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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