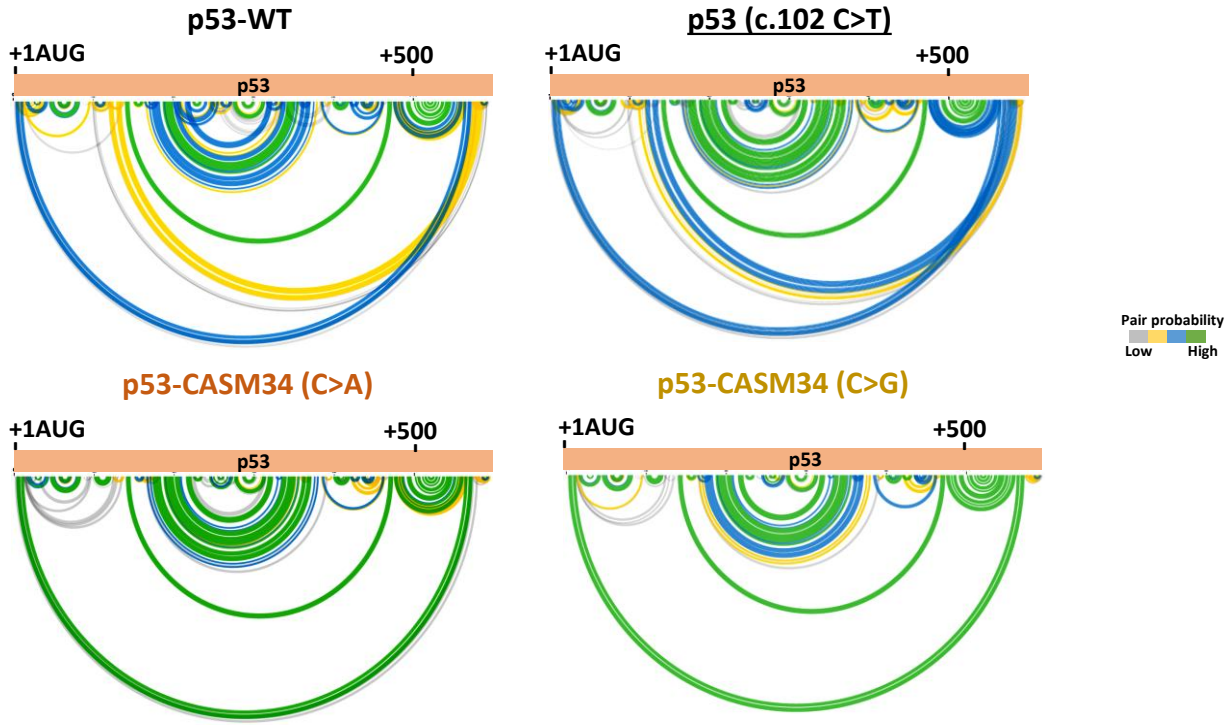
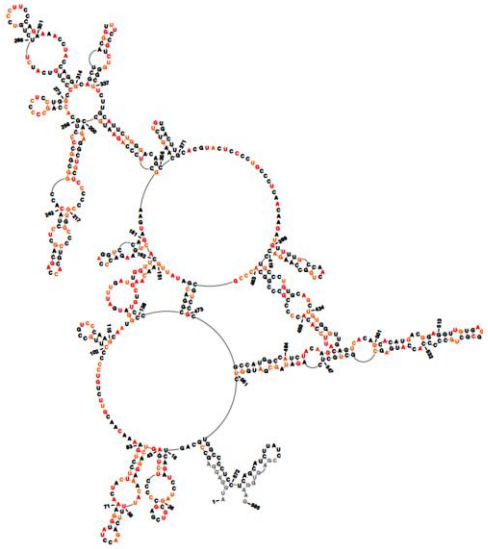
Supplementary Figure 1



