Mol Cell Biochem (2013) 382:225–235
DOI 10.1007/s11010-013-1738-z

# Distinctive microRNA expression signatures in proton-irradiated mice

**Shahid Yar Khan · Muhammad Akram Tariq · James Patrick Perrott · Christopher Drew Brumbaugh · Hyunsung John Kim · Muhammad Imran Shabbir · Govindarajan T. Ramesh · Nader Pourmand**

Received: 16 April 2013 / Accepted: 14 June 2013 / Published online: 2 July 2013


**Abstract** Proton particles comprise the most abundant ionizing radiation (IR) in outer space. These high energy particles are known to cause frequent double- and single-stranded DNA lesions that can lead to cancer and tumor formation. Understanding the mechanism of cellular response to proton-derived IR is vital for determining health risks to astronauts during space missions. Our understanding of the consequences of these high energy charged particles on microRNA (miRNA) regulation is still in infancy. miRNAs are non-coding, single-stranded RNAs of $\sim$22 nucleotides that constitute a novel class of gene regulators. They regulate diverse biological processes, and each miRNA can control hundreds of gene targets. To investigate the effect of proton radiation on these master regulators, we examined the miRNA expression in selected mice organs that had been exposed to whole-body proton irradiation (2 Gy), and compared this to control mice (0 Gy exposure). RNA was isolated from three tissues (testis, brain, and liver) from treated and control mice and subjected to high-throughput small RNA sequencing. Bioinformatics analysis of small RNA sequencing data revealed dysregulation of ($p < 0.05$; 20 up- and 10 down-regulated) 14 mouse testis, 8 liver, and 8 brain miRNAs. The statistically significant and unique miRNA expression pattern found among three different proton-treated mouse tissues indicates a tissue-specific response to proton radiation. In addition to known miRNAs, sequencing revealed differential expression of 11 miRNAs in proton-irradiated mice that have not been previously reported in association with radiation exposure and cancer. The dysregulation of miRNAs on exposure to proton radiation suggest a possible mechanism of proton particles involvement in the onset of cell tumorgenesis. In summary, we have established that specific miRNAs are vulnerable to proton radiation, that such differential expression profile may depend upon the tissue, and that there are more miRNAs affected by proton radiation than have been previously observed.

**Keywords** miRNA · Differential expression · Proton radiation · Mice

S. Y. Khan · M. A. Tariq · J. P. Perrott · C. D. Brumbaugh · H. J. Kim · M. I. Shabbir · N. Pourmand (✉)
Department of Biomolecular Engineering, University of California Santa Cruz, Santa Cruz, CA 95064, USA
e-mail: shahidyarkhan@hotmail.com; pourmand@soe.ucsc.edu

M. A. Tariq
Center for Bionanotechnology and Environmental Research, Texas Southern University, Houston, TX 77004, USA

*Present Address:*
M. I. Shabbir
Department of Bioinformatics and Biotechnology, Faculty of Basic Applied Sciences, International Islamic University, Sector H10, Islamabad, Pakistan

G. T. Ramesh
Molecular Toxicology Laboratory, Center for Biotechnology and Biomedical Sciences, Norfolk State University, 700 Park Avenue, Norfolk, VA 23504, USA

## Introduction

The space radiation environment consists mainly of trapped particle radiation, solar particle radiation, galactic cosmic radiation (GCR), and also ionizing radiation (IR). IR is a well-known modality used in cancer treatment that also induces oxidative genotoxic stress. It is known that IR causes cellular damage by either directly damaging DNA, or by the formation of free radicals [1]. Among IR, protons