

## Biochemical studies of the effect of arsenic trioxide on Ehrlich ascites tumor

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**Background:** Hexokinase 2 enzyme catalyzes the rate-limiting step in glycolysis. It is overexpressed in several carcinomas including breast cancer to sustain energy for rapidly dividing cells and associates with chemoresistance. However, impact of chemo drugs alone or in combination on hexokinase activity and autophagic cell death is unclear. Arsenic trioxide ( $\text{As}_2\text{O}_3$ ) (ATO) is a metalloid with potent antineoplastic effects in several types of cancer especially acute promyelocytic leukemia and breast cancer. Due to the cytotoxicity and low efficacy of ATO when it is used alone, a combination of ATO with other chemotherapeutic drugs may provide a rational basis for novel therapeutic combinations.

**Aim:** Examine the specific cellular events that account for differential effects of ATO on cancer cell viability and the possible therapeutic combinations remain to be well-defined. **Materials and Methods:** In this report, we used an *in vivo* murine adenocarcinoma model to validate the effects of  $\text{As}_2\text{O}_3$  and cisplatin on hexokinase activity and autophagic cancer cell death. **Results:** We found that the two drugs inhibit hexokinase activity and induce autophagic marker, beclin 1 expression. Interestingly, combining  $\text{As}_2\text{O}_3$  with cisplatin synergistically enhanced these effects and alleviated oxidative stress often encountered in  $\text{As}_2\text{O}_3$  treatment. Altogether, our data provide direct evidence that inhibition of hexokinase activity and induction of autophagic cell death are mediating the antineoplastic effects of  $\text{As}_2\text{O}_3$  and cisplatin. **Conclusion:** findings raise the potential of combining  $\text{As}_2\text{O}_3$  with cisplatin as an approach to augment cisplatin-induced cell death and combat cisplatin chemo-resistance in cancer.

**Keywords:** Arsenic Trioxide; Autophagy; Beclin 1; Cisplatin; Hexokinase

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