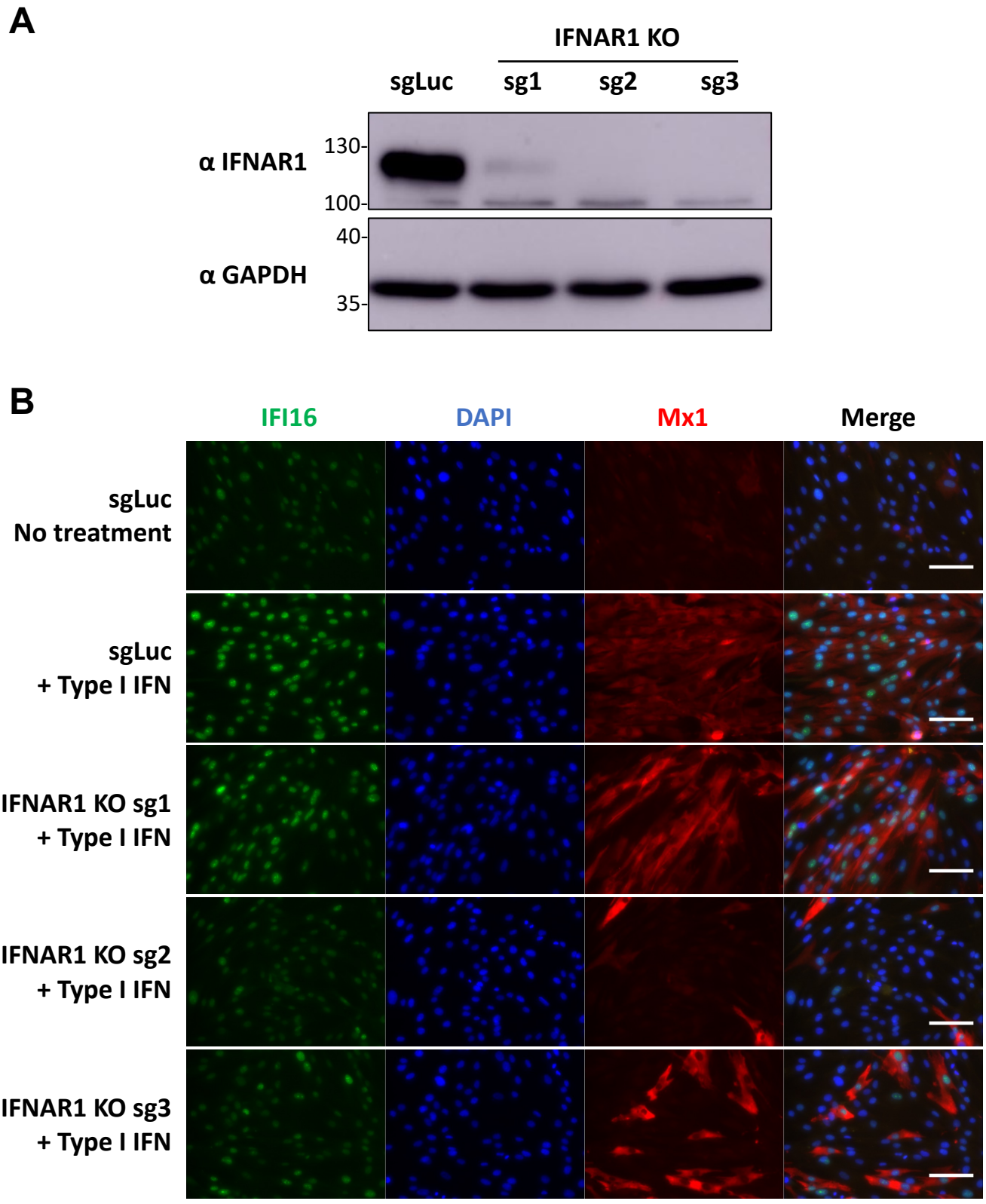
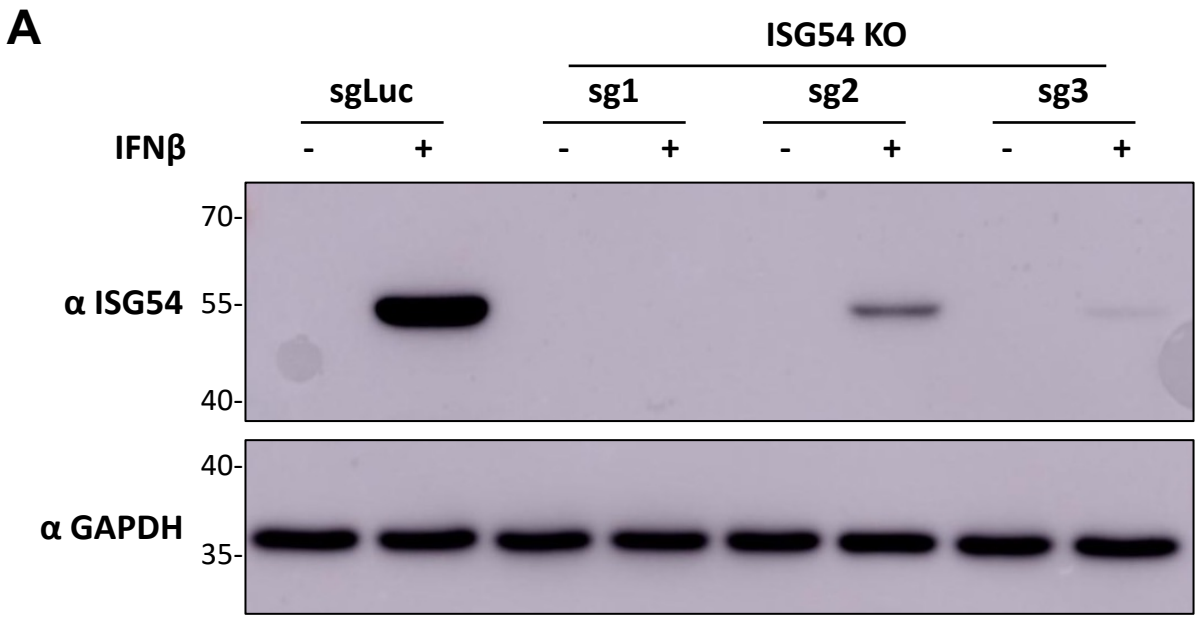