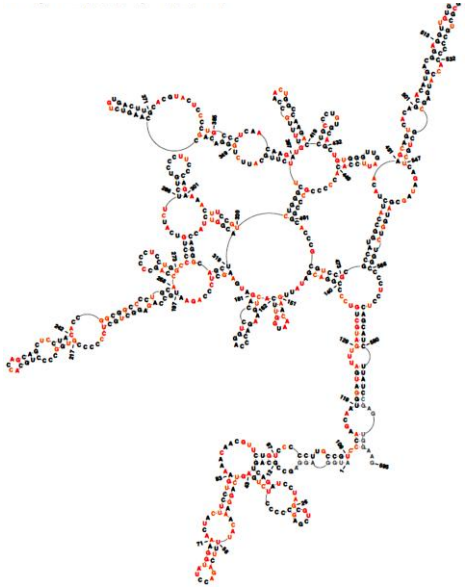
Supplementary Figure 1. Arc plots showing the probability of base pairings based on the SHAPE-MaP of indicated *p53* mRNAs, highly probable base-pairings are indicated in green color. Related to main figure 1

Supplementary Figure 2

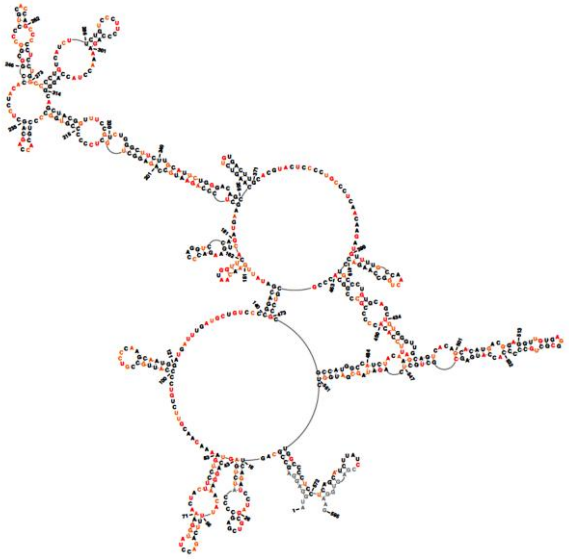
p53-WT + DMSO



