

Abstract Submitted  
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**Experimental test of specific predictions of a model for the oscillatory response of p53 to DNA damage.** GUSTAVO STOLOVITZKY, IBM T.J. Watson Research Center, Yorktown Heights, New York; JOHN WAGNER, J. JEREMY RICE, IBM T.J. Watson Research Center, Yorktown Heights, New York, LAN MA, The Univ. of Texas Southwestern Medical Center, Dallas, Texas, WENWEI HU, ZHAOHUI FENG, Cancer Inst of New Jersey, Univ. of Med and Dent. NJ, New Brunswick, New Jersey, ARNOLD LEVINE, School of Natural Sciences, Institute for Advanced study, Princeton, New Jersey — We have proposed a model for radiation-induced oscillations of the p53-mdm2 system that makes specific predictions about the range of both p53 and mdm2 transcription rates that support oscillation. Our model predicts that in cells with a polymorphism in the mdm2 gene (SNP309) that enhances mdm2 transcription levels, oscillations disappear. The kinetics of the p53 and Mdm2 levels measured in cells with different genotype at the SNP309 locus show that oscillations of p53 and Mdm2 are observed in the cells wild type for mdm2 SNP309 but not in cells homozygous for mdm2 SNP309. By using H1299 cell line expressing wild-type p53 under a tetracycline-regulated promoter we found that only when p53 levels are in a certain range, oscillation can be observed after stress. This study provides evidence that proper range of the p53 and Mdm2 levels are required for the coordinated p53-Mdm2 oscillation upon stress.

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