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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 results 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 system [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].

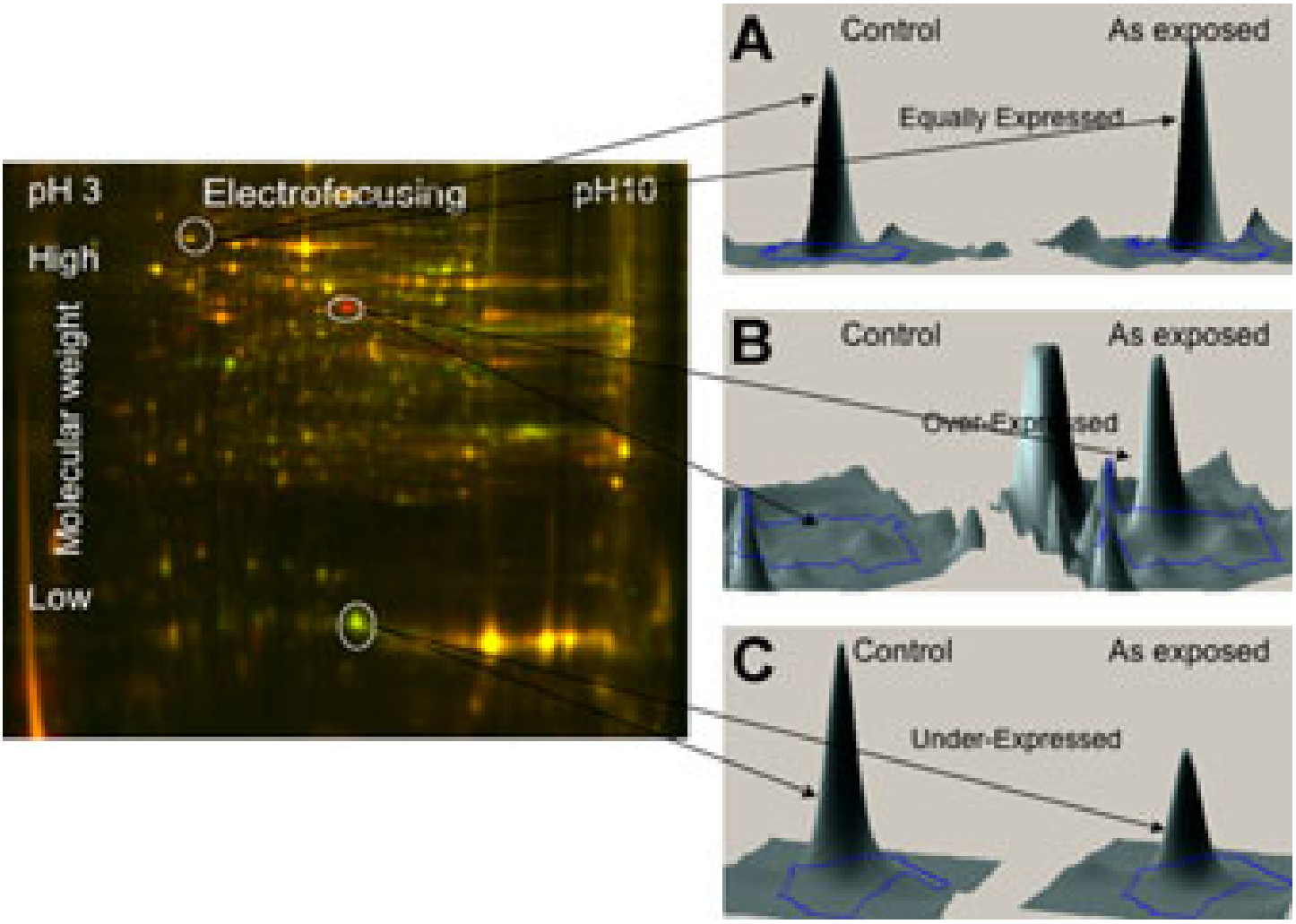

Figure. Three-dimentional simulation of over-and under expressed protein spots in the livers of hamsters using Decyder software.

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].

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.

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