Expanded View Figures

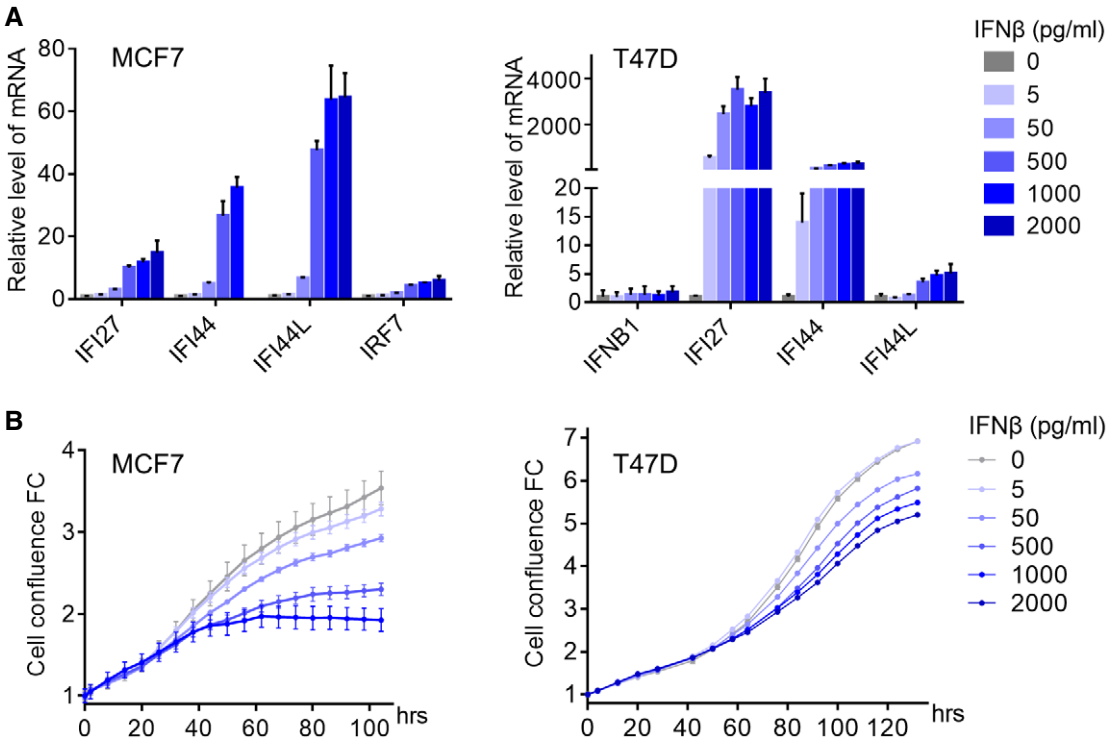

Figure EV1. IFNβ treatment up-regulated the expressions of ISGs and inhibited proliferation of breast cancer cells.

A The expression levels of ISGs were measured in MCF7 (left) and T47D (right) cells treated with different concentrations of IFNβ. Data represent mean ± SD.

B Growth curves of MCF7 (left) and T47D (right) cells treated with different concentrations of IFNβ. Data represent mean ± SD.

