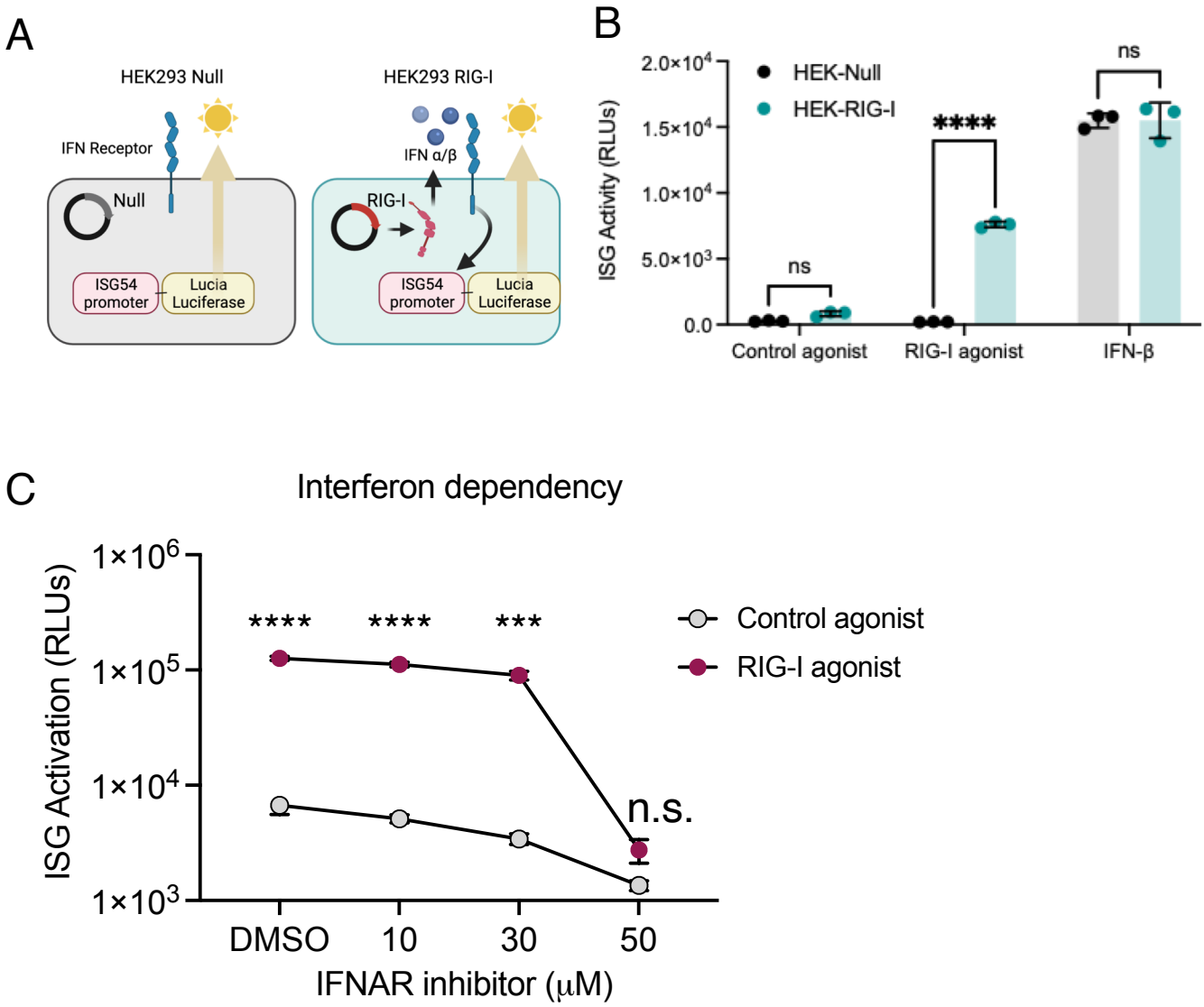
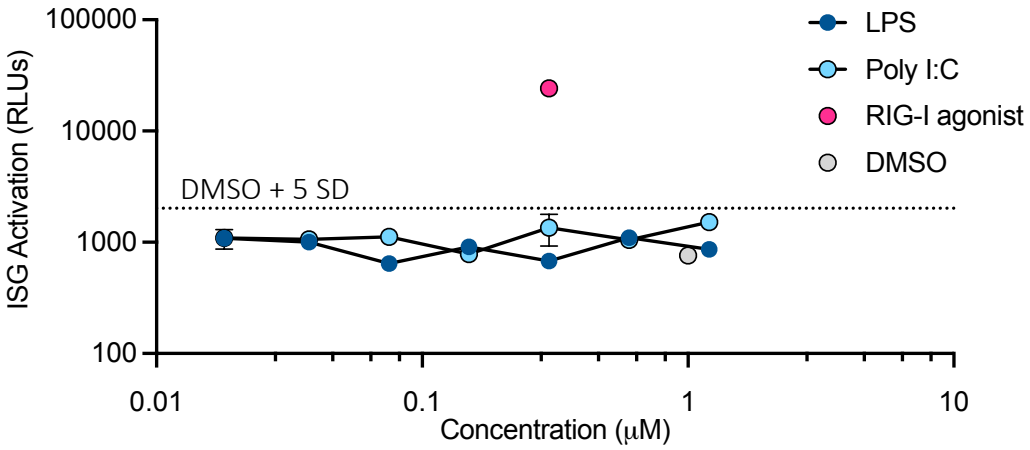
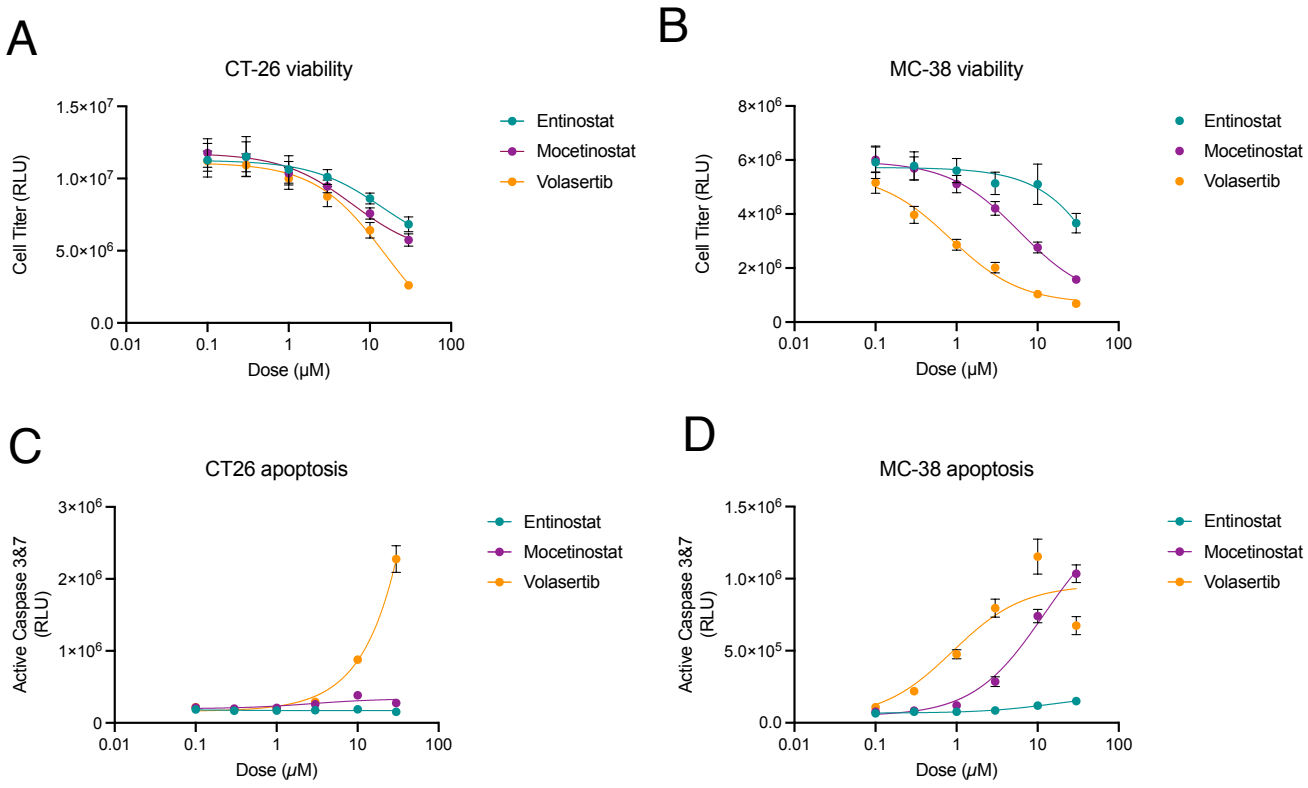


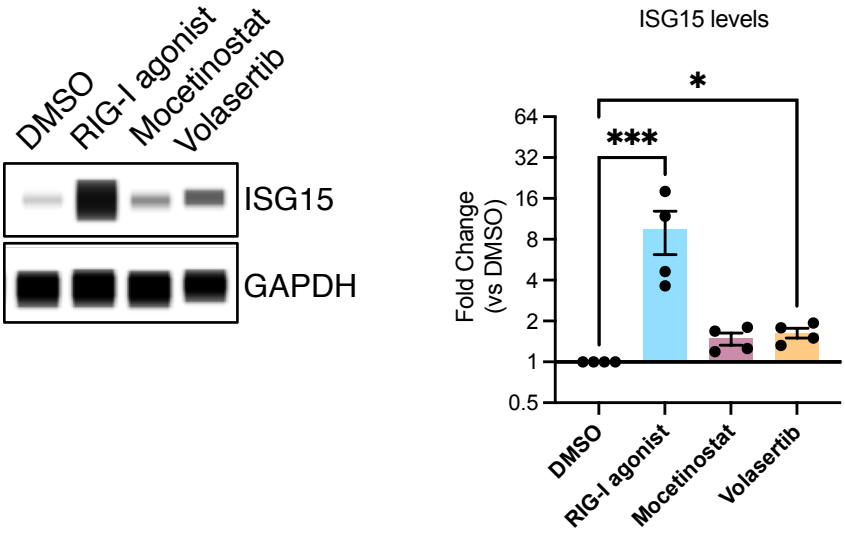
Supplementary Figure 1. RIG-I and IFN dependent activation of an ISG54 luciferase reporter cell line. A-B) HEK293 reporter cell lines with an ISG54 responsive luciferase gene and a null vector or RIG-I expressing vector were treated with a control agonist or RIG-I agonist or IFN-β as a positive control. ISG activity was assessed using luminescence at 24h in the null cell line and the RIG-I expressing cell lines. ****P<0.0001 using ANOVA with post-hoc Sidak's test. C) HEK293 RIG-I cells were treated with a control agonist