

題名:Molecular Epidemiologic Studies on Arsenic-Induced Skin Cancer.

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摘要:Millions of individuals worldwide are chronically exposed to arsenic through their drinking water. In this study, the effect of arsenic exposure and arsenical skin lesion status on genome-wide gene expression patterns was evaluated using RNA from peripheral blood lymphocytes of individuals selected from the Health Effects of Arsenic Longitudinal Study. Affymetrix HG-U133A GeneChip (Affymetrix, Santa Clara, CA) arrays were used to measure the expression of approximately 22,000 transcripts. Our primary statistical analysis involved identifying differentially expressed genes between participants with and without arsenical skin lesions based on the significance analysis of microarrays statistic with an a priori defined 1% false discovery rate to minimize false positives. To better characterize differential expression, we also conducted Gene Ontology and pathway comparisons in addition to the gene-specific analyses. Four-hundred sixty-eight genes were differentially expressed between these two groups, from which 312 differentially expressed genes were identified by restricting the analysis to female never-smokers. We also explored possible differential gene expression by arsenic exposure levels among individuals without manifest arsenical skin lesions; however, no differentially expressed genes could be identified from this comparison. Our findings show that microarray-based gene expression analysis is a powerful method to characterize the molecular profile of arsenic exposure and arsenic-induced diseases. Genes identified from this analysis may provide insights into the underlying

processes of arsenic-induced disease and represent potential targets for chemoprevention studies to reduce arsenic-induced skin cancer in this population.