

Expanded View Figures

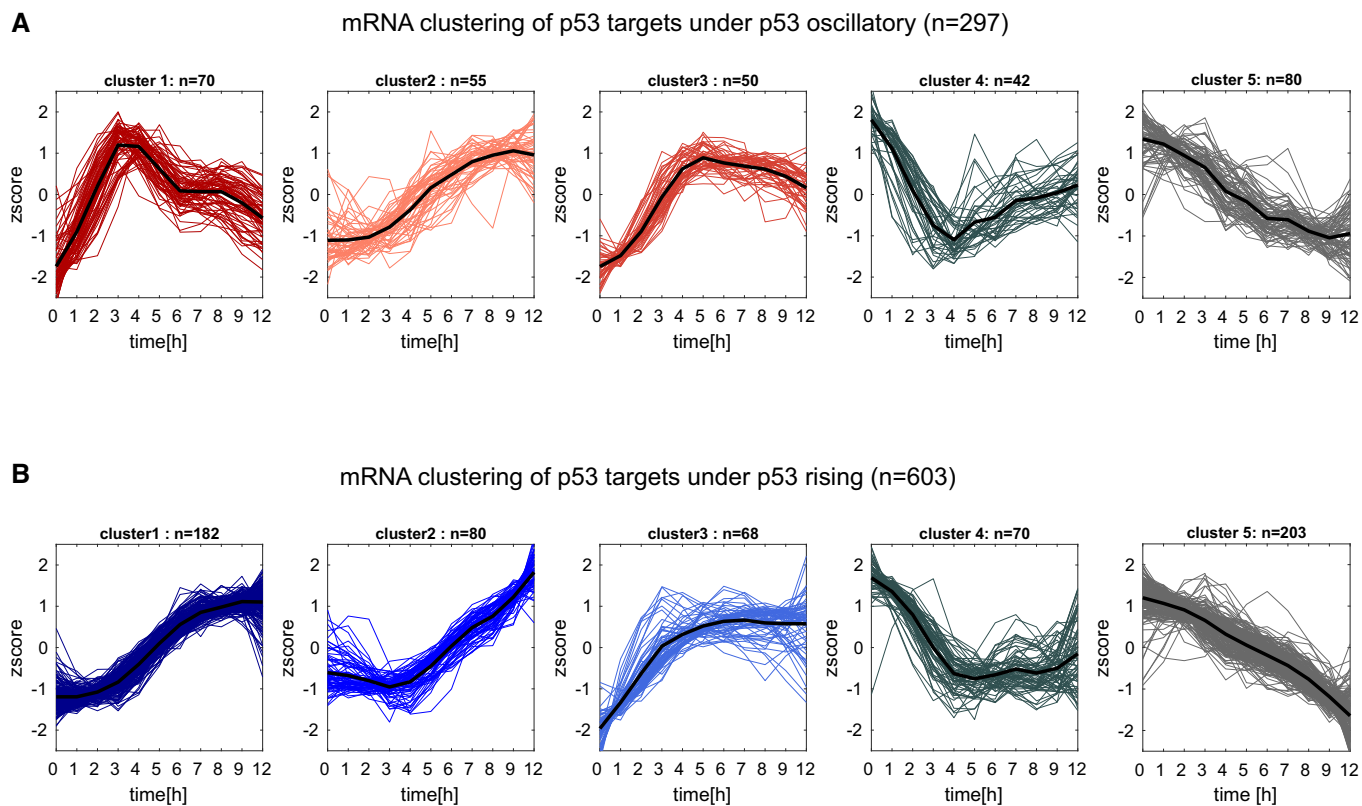


Figure EV1. Clustering of p53 mRNA targets under oscillating and pulsatile p53 expression.

A, B p53 target genes were clustered via fuzzy c-means clustering according to their mRNA expression profiles under (A) oscillatory or (B) rising p53 expression. Differential mRNA expression was defined as fold change > 1.5 and FDR < 0.2 (t-test, Benjamini–Hochberg corrected) based on two independent experiments. mRNAs were clustered based on their normalized time traces (z score) into five expression clusters under oscillatory and rising p53.

