

Author's Accepted Manuscript

On p53 Revival using System Oriented Drug Dosage Design

Muhammad Haseeb, Shumaila Azam, A.I. Bhatti, Rizwan Azam, Mukhtar-Ullah, Sahar Fazal



PII: S0022-5193(16)30416-7
DOI: <http://dx.doi.org/10.1016/j.jtbi.2016.12.008>
Reference: YJTBI8891

To appear in: *Journal of Theoretical Biology*

Received date: 17 December 2015
Revised date: 26 November 2016
Accepted date: 10 December 2016

Cite this article as: Muhammad Haseeb, Shumaila Azam, A.I. Bhatti, Rizwan Azam, Mukhtar-Ullah and Sahar Fazal, On p53 Revival using System Oriented Drug Dosage Design, *Journal of Theoretical Biology*, <http://dx.doi.org/10.1016/j.jtbi.2016.12.008>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

On p53 Revival using System Oriented Drug Dosage Design

Muhammad Haseeb^{1,4*}, Shumaila Azam¹, A I Bhatti², Rizwan Azam², Mukhtar-Ullah³, Sahar Fazal¹

¹Department of Bioinformatics and Biosciences, Capital University of Science & Technology, Islamabad, Pakistan

² CASPR, Department of Electronics Engineering, Capital University of Science & Technology, Islamabad, Pakistan

³Department of Electrical Engineering, National University of Computer & Emerging Sciences, Islamabad, Pakistan

⁴Department of Molecular Science and Technology, Ajou University, Suwon, Korea

aamer987@gmail.com

Abstract

We propose a new paradigm in the drug design for the revival of the p53 pathway in cancer cells. It is shown that the current strategy of using small molecule based Mdm2 inhibitors is not enough to adequately revive p53 in cancerous cells, especially when it comes to the extracting pulsating behavior of p53. This fact has come to notice when a novel method for the drug dosage design is introduced using system oriented concepts. As a test case, small molecule drug Mdm2 repressor Nutlin 3a is considered. The proposed method determines the dose of Nutlin to revive p53 pathway functionality. For this purpose, PBK dynamics of Nutlin have also been integrated with p53 pathway model.

The p53 pathway is the focus of researchers for the last thirty years for its pivotal role as a frontline cancer suppressant protein due to its effect on cell cycle checkpoints and cell apoptosis in response to a DNA strand break. That is the reason for finding p53 being absent in more than

Download English Version:

<https://daneshyari.com/en/article/5760102>

Download Persian Version:

<https://daneshyari.com/article/5760102>

[Daneshyari.com](https://daneshyari.com)