Figure S1. Characterization of IFNAR1 CRISPR knockout (KO) HDF cells. A. HDFs stably expressing Cas9 and a sgRNA targeting either the IFNAR1 gene (sg1, sg2, and sg3) or the nonmammalian luciferase gene (sgLuc) were immunoblotted for IFNAR1 and GAPDH. **B.** sgLuc or IFNAR1 KO sg1/2/3 HDF cells were treated with 500 U/ml type I IFN for 21 h, fixed, immunostained for IFI16 and Mx1, and counterstained with DAPI. Scale bar, 100 μm.



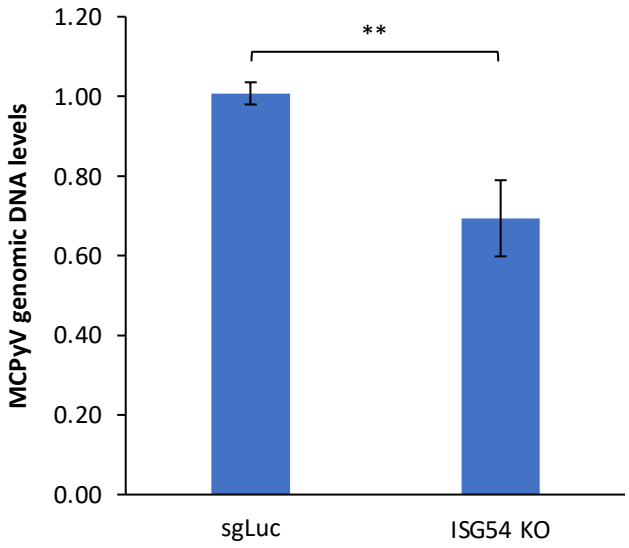


Figure S2. ISG54 knockout does not significantly affect MCPyV infection. A. HDFs stably expressing Cas9 and a sgRNA targeting either the ISG54 gene (sg1, sg2, and sg3) or the luciferase gene (sgLuc) were treated with IFNβ for 20 h and immunoblotted for ISG54 and GAPDH. **B.** MCPyV infected sgLuc or ISG54 KO (sg1) HDF cells were harvested for DNA extraction on day 5 post-infection. MCPyV genomic DNA levels were determined by qPCR quantification and normalized to the GAPDH genomic DNA levels. The value for one of the MCPyV-infected sgLuc HDF groups was set as 1. Error bars represent the standard deviation from three independent experiments. **p<0.01.