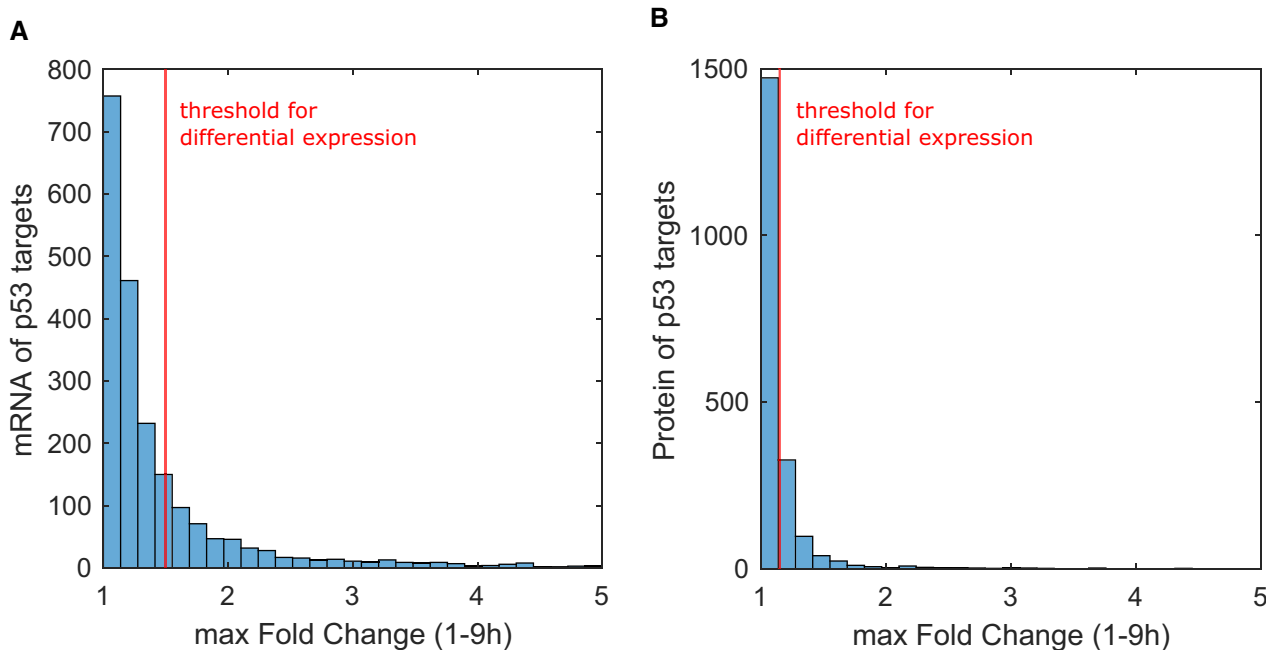


Figure EV2. Fold change in expression of mRNA and protein levels of p53 targets.

A, B Maximum fold-change (FC) distribution of mRNA and protein levels of p53 targets under both oscillatory and rising p53. Maximum fold change is calculated as the largest FC value from 1 to 9 h. Red vertical lines indicate fold-change threshold to consider an mRNA ($FC > 1.5$) or protein ($FC > 1.15$) differentially expressed.