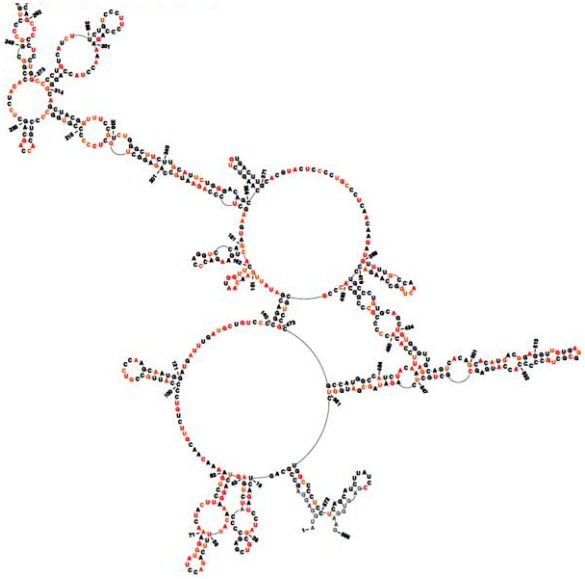
p53-WT + DOXO



CASM34 (C>A) + DMSO

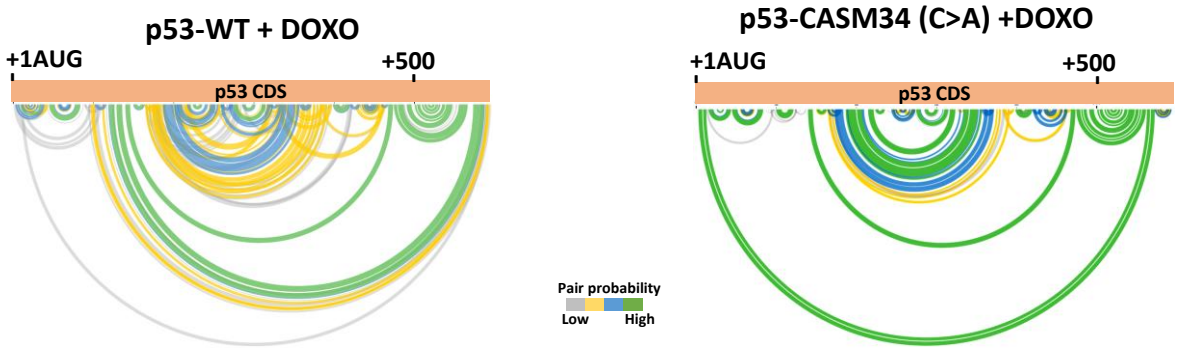


CASM34 (C>A) + DOXO



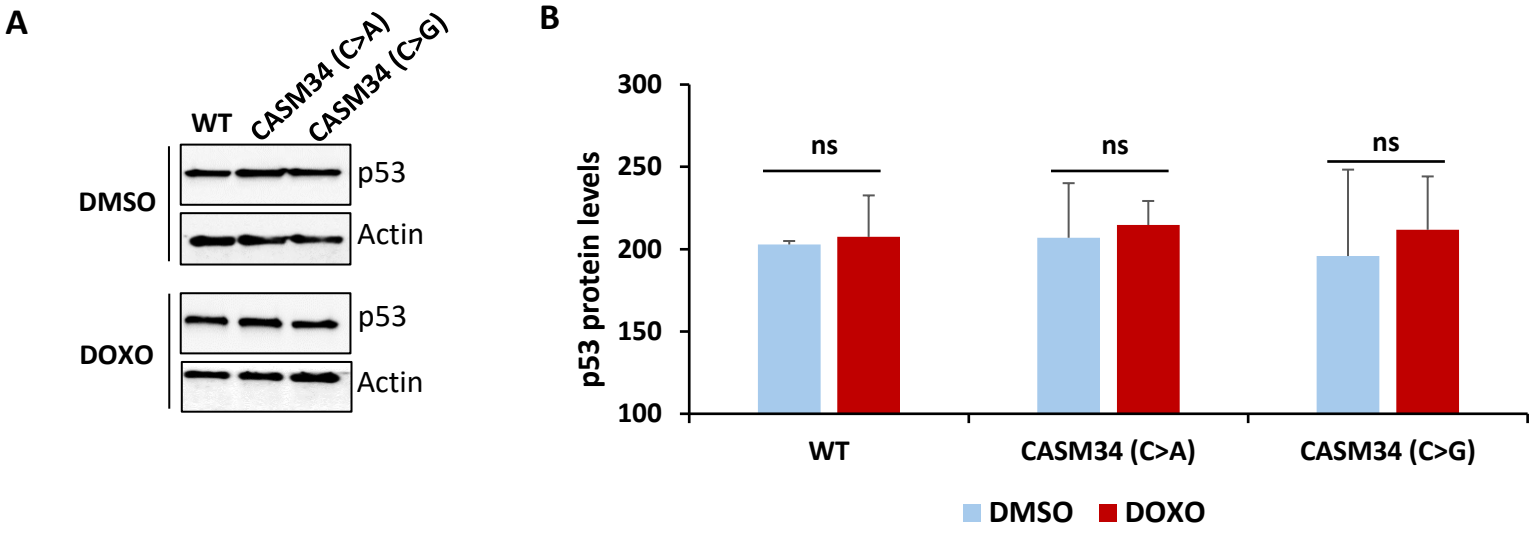
Supplementary Figure 2. Secondary structures of the *p53* WT and *CASM34* mRNAs under normal (DMSO) and DNA damage (DOXO) conditions. Related main figure 2.

