Predicting Paths to Prostate Cancer: The Role of Inorganic Arsenic in Estrogen Receptor Mediated Signaling Pathways

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Although studies have found that inorganic arsenic (iAs), a potent carcinogen and estrogen-mimicking endocrine disruptor, is directly associated with prostate cancer incidence and mortality, the mechanism by which iAs affects prostate stem-progenitor cells remains unclear. Moreover, it has yet to be determined whether the interaction between iAs and estrogen receptors (ERs) in prostate stem-progenitor cells and whether this potential signaling induces carcinogenic effects on the prostate gland. Thus, the aim of this study was to identify whether biochemical signals are transduced via ERs in normal prostate stem-progenitor cells due to iAs exposure. Prostate stem-progenitor cells were derived from normal human prostate epithelial cells, exposed to 1μM iAs +/- ER inhibitors ICI, MPP, or PHTPP for 60 minutes and 24 hours, and harvested after 7 days. Western blotting was performed to measure phosphorylation of kinase proteins involved in ER-mediated signaling pathways, and RT-qPCR was performed to measure the expression of genes regulated by those pathways. The results suggested that iAs induces differential effects in normal prostate stem-progenitor cells with short-term, rapid exposure and long-term, sustained exposure. While the data revealed that iAs might interact with ERs at the 24 hour time point by activating phosphatases to withhold phosphorylation, the data appeared to be variable at the 60 minute time point.