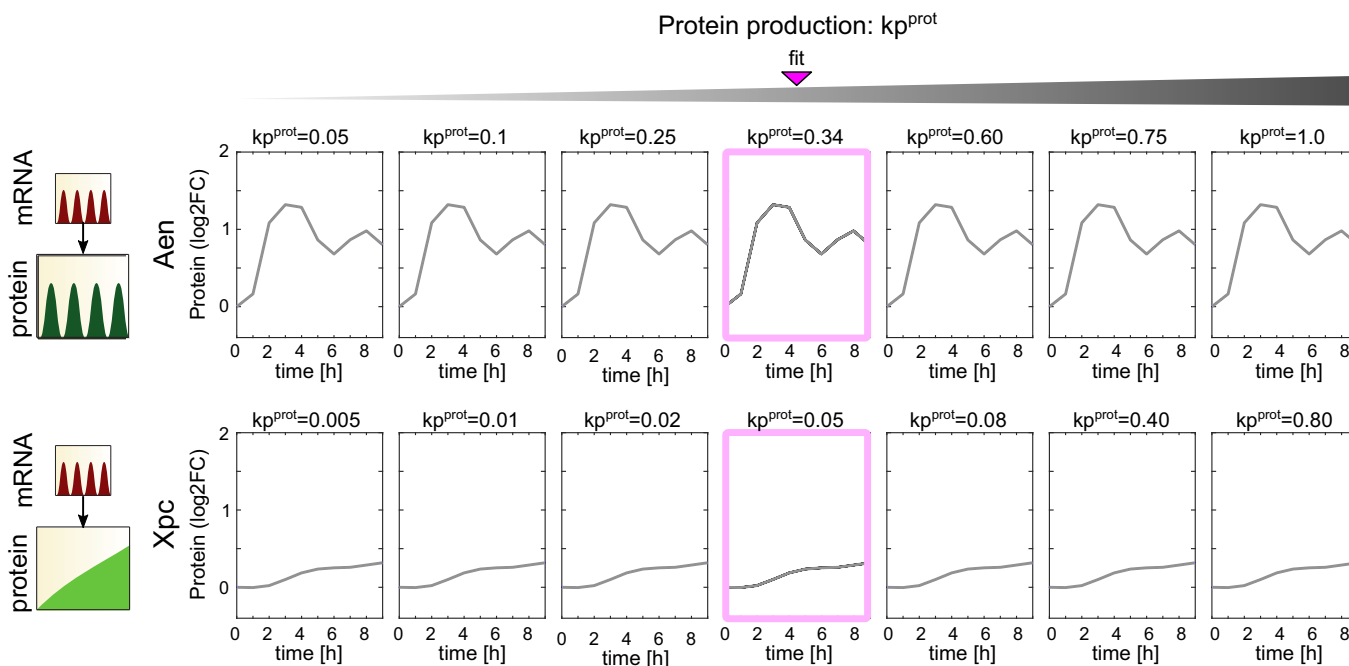


Figure EV3. Predicted protein expression trajectories of two representative p53 target genes for different values of k_p^{prot} .

Protein expression trajectories for targets showing the mRNA and protein dynamics indicated at the left were modeled for the indicated values of k_p^{prot} (with k_d^{prot} fixed at the value determined in Fig 3C). Pink box shows the value of k_p^{prot} that best fits the experimentally measured protein levels.

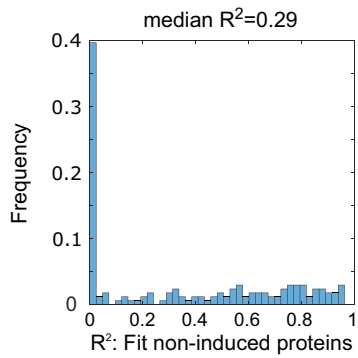


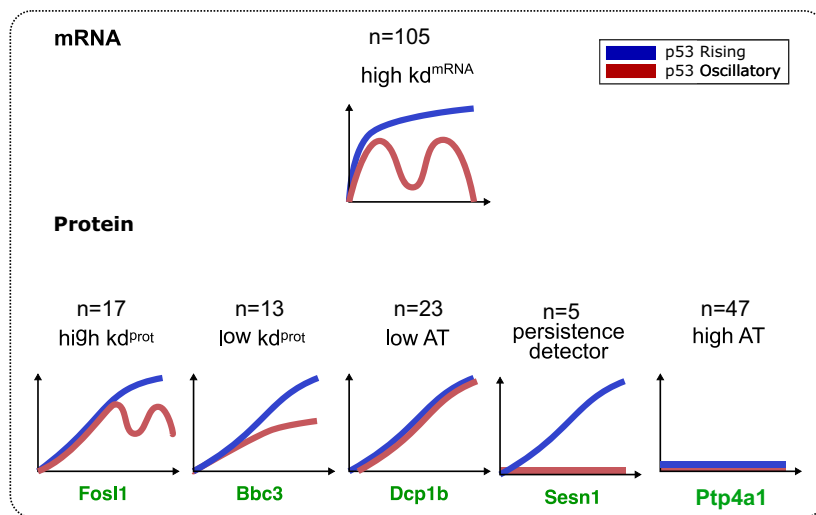
Figure EV4. Distribution of R^2 values for the fitting of expression of p53 target proteins not induced under oscillatory conditions.