Supplementary Figure 3



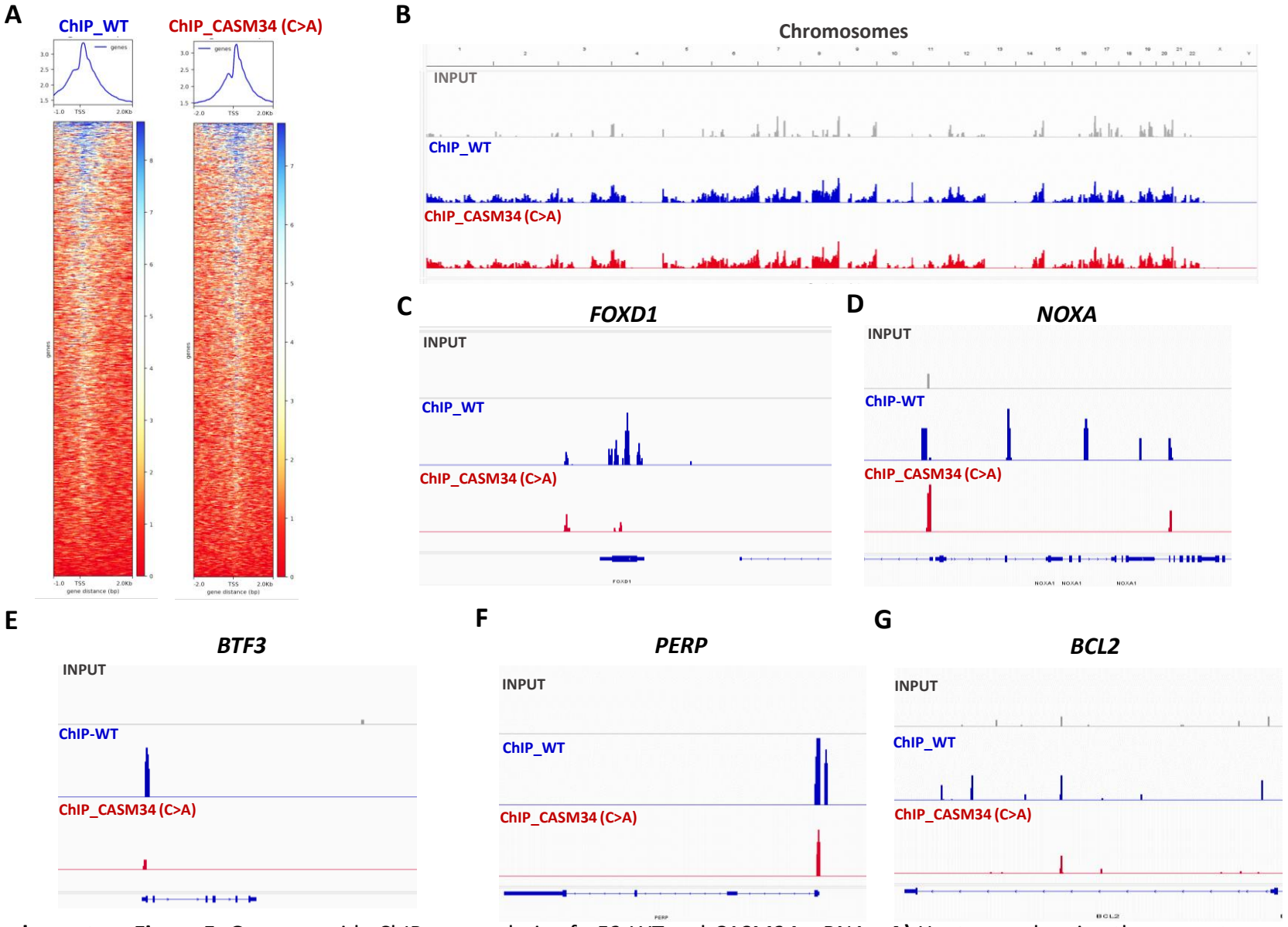
Supplementary Figure 3. Arc plots showing the probability of base pairings observed in the corresponding circos plots in Figure 2, highly probable base-pairings are indicated in green color. Related to main figure 2.

