ARSENIC SKIN KERATINOCYTE CARCINOGENESIS

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Abstract: Arsenic is a known environment contaminant of public health concern. Exposure to a chronic low dose of arsenic has been reported to induce skin cancer and cancers of the bladder, lung, kidney, and liver. The cancers of the skin associated with arsenic exposure are intraepidermal carcinomas (Bowen disease), squamous cell carcinomas (SCC), basal cell carcinomas (BCC), Merkel cell carcinoma (MCC) and benign skin lesions such as hyperpigmentation and hyperkeratosis, which are the trademarks of chronic arsenic exposure. The adverse effects on health due to chronic arsenic exposure may depend on the cumulative dose of arsenic and different chemical forms of arsenic in drinking water, medication, food or the workplace. Other factors may include population groups, individual susceptibility, genetic factors, age, gender, nutritional status, and lifestyle. Some of the proposed mechanisms of action are: inhibition of enzymes by generating reactive oxygen species that inactivate proteins through direct binding to the sulphydryl group and also binding to vicinal cysteines and the activation of NF-κB. Arsenic induces polymorphisms in several genes encoding members of the GSH transferase (GST) family, interaction with phosphates, DNA damage and alteration of DNA repair, and as a co-carcinogen. Arsenic also interacts with zinc finger motifs of proteins, stimulate cell proliferation, alter DNA methylation and induce aberration in gene expression. The precise mechanism of arsenic-related carcinogenicity is unknown and research in this area is ongoing. It is essential to understand the mechanism of arsenic carcinogenesis so as to determine the appropriate human risk assessment and mitigation model. This review reports the latest advances in the mechanism of arsenic carcinogenicity in skin keratinocytes.

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