Arsenic and Protein Expression: It might help to know the mechanism of As toxicity

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ABSTRACT

Arsenic and Protein Expression: It might help to know the mechanism of As toxicity is described.

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Introduction

One of the largest public health problems at present is the drinking of water containing levels of Inorg-As that are known to be carcinogenic. The chronic ingestion of Inorg-As can result in skin cancer, urinary bladder cancer, lungs cancer, kidneys cancer, liver cancer, and cancer of other human organs 1-6.

The molecular mechanisms of the carcinogenicity and toxicity of inorganic arsenic are not well understood 7-9. Many mechanisms of arsenic toxicity and carcinogenicity have been suggested 1, 7, 10 including chromosome abnormalities 11, oxidative stress 12, 13, altered growth factors 14, cell proliferation 15, altered DNA repair 16, altered DNA methylation patterns 17, inhibition of several key enzymes 18, gene amplification 19 etc. Some of these mechanisms result in alterations in protein expression.

Proteomics is a powerful tool developed to enhance the study of complex biological systems 20. This technique has been extensively employed to investigate the proteome response of cells to drugs and other diseases 21, 22. A proteome analysis of the Na-As (III) response in cultured lung cells found in vitro oxidative stress-induced apoptosis 23.

In one of the study, hamsters were exposed to sodium arsenite (173 mg As/L) in drinking water for 6 days and several protein spots were over expressed and several were under expressed in the livers and urinary bladders of hamsters (Fig.) 24, 25. Hamsters were exposed to sodium arsenite (173 mg As/L) in drinking water for 6 days. The control hamsters were given tap water. The spot pairs of (A) equally expressed, (B) overexpressed, and (C) under expressed proteins in the liver tissues were shown. The amount of the protein is proportional to the volume of the protein peak.

Transgelin was down-regulated, and GST-pi was up-regulated in the urinary bladder tissues of hamsters. In the liver tissues ornithine aminotransferase (OAT) was up-regulated, and senescence marker protein 30 (SMP 30), and fatty acid binding protein (FABP) were down-regulated.

Down-regulation of transgelin has been noted in the urinary bladders of rats having bladder outlet obstruction 26. Ras-dependent and Ras-independent mechanisms can cause the down regulation of transgelin in human breast and colon carcinoma cell lines and patient-derived tumor samples 27. The loss of transgelin expression has been found in prostate cancer cells 28 and in human colonic neoplasms 29. It has been suggested that the loss of transgelin expression may be an important early event in tumor progression and a diagnostic marker for cancer development 26-29.
Over-expression of GST-pi has been found in colon cancer tissues 30. Strong expression of GST-pi also has been found in gastric cancer 31, malignant melanoma 32, lung cancer 33, breast cancer 34 and a range of other human tumors 35. GST-pi has been up-regulated in transitional cell carcinoma of human urinary bladder 36.

OAT has a role in regulating mitotic cell division and it is required for proper spindle assembly in human cancer cell 37. Ornithine amino transferase knockdown in human cervical carcinoma and osteosarcoma cells by RNA interference blocks cell division and causes cell death 37. It has been suggested that ornithine amino transferase has a role in regulating mitotic cell division and it is required for proper spindle assembly in human cancer cells 37.

SMP 30 expressed mostly in the liver. By stimulating membrane calcium-pump activity it protects cells against various injuries 38.

Figure. Three-dimentional simulation of over-and under expressed protein spots in the livers of hamsters using Decyder software.

High levels of saturated, branched chain fatty acids are deleterious to cells and resulting in lipid accumulation and cytotoxicity. FABP expression has protected the cells against branched chain saturated fatty acid 39.

Proteomics would be a powerful tool to know the unknown cellular mechanisms of arsenic toxicity in humans.

References.