Supplementary Figure 4



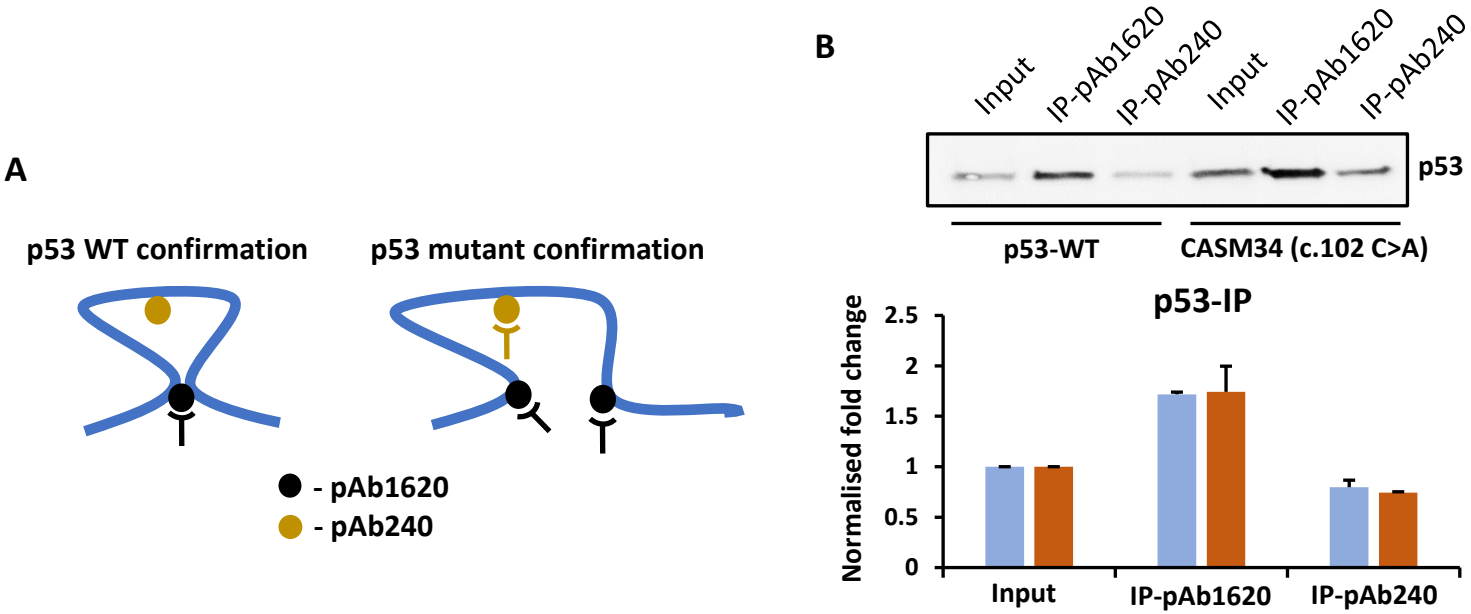
(A) Western blot analysis showing steady-state p53 protein levels for the indicated constructs under normal (DMSO) and DNA damage (DOXO) conditions. Actin was used as a loading control. (B) Quantification of p53 protein levels under the indicated conditions. Band intensities were measured using ImageJ, and relative p53 levels are plotted. Data are shown as mean ± s.d. from three independent experiments. Statistical significance was determined using an unpaired *t*-test (**$p < 0.001$; *$p < 0.01$; $p < 0.05$; ns, not significant). Related to Figure 3A.

