GENOMIC CHANGES IN HUMAN EPIDERMAL CELLS EXPOSED TO ARSENIC TRIOXIDE

Udensi K. Udensi, Barbara G. Graham-Evans, Raphael D. Isokpehi and Hari H. P. Cohly

RCMI Center for Environmental Health & Department of Biology, Jackson State University, Jackson Mississippi 39217, USA

Abstract: Arsenic is recognized as an environmental toxicant of global public health concern and a leading cause of toxicity and carcinogenicity. Arsenic targets the human skin and long-term exposure to arsenic principally through drinking water has been correlated with increased risk to skin cancer. The cellular toxicity of arsenic has been well documented through poisoning incidents and medicinal use. However, due to increased epidemiological reports of arsenic related cancers in places such as southeastern Michigan USA, Taiwan, China, India and Bangladesh, public health concerns about long-term exposure have arisen. The human skin is the critical organ of arsenic toxicity because arsenic has a strong affinity for the keratin proteins and is excreted by desquamation of skin and in sweat. Chronic exposure to arsenic induces sequential changes in the skin epithelium, proceeding from hypopigmentation to hyperkeratosis which may eventually lead to skin cancer. We are using the HaCaT keratinocyte cell line cultured on mitomycin treated 3T3 fibroblast (feeder layer) as a model to study time course (Day 2, 5, 8 and 14) alteration of global gene expression in human epidermal cells exposed to chronic concentration (after 8 passages) of arsenic trioxide. We have established chronic HaCaT cell cultures with 0.5ppm of arsenic trioxide and have designed experiments to investigate DNA damage associated with each passage compared to untreated cells. The long-term goal of the research is to understand the contribution of the epidermal cellular elements of the skin, namely basal keratinocytes and squamous cells to skin cancer. Our approach will allow us to identify potential pathways that are part of the initial response of the cell line after chronic exposure to arsenic trioxide and provide a better integrated picture of how the pathways change as the cells adapt to arsenic. Chronically exposed arsenic trioxide treated cells in the laboratory provides a model to understand the mechanism of arsenic-induced carcinogenesis.

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