

Figure S1, Related to Figure 1: A model of p53-mdm2 oscillations suggests that Mdm2 transcription and p53 degradation regulate the period of p53 oscillations. (A) Schematic of a mathematical model including the core p53 and MDM2 feedback loop. (B) The indicated parameters were varied +/- 5 log2 around parameters that approximated the human-like oscillatory period (C) the dependency between each parameter range and period for parameter sets that show oscillations.



Figure S2, Related to Figure 3: Treatment of human and mouse cells with Nutlin3 results in different dynamics. Human (MCF7) and Mouse (NIH3T3) cells expressing p53-YFP were treated with  $5\mu$ M Nutlin3 and the response was quantified in individual cells over time. Faint lines indicate single cells. Bold lines indicate the average (N>30).



**Figure S3, Related to Figure 4: p53 binding site conservation.** (A, B) The conservation of p53 binding sites across eight species (with opossum included as an outgroup) was computed from ChIP-Seq data sets (4 human, 2 mouse) and scoring of conservation of binding sites with a PWM matrix. Bars represent the average of the datasets. Dots represent individual datasets. (C) The sequence of p53 binding site in the MDM2 promoter across species.