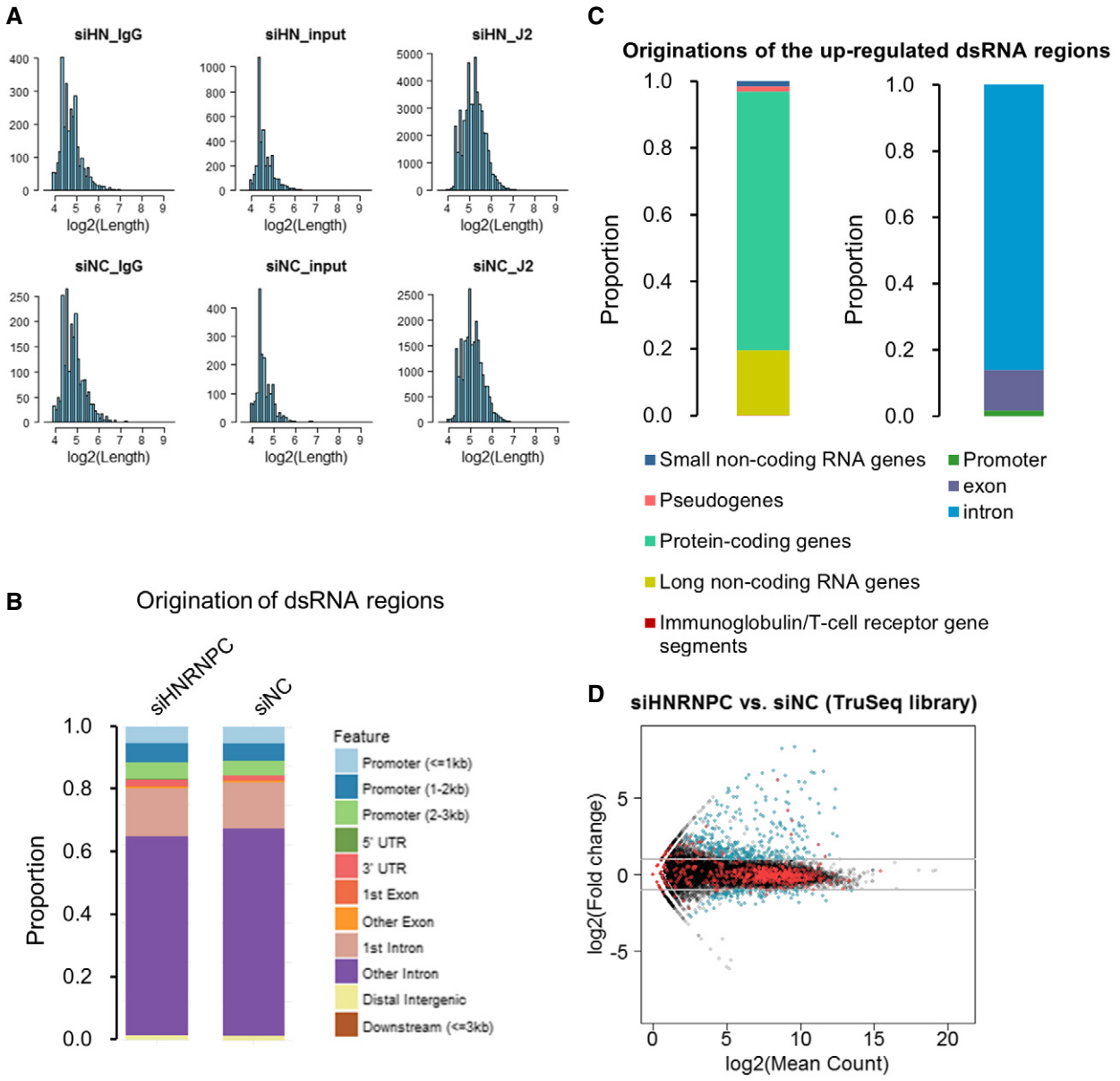

Figure EV2. Features of the dsRNA regions.

A Distributions of the lengths of the dsRNA regions identified in the dsRNA-enriched libraries (siHN_J2 and siNC_J2) or in the two types of control libraries (input and IgG controls).

B Percentages of the dsRNA regions identified in control or HNRNPC KD cells, which were divided into different categories according to the intra-genic locations of the dsRNAs.

C Percentages of the up-regulated dsRNA regions upon HNRNPC knock-down, which were divided into different categories according to the type of their host genes (left) or intra-genic locations (right).

D MA plot showing differential expression of the genes, upon HNRNPC knock-down. The *x*-axis represents the average read count of each gene (in logarithm scale), and the *y*-axis represents log2 fold change of the read count in siHNRNPC vs. siNC. The differentially expressed genes, identified by DESeq2 and shown in Fig 2A, were marked in blue. The host genes of the up-regulated dsRNA regions upon HNRNPC knock-down were marked in red.

