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SIMULATION ANALYSIS OF THE ATR MODULE AS A DETECTOR OF UV-INDUCED DNA DAMAGE

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ABSTRACT

Maintaining the integrity of the DNA in the cell is essential for the proper functioning of the organism. For this purpose detection, amplification and transduction of the signal about DNA damage to the effector module is necessary. This results with cell cycle arrest, DNA repair or apoptosis. In some of the eukaryotic cells, like human, two modules play roles as DNA damage detectors: ATM (ataxia telangiectasia mutated), which responds to the formation of double DNA strand breaks and ATR (ataxia telangiectasia mutated and Rad3-related), which is responsible for detecting single-strand damage. Simulation analysis of a constructed mathematical model of ATR pathway is a subject of this study. Our results show that ATR is an effective system for damage detection and amplification of the signal. The activation of this module is fast: detection takes place within a few seconds after the occurrence of the damage. The created novel mathematical model explains the mechanism of single-strand breaks detection, enables testing of the impact of modifications of proteins belonging to the ATR-p53 signaling pathway. Additionally the model explains that the basic activation of p53 protein signaling pathway observed in cells, may be caused by persistent cellular stress levels.

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