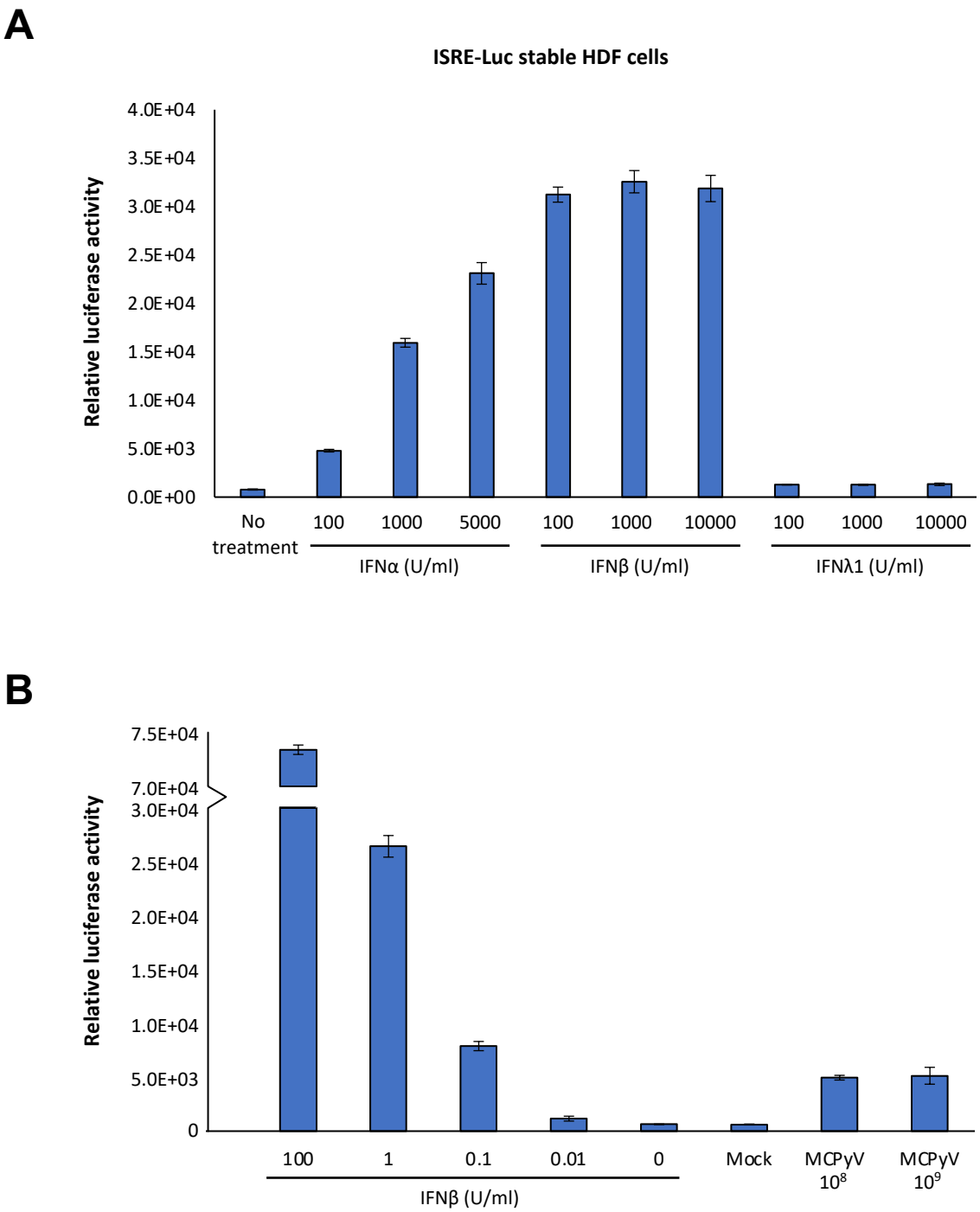


Figure S3. Quantification of IFNβ induction by MCPyV infection. A. HDF ISRE-Luciferase reporter stable cells were treated with the indicated doses of IFNs for 18h. Cell lysates were analyzed using luciferase assays. **B.** Cell culture medium collected from mock-infected HDFs or HDFs infected with 10^8 or 10^9 viral genome equivalents in each well of a 96-well plate were harvested on day 6 post-infection. The cell culture medium or different doses of IFNβ were used to treat HDF ISRE-Luciferase reporter stable cells for 6 h. Cell lysates were harvested for luciferase assays.