Epstein-Barr virus enhances sensitivity of Burkitt Lymphoma Akata cells to etoposide


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Burkitt lymphoma (BL) is usually associated with latent EBV chronic infection. Even though resistance to apoptosis has been described in acute EBV models of infection, the effect of latent EBV infection on apoptosis induced by anti-cancer drugs is not well defined. To determine this, we have studied the apoptotic responses of the Akata EBV- and its parental type I latency EBV+ cell line [1, 2].

The responses to etoposide of Akata EBV+ cells (with basal or siRNA downregulation of EBNA-1) and of Akata EBV- cells were analysed (trypan blue). Apoptosis (TUNEL assay and Western Blot-WB), cellular and viral protein expression were assessed (WB and/or Immunofluorescence). EBNA-1, Bcl-xL and Mcl-1 mRNAs were quantified (qPCR). MG132 and zVAD.fmk were used to study degradation of BCL-XL. Methylation status of BCL-XL promoter was evaluated (bisulfite treatment and DNA sequencing). Mitochondrial integrity (Mitotracker labelling, Fluorescence Microscopy) and alterations in cellular morphology were verified (electron microscopy).

Decreasing EBNA-1 expression with siRNAs reduced cellular sensitivity to etoposide. This is in accordance with Akata EBV+ cells showing more sensitivity to etoposide, more levels of apoptosis and less Bcl-xL mRNA and protein levels, when compared to the Akata EBV- cells. Furthermore, Akata EