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# p16/Rb Pathway Plays Critical Role in the Inhibition of Gh3 Cell Cycle Induced by T-2 Toxin

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T-2 toxin is a worldwide trichothecenetoxin and can cause various toxicities. T-2 toxin is involved in G1 phase arrest in several cell lines but molecular mechanism is still not clear. In present study, we used rat pituitary GH3 cells to investigate the mechanism involved in cell cycle arrest against T-2 toxin (40 nM) for 12, 24, 36 and 48 has compared to control cells. GH3 cells showed a considerable increase in reactive oxygen species (ROS) as well as loss in mitochondrial membrane potential (ΔYm) upon exposure to the T-2 toxin. Flow cytometry showed a significant time-dependent increase in percentage of apoptotic cells and gel electrophoresis showed the hallmark of apoptosis oligonucleosomal DNA fragmentation. Additionally, T-2 toxin-induced oxidative stress and DNA damage with a time-dependent significant increased expression of p53 favors the apoptotic process by the activation of caspase-3 in T-2 toxin treated cells. Cell cycle analysis by flow cytometry revealed a time-dependent increase of G1 cell population along with the significant time-dependent up-regulation of mRNA and protein expression of p16 and p21 and significant down-regulation of cyclin D1, CDK4 and p-RB levels further verify the G1 phase arrest in GH3 cells. Morphology of GH3 cells by TEM clearly showed the damage and dysfunction to mitochondria and the cell nucleus. These findings for the first time demonstrate that T-2 toxin induces G1 phase cell cycle arrest by the involvement of p16/Rb pathway, along with ROS mediated oxidative stress and DNA damage with p53 and caspase cascade interaction, resulting in apoptosis in GH3 cells.

**Keywords:** Cell cycle· T-2 toxin· G1 phase arrest· p16/Rb pathway· Reactive oxygen species· p53

## Biography:

Dr. Xu Wang got the doctor's degree from Huazhong University of Science and Technology, China in 2006. During 2007-2015, he served as lecturer, associate Professor of National Reference of National Reference Laboratory of Veterinary Drug Residues of Huazhong Agriculture University (HZAU) in China. During 2015-2016, Dr. Xu has studied as a visiting scholar at Department of Toxicology and Pharmacology, Faculty of Veterinary Medicine, Universidad Complutense de Madrid, Spain. Since 2016, he served as a full Prof. in HZAU. His research interest is metabolism, pharmacokinetics, toxicokinetics, immunotoxicity and food evaluation. Dr. Xu has published more than 80 peer-reviewed articles in the field of metabolism and toxicology.