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MicroRNAs in urothelial cells as potential biomarkers of arsenic exposure and related cancer risk

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Worldwide, millions of people are exposed to potentially carcinogenic levels of arsenic, a metalloid drinking water contaminant with wide-ranging adverse health effects. The mechanisms by which ingested arsenic induces cancer are complex and remain largely unknown. In search of biomarkers of arsenic exposure and related diseases, we focused on arsenic's effects on the expression of microRNAs (miRNAs), small noncoding RNA molecules that control gene expression. Because miRNAs are relatively stable in the harsh urinary milieu, they may serve as easily obtainable biomarkers of arsenic exposure and arsenic-induced bladder and kidney cancer. We therefore evaluated miRNA expression in exfoliated urinary epithelial cells of individuals exposed to arsenic in early childhood. A screen for 20,715 miRNA targets on an Affymetrix 2.0 miR microarray revealed several miRNA targets that showed significant differences in expression between unexposed and currently arsenic exposed Bangladeshi children. The top significant miRNAs from the microarray as well as six additional candidate miRNAs that were previously found to be associated with bladder cancer or kidney cancer were further tested in urothelial samples from early-life arsenic-exposed Chilean adults. miRNA expression was measured using qScript Reverse Transcription Quantitative Polymerase Chain Reaction (RT-qPCR). Of the selected miRNAs that are associated with bladder or kidney cancer, two also showed significant changes in adults exposed to high levels of arsenic during early childhood. We are currently validating whether the expression of these miRNAs remains consistent in time in arsenic-exposed individuals. Future studies will confirm the potential of these miRNAs to predict arsenic-induced cancer risk.

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