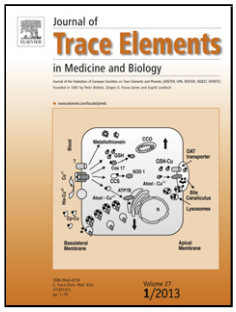

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Authors: M. Ramdas, S. Sharma, D. Kaul, A. Bhatia

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Possible role of miR-2909 RNomics in Arsenic mediated pancreatic β-cell dysfunction

BY

M. Ramdas, S. Sharma, D. Kaul *, A. Bhatia

Department of Experimental Medicine & Biotechnology, Post-graduate Institute of Medical Education & Research,CHANDIGARH-160012 (INDIA)

*Author for correspondence & reprint request.
E-mail: dkaul235@gmail.com, Fax: +91-0172-2744401

ABSTRACT

Chronic exposure of humans to inorganic arsenic as a potential risk for the incidence of diabetes has received wide attention. However, the biological mechanism through which arsenic plays a role in the development of diabetes is still being evaluated. One of the hallmark of diabetes is the β-cell dysfunction followed by the changes in the insulin secretion. Pancreatic duodenal homeobox 1 (PDX1) has been widely recognized to play crucial role in the β-cell development, survival and its regulation of insulin gene expression. Many of the arsenic mediated cellular affects have been shown to be regulated by miR-2909 in vitro. Our present study provides evidence to reveal that arsenic affects miR-2909 expression in the pancreatic β-cell and this novel miRNA regulates PDX1 transcriptional expression indirectly through genes coding for c-Jun, MafA, PI3K and directly at the translational level by targeting the PDX1 mRNA. We provide further evidence for this miR-2909RNomics in pancreatic tissue obtained from NOD mice where the expression of miR-2909 was high compared to the control mice. Keeping in view the fact that arsenic is known to cause β-cell dysfunction and most of the cellular effects of arsenic have been shown to be mediated through miR-2909 RNomics,