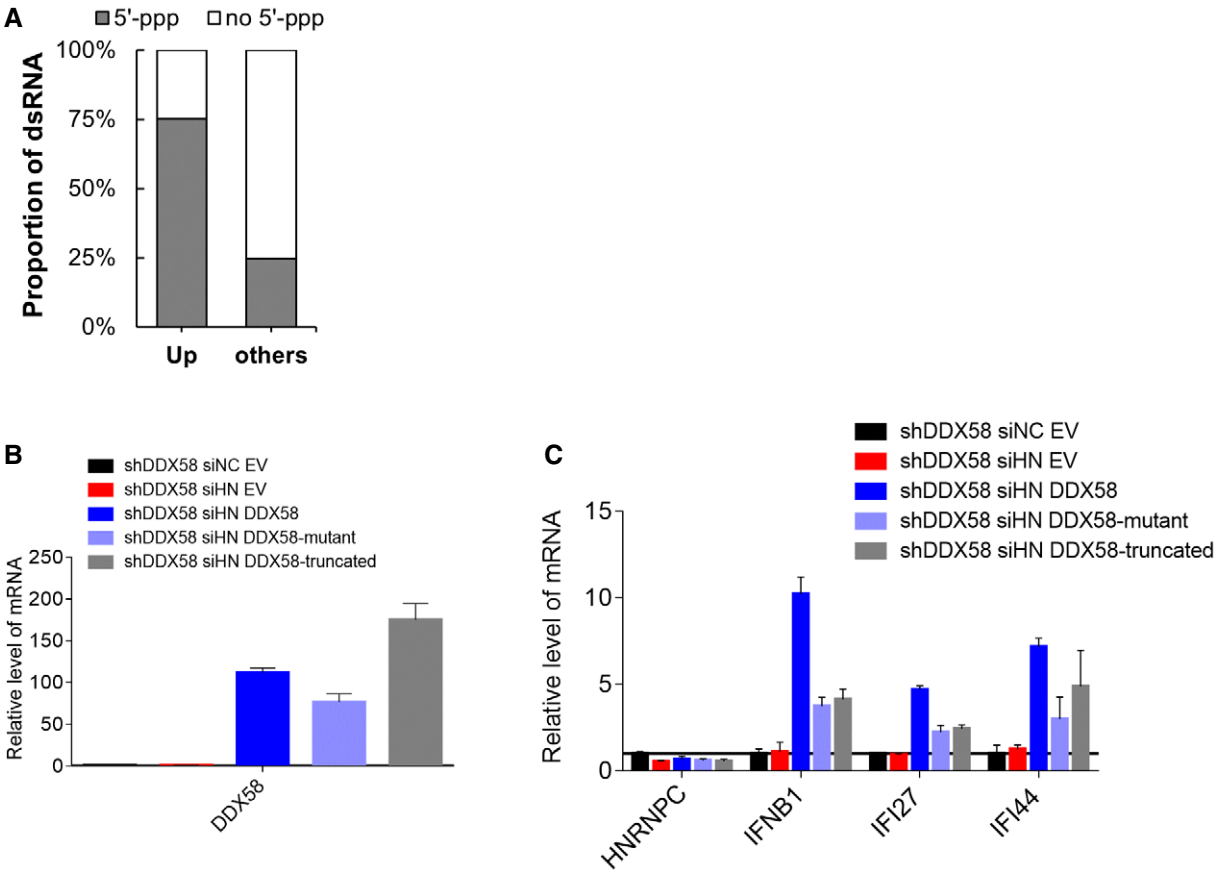

Figure EV3. Involvement of 5′ppp reorganization unit of RIG-1 in mediating interferon response upon HNRNPC KD.

A RNA pulled down by J2 antibody from the small RNA fraction (< 500 nt) was subjected to further enrichment of 5′ppp modifications. According to Fig 6C, the dsRNA species identified by J2 dsRNA-seq were divided into two sets (up-regulated by HNRNPC KD and the others). For each set, the percentages of the dsRNA species that have 5′ppp ends were shown as bar plots.

B Rescue of DDX58 expression after double KD of HNRNPC and DDX58, with wild-type RIG-I or RIG-I with its 5′ppp RNA recognition domain mutated or truncated. Data represent mean ± SD.

C mRNA expression of ISG signatures upon rescue of DDX58 expression after double KD of HNRNPC and DDX58, with wild-type RIG-I or RIG-I with its 5′ppp RNA recognition domain mutated or truncated. Data represent mean ± SD.

