Arsenite Inhibits Adipogenic Differentiation of Mesenchymal Stem Cells by Down-regulation of CCAAT Enhancer-Binding Proteins through MEK dependent Pathway

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Abstract

Predominantly in bone marrow two distinct stem cell types are reside first hematopoietic stem cells responsible for hematopoiesis and non hematopoietic stem cells such as mesenchymal stem cells (MSCs) responsible for maintenance of the non-hematopoietic bone marrow elements such adipocytes and osteogenic cells. Transcription factors drive MSCs to differentiate into either osteoblasts or adipocytes, and the differentiation of each lineage appears to be mutually exclusive and transcriptionally regulated. The balance between osteoblast and adipocyte differentiation is disrupted in various human diseases. Moreover, presences of environmental carcinogens can lead imbalance between these two antagonistic processes. Arsenite is a double edged sword: on the one edge it is a well recognized human carcinogen (IARC, 1980) and on the other edge it tested successfully in the treatment of acute promyelocytic leukemia. Present study was designed to explore the effect (s) of arsenite on the adipogenic differentiation potential of MSCs. Materials and Methods: MSCs were differentiated into the adipogenic lineage using dexamethasone in the presence or absence of arsenite. The effects of arsenite on lipid accumulation, adipogenic transcription factors such as C/EBP family proteins, PPAR-γ and MEK expression were investigated. Results: arsenite inhibited adipocyte differentiation as evidenced by decreased lipid accumulation, down-regulation master adipogenic transcription factors such as C/EBP family proteins and PPAR which is mediated by via the MEK dependent pathway. Conclusion: Arsenite has significant effects on the adipogenic differentiation potential of mesenchymal stem cells.