or RIG-I agonist in the presence of indicated concentrations of an interferon alpha receptor antagonist. ISG activity was assessed by luminescence at 24h. ****P<0.0001 using Welch's T-test with post-hoc Bonferroni-Sidak's test.



Supplementary Figure 2. TLR ligands do not activate ISG54 luciferase in our reporter assay. HEK293 reporter cell lines were treated with different Poly I:C, TLR 3 agonist or LPS a TLR4 and TLR2 agonist at the indicated concentrations. RIG-I agonist was used at 0.3 ug/ml as a positive control and 1% DMSO as negative control. Dotted line indicates our hit criteria at 5 SD above the mean of negative control wells.



Supplementary Figure 3. Viability of tumor cell lines in response to HDAC and PLK inhibitors. CT26 or MC38 Colorectal carcinoma cells were treated with the indicated concentrations of the HDAC inhibitors or Plk1 inhibitor. 24h later A-B) viability was measured using a Cell Titer glo assay C-D) cell death was measured by a CaspaseGlo assay.



Supplementary Figure 4. Activation of RIG-I signaling in response to HDAC and PLK inhibitors. A) MC38 Colorectal carcinoma cells were treated with RIG-I agonist (0.5 ug/ml), Mocetinostat (5uM) or Volasertib (1uM). Simple Wes western blot for ISG15 or GAPDH is shown. Right panel depicts quantitation from 4 independent biological replicates. * P<0.05, *** P <0.005 by Kruskal-Wallis test