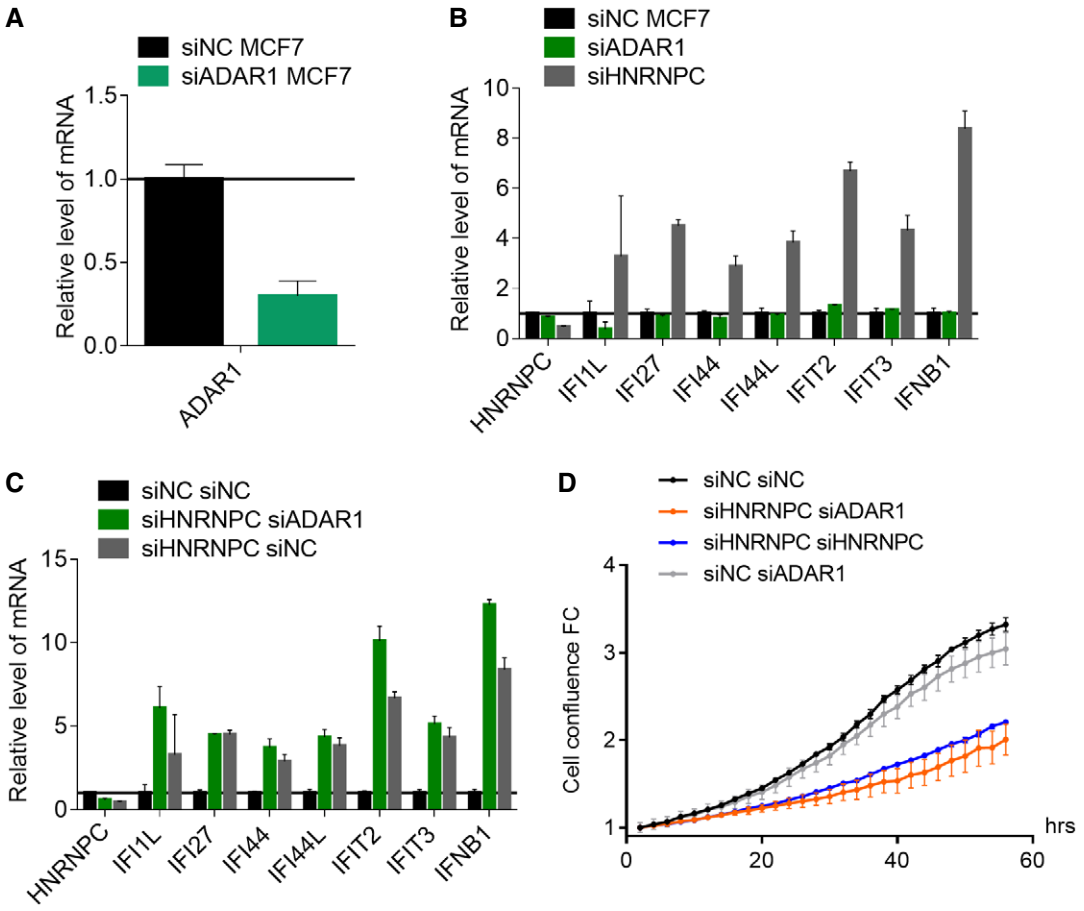

Figure EV4. Effects of ADAR1 in interferon response upon HNRNPC KD.

A mRNA silencing efficiency of ADAR1 siRNA. Data represent mean ± SD.
B Expression levels of ISGs upon HNRNPC or ADAR1 silencing in MCF7 cells. Data represent mean ± SD.
C Expression levels of ISGs upon double knock-down of HNRNPC and ADAR1 in MCF7 cells. Data represent mean ± SD.
D Cell proliferation upon single knock-down of HNRNPC or double knock-down of HNRNPC and ADAR1 in MCF7.