All proteins that were detectable but not induced under oscillatory p53 were fit for k_p^{prot} and k_d^{prot} based on mass spectrometry data collected under oscillatory conditions. The distribution of R^2 values for these fits is shown.

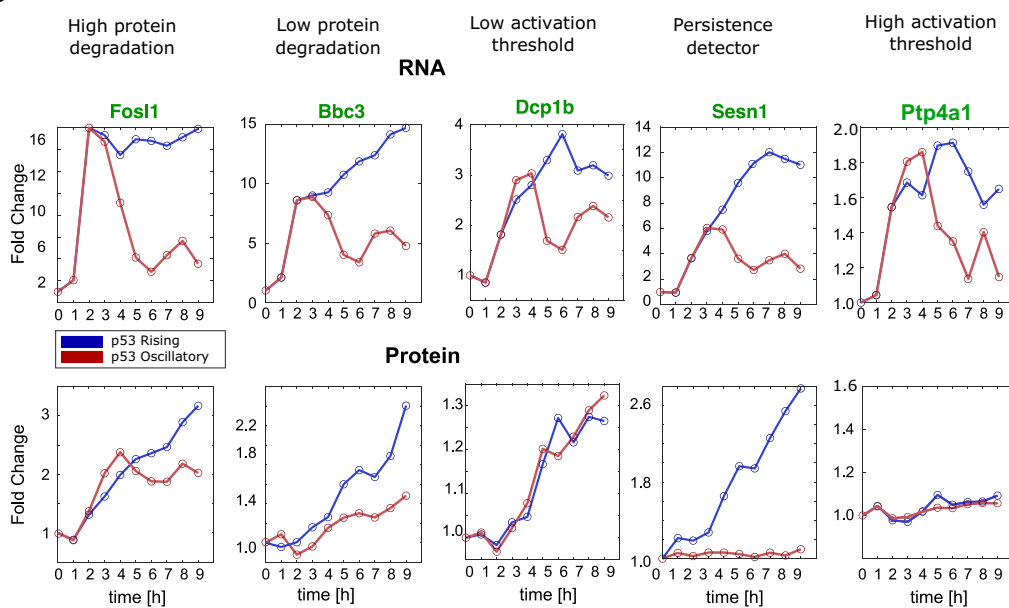
Figure EV5. Expanded view of mechanisms decoding p53 dynamics.

- A Schematics showing relationship between dynamical mRNA and protein responses for oscillatory mRNA.
- B Four targets with similar mRNA expression profiles—high mRNA degradation rate—but distinct protein profiles due to differences in protein degradation rates, activation thresholds (AT), or existence of cFFLs are shown.
- C, D Venn diagrams showing exclusive or pervasive induction of mRNA and protein. Fifteen percent of mRNA ($28/191 = 15\%$) and 20% ($16/82 = 20\%$) of proteins show exclusive induction. A total of 109 of the 191 mRNAs in (C) failed to induce proteins under either p53 dynamic.

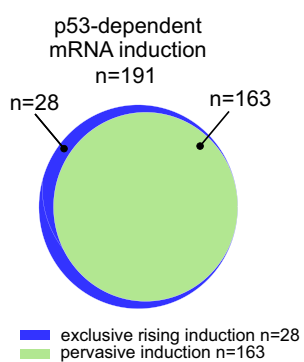
A



B



C



D

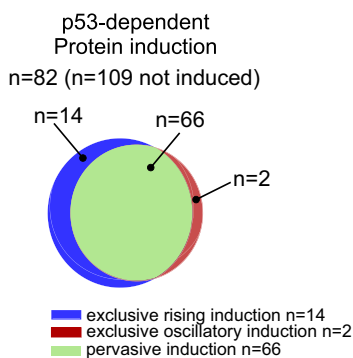


Figure EV5.