UAEU جامعة الإمارات العربية المتحدة United Arab Emirates University

The College of Graduate Studies and the College of Medicine and Health Sciences Cordially Invite You to a

Master Thesis Defense

Entitled

UNDERSTANDING THE ROLE OF EPSTEIN-BARR VIRUS ENCODED RNA-1 (EBER-1) IN THE CELL PROLIFERATION

by

Yasmeen Atta Abdelmoulla

Faculty Advisor

Prof. Gulfaraz Khan, Department of Microbiology and Immunology
College of Medicine and Health Sciences

Date & Venue

01:00 PM
Wednesday, 18 December 2019
Yanah Theater, College of Medicine Building

Abstract

Epstein-Barr virus (EBV) is a human herpesvirus that infects and persists in > 90% of human adults, generally without causing disease. However, EBV has oncogenic properties and is associated with several malignancies of epithelial and lymphoid origin. The details of the molecular steps leading to these different malignancies are poorly understood. It is believed that some of the EBV latent gene products are involved. Two small EBV-encoded RNAs, referred to as EBER1 and EBER2 have been shown to be expressed in all forms of EBV latent infection. These non-polyadenylated and non-protein coding RNAs are by far the most abundant transcripts expressed in EBV infected cells (>106 copies), but their function remains unknown. Although, not directly involved in cell transformation, a number of studies have reported that these RNAs may be involved in inhibiting apoptosis and providing a proliferative advantage to EBV infected cells. The molecular mechanisms involved in these processes are unclear. The aim of this study was to investigate the role of EBER1 in cell proliferation. We prepared stable EBER1 transfectants of different cell types (epithelial, B-cell and T-cell), together with corresponding control cell lines transfected with the control plasmid only. After confirming that EBER1 was expressed in all EBER1 transfected cells, we investigated their proliferative properties using a range of different approaches and methodologies. Cell proliferation was measured by trypan blue exclusion assay, after subjecting the cells to either normal growth requirements or serum-deprived condition. ATP activity, as an indicator of cell proliferation, was measured using Glo-cell viability assay. Soft agar assay was used to determine the colony forming ability of EBER1 transfected cells. Molecular mechanism underlying EBER1 induced proliferation was assessed by Real-Time qPCR, immunocytochemistry and western blot for known proliferation markers, namely Ki67, PCNA and MCM2. Finally, in an attempt to understand the potential intracellular pathways that may be activated in EBER1 transfected cells, we examined for the expression of genes involved in cell proliferation using microarray methodology. The results from these investigations indicated that EBER1 transfected cells, compared to controls, had higher ATP activity, proliferated at significantly higher rate, expressed higher levels of RNAs and proteins associated with cell proliferation and formed larger and more colonies in soft agar. Our study also suggested that EBER1 could be inducing some of these changes by triggering the production of pro-inflammatory cytokines and anti-apoptotic signals.

Keywords: EBV, Epstein-Barr virus encoded RNA-1 (EBER1), cell proliferation, Ki67, PCNA, MCM2.