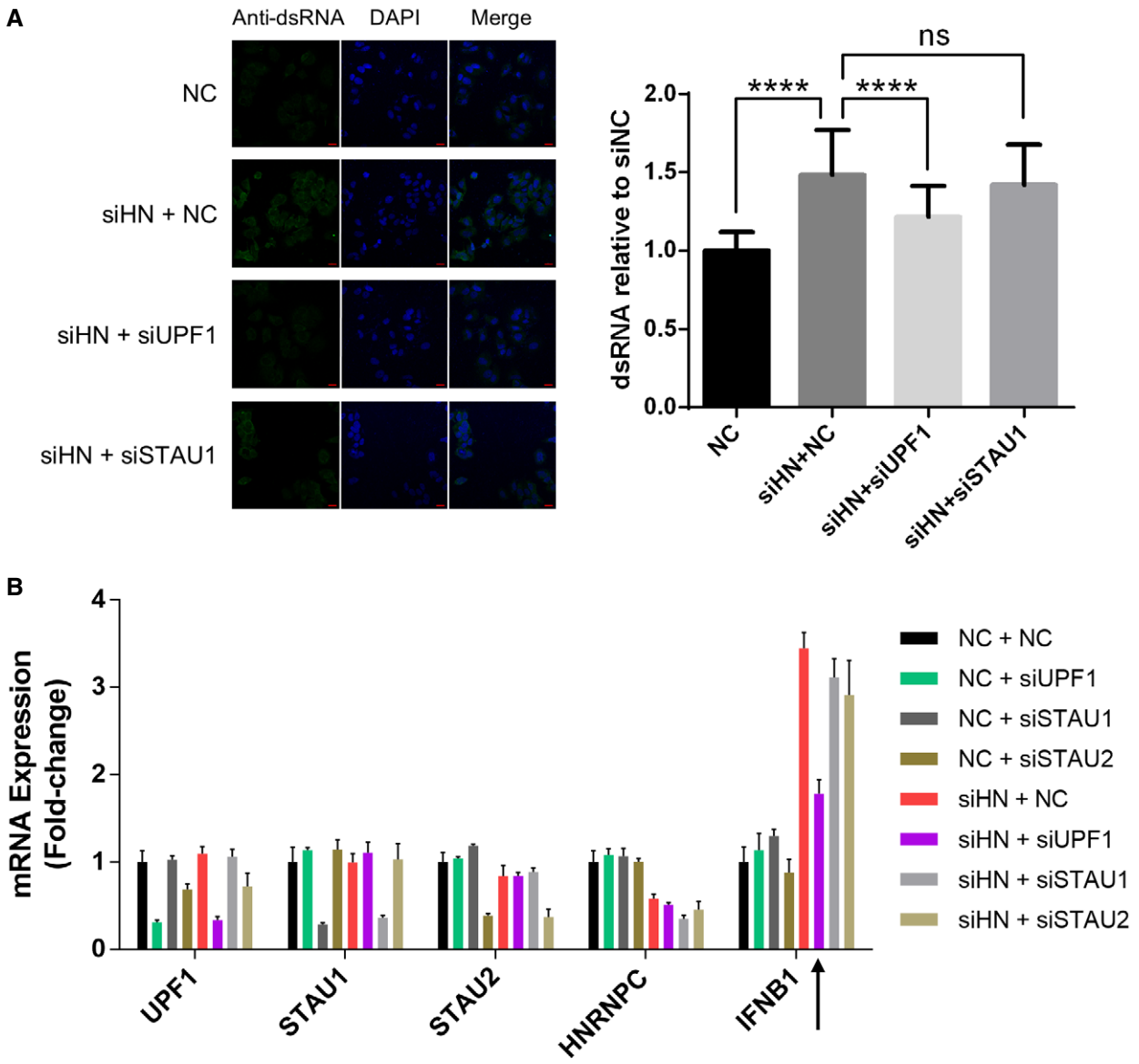

Figure EV5. dsRNA accumulation and IFNB1 expression in response to HNRNPC repression and silencing of UPF1 and STAU1.

A Immunofluorescence analysis of the dsRNA in MCF7 cells after knock-down of HNRNPC only or double knock-down of HNRNPC & UPF1 or HNRNPC & STAU1, with 4′,6-diamidino-2-phenylindole (DAPI) staining (blue) and anti-dsRNA antibody J2 (green).

B mRNA expressions of UPF1, STAU1, STAU2, HNRNPC, and IFNB1 upon knock-down of UPF1, STAU1, and STAU2 or double knock-down of HNRNPC & UPF1, HNRNPC & STAU1, or HNRNPC & STAU2 in MCF7 cells. Data represent mean ± SD.