Abstract Submitted for the MAR17 Meeting of The American Physical Society

An adaptive molecular timer in p53-meidated cell fate decision<sup>1</sup> XIAO-PENG ZHANG, PING WANG, FENG LIU, WEI WANG, Nanjing University — The tumor suppressor p53 decides cellular outcomes in the DNA damage response. It is intriguing to explore the link between p53 dynamics and cell fates. We developed a theoretical model of p53 signaling network to clarify the mechanism of cell fate decision mediated by its dynamics. We found that the interplay between p53-Mdm2 negative feedback loop and p53-PTEN-Mdm2 positive feedback loop shapes p53 dynamics. Depending on the intensity of DNA damage, p53 shows three modes of dynamics: persistent pulses, two-phase dynamics with pulses followed by sustained high levels and straightforward high levels. Especially, p53 shows twophase dynamics upon moderated damage and the required number of p53 pulses before apoptosis induction decreases with increasing DNA damage. Our results suggested there exists an adaptive molecular timer that determines whether and when the apoptosis switch should be triggered. We clarified the mechanism behind the switching of p53 dynamical modes by bifurcation analysis. Moreover, we reproduced the experimental results that drug additions alter p53 pulses to sustained p53 activation and leads to senescence. Our work may advance the understanding the significance of p53 dynamics in tumor suppression.

<sup>1</sup>This work was supported by National Natural Science Foundation of China (Nos. 11175084, 11204126 and 31361163003).

Xiao-Peng Zhang Nanjing University

Date submitted: 08 Nov 2016

Electronic form version 1.4