ARSENIC TRIOXIDE MODULATES P38 MAPK PATHWAY OF SIGNALING IN ACUTE PROMYELOCYTIC LEUKEMIA

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Abstract: Arsenic trioxide (ATO) has been used successfully in the treatment of acute promyelocytic leukemia (APL) patients alone or combination with all trans retinoic acid (ATRA). It induced oxidative stress and DNA damage leading to cell cycle arrest and apoptosis in APL cells. However, ATO induced P38 MAPK signaling cascade involvement in cell cycle arrest and apoptosis are poorly understood. We hypothesized that ATO induced cell cycle regulation and apoptosis mediated by P38 MAPK signaling in APL cells. To test the hypothesis, we used western blotting, confocal imaging and other molecular techniques for investigation of ATO induced modulation of p38 MAPK signaling cascade in APL cells. We found that the phosphorylation levels of p38 and Erk modulated in HL-60 and NB4 cells treated with ATO concentration dependent manner. Whereas, phosphorylation of JNK was increased in HL-60 cells, but down regulated in NB4 cells concentration dependent manner. Our specific inhibitor studied of p38 and JNK phosphorylation revealed p38 MAPK signaling pathway involved in ATO induced cell cycle regulation and apoptosis in APL cells. It is a novel target for treatment of APL patients by ATO and also designing of new anti-leukemic drugs.

Keywords: ATO, p53, p-JNK, p-P38MAPK, p-Erk, APL treatment.

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