Supplementary Figure 5



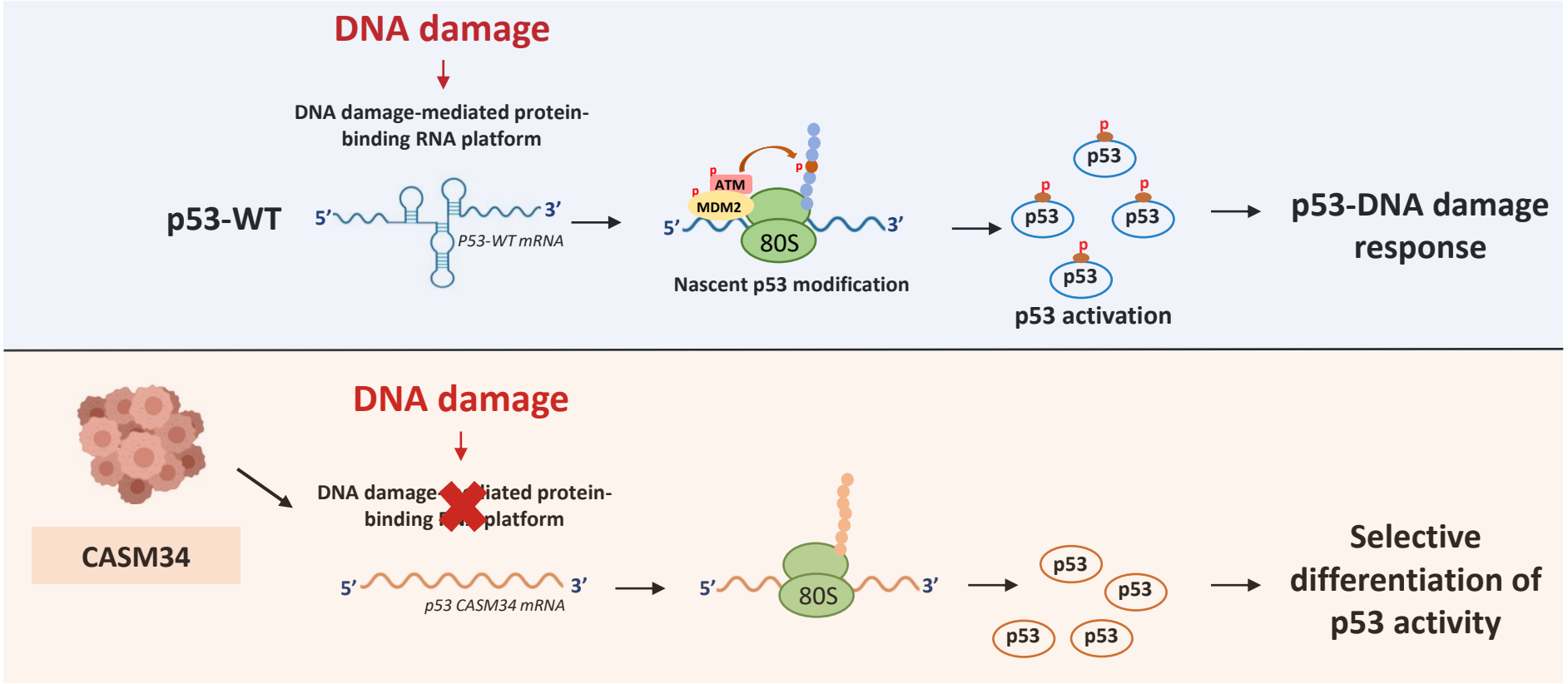
Supplementary Figure 5. Genome-wide ChIP-seq analysis of *p53-WT* and *CASM34* mRNAs. **A)** Heat-map showing the promoter occupancy profiles of p53 under indicated conditions. **B)** Genome-wide ChIP profile of WT and CASM34. **C-G** Selected representation of p53-downstream targets showing lesser p53 binding in CASM34 compared to p53-WT. ChIP-seq data are representative of at least two independent biological replicates. Related to main figure 4, see also supplementary information.

Supplementary Figure 6



Supplementary Figure 6. A) Schematics showing the conformations of p53 WT and mutant proteins masking the epitope of conformation specific antibodies (pAb240). B). Western blot showing the p53 pulldown levels with indicated antibodies. Graph below shows the semi-quantitative levels of p53 based on densitometric analysis of corresponding p53 band intensity as indicated. Signal ratio was normalized using the corresponding input samples.

Supplementary Figure 7



Supplementary Figure 7. A model on how CASM34s might confer functional selectivity of the encoding protein by targeting *p53* mRNA folding. Upper panel: Previous data have shown that the *p53-WT* mRNA undergoes riboswitch-like RNA structural alterations during DNA damage to form a protein-binding platform that results in induced p53 synthesis and modification of the nascent protein at serine 15 by the ATM kinase[13,15]. Lower panel: In a similar concept, CASM34 mutants target *p53* mRNA structures and possibly prevent the recruitment of an enzyme that selectively differentiates p53 activity towards certain target genes. (Created in BioRender. Vadivel Gnanasundram, S. (2026) https://BioRender.com/kuf8xvs)