EBV LATENCY III PROGRAM INDUCES EXPRESSION OF HERVK(HML2) LOCI IN BURKITT LYMPHOMA CELL LINES

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Burkitt Lymphoma (BL) is the most common type of non-Hodgkin lymphoma (NHL) in children and a subset of these pediatric BL is associated with Epstein-Barr Virus (EBV) infection [1]. Following infection of B cells, EBV can establish different latency programs by expressing varying degrees of viral genes. The latency III program is defined by expression of most viral genes, many of which support cell survival [2]. While some of these viral genes have been associated with EBV-mediated oncogenesis, host factors have also been implicated [3]. Human endogenous retroviruses (HERVs) contribute up to 8% of the human genome and their expression is tightly controlled in healthy tissue. However, previous research has shown that the expression of these retroviral sequences is dysregulated after exogenous viral infection, including EBV, and in various malignancies [4,5]. Members of the HERVK(HML2) family have been shown to encode two oncogenes: Rec and Np9 [6,7]. To determine whether EBV latency III program induces expression of Np9-encoding HERVK(HML2) transcripts, we performed RNA-seq on matched Latency I/Latency III pairs from two different BL cell lines, Mutu and Kem. We utilized a bioinformatic tool, Telescope, to analyze differential expression of locus-specific retroelements between latency programs [8]. We show that Mutu cell lines expressing Latency III viral genes upregulated the expression of 3 HERVK(HML2) loci and downregulated 3 loci. Similarly, Kem cell lines in Latency III upregulated 3 loci and downregulated 7 loci. Although none of the Latency III upregulated HERVK(HML2) transcripts were shared between cell lines, each induced upregulation of HERVK(HML2) loci with coding potential for the Np9 oncogene. These results demonstrate that Latency III EBV gene expression may promote the expression of HERVK(HML2) loci encoding the Np9 oncogene. This finding may serve as a novel target for the treatment of EBV+ lymphoma.

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