ARSENIC TRIOXIDE INDUCES CHANGES IN INDUCED PLURIPOTENT STEM CELLS

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Abstract: Induced pluripotent stem cells (iPSCs) are an artificially derived type of pluripotent stem cell from a non-pluripotent cell, typically an adult somatic cell, by inducing a "forced" expression of certain genes[1]Induced pluripotent stem cells (iPSCs) are somatic cells reprogrammed to a pluripotent or embryonic stem cell–like state with factors important for maintaining the defining properties of embryonic stem cells. IPSCs show many of the same characteristics as natural pluripotent stem cells, such as the expression of certain stem cell genes and proteins, chromatin methylation patterns, doubling time, embryoid body formation, teratoma formation, viable chimera formation, potency and differentiability. IPSCs are a hopeful therapeutic model; there is a critical need to determine the effect that environmental factors will have on reprogrammed cells in a self-renewing induced state. Effects of arsenic on skin cells have been studied extensively, however, its effect on growth and molecular pathways of iPSCs is uncertain. Investigating the effect that arsenic will have on human (h) iPSCs will further our knowledge on its potential mechanism of action. We hypothesize that arsenic will induce alterations in gene expression involved in pluripotency and self renewal of human induced pluripotent stem cells (hiPSCs). MTT assay and trypan blue exclusion assay will be used to determine the relative toxicity of arsenic trioxide (ATO) on hiPSCs. By determining relative toxicity, information will be gathered on how much ATO will affect proliferation and viability of reprogrammed-iPSC. Pluripotency and self-renewal are traits regulated by a number of cell signaling pathways. In hESCs, the predominant signaling pathways involved are TGF-β, FGFR, and Wnt resulting in the expression and activation of Oct-4, Sox2, and Nanog. Arsenic is known to affect signal transduction pathways and cause a wide range of alterations leading to apoptosis and other immunotoxic effects. Overall, it is anticipated that this study will provide important insight into the carcinogenic potential of arsenic on reprogramming, self-renewal and continued pluripotency of human induced pluripotent stem cells.

Keywords: Human Induced Pluripotent Stem Cells, Arsenic, pluripotency, differentiation

Acknowledgements: This research was financially supported by the NIH-RCMI Grant No. 5G12RR13459-15, NIH-NIMHD Grant No. 8G12MD007581-15.