題名:Human carcinogenicity of inorganic arsenic.

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摘要:Arsenic toxicity is dependent on its chemical species. In humans, the bladder is one of the primary target organs for arsenic-induced carcinogenicity. However, little is known about the mechanisms underlying arsenic-induced carcinogenicity, and what arsenic species are responsible for this carcinogenicity. The present study aimed at comparing the toxic effect of DMMTA(V) with that of inorganic arsenite (iAs(III)) on cell viability, uptake efficiency and production of reactive oxygen species (ROS) toward human bladder cancer EJ-1 cells. The results were compared with those of a previous study using human epidermoid carcinoma A431 cells. Although iAs(III) was known to be toxic to most cells, here we show that iAs(III) (LC(50)=112 microM) was much less cytotoxic than DMMTA(V) (LC(50)=16.7 microM) in human bladder EJ-1 cells. Interestingly, pentavalent sulfur-containing DMMTA(V) generated a high level of intracellular ROS in EJ-1 cells. However, this was not observed in the cells exposed to trivalent inorganic iAs(III) at their respective LC(50) dose. Furthermore, the presence of N-acetyl-cysteine completely inhibited the cytotoxicity of DMMTA(V) but not iAs(III), suggesting that production of ROS was the main cause of cell death from exposure to DMMTA(V), but not iAs(III). Because the cellular uptake of iAs(III) is mediated by aquaporin proteins, and because the resistance of cells to arsenite can be influenced by lower arsenic uptake due to lower expression of aquaporin proteins (AQP 3, 7 and 9), the expression of several members of the aquaporin family was also examined. In human bladder EJ-

1 cells, mRNA/proteins of AQP3, 7 and 9 were not detected by reverse transcription polymerase chain reaction (RT-PCR)/western blotting. In A431 cells, only mRNA and protein of AQP3 were detected. The large difference in toxicity between the two cell lines could be related to their differences in uptake of arsenic species.