P53 AND BCL-2 EXPRESSION AND DNA SYNTHESIS IN BREAST AND LUNG CARCINOMA CELLS EXPOSED TO ARSENIC TRIOXIDE

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Abstract: Arsenic is a semi-metal commonly found in water, soil, and air. The toxicity of arsenic depends upon its valence state. The inorganic form in particular the trivalent state is more toxic than the organic form. The source of human exposure is through drinking water and food. p53 plays a key role in mediating cell response to various stresses, mainly by inducing or repressing a number of genes involved in cell cycle arrest, senescence, apoptosis, DNA repair, and angiogenesis. p53 exerts its anti-proliferative action by inducing reversible or irreversible (senescence) cell cycle arrest or apoptosis. It may also enhance DNA repair and inhibit angiogenesis. Bcl-2 can act as a pro or anti-apoptotic regulator that is involved in wide variety of cellular activities. The Bcl-2 gene has been implicated in several cancers such as melanoma, breast, prostate and lung. Arsenic has also shown to be cytotoxic and able to induce stress-related genes and proteins in a number of cell lines, mainly of the skin and liver. Although arsenic has been reported to cause DNA damage to liver and hematopoietic cells, its effects on breast and lung cells are not well elucidated. The primary objective of this research is to evaluate the effects of arsenic trioxide on p53 and Bcl-2 expression and DNA synthesis in breast and lung carcinoma cells. To achieve this goal, breast cancer (MCF-7) and lung cancer (A549) cells were cultured following standard protocols, and exposed to various doses (0, 2, 4, 6, 8, and 10 µg/ml) of arsenic trioxide for 48h. Thymidine [³H] incorporation was performed to investigate DNA synthesis. Thymidine [³H] incorporation, protein and western blot analyses were performed using standard protocols. The DNA synthesis revealed a dose-response to arsenic trioxide in the lung cell line whereas it revealed a biphasic response in the breast cell line. The Western blot analysis revealed an up-regulation of p53 with the exposure of arsenic trioxide, showing a peak expression at 4µg/ml. Experiments on Bcl-2 expression are underway, and it is anticipated that arsenic exposure would induce its down–regulation in arsenic-treated cells.

Keywords: Arsenic, p53 activation, Bcl-2 repression, MCF-7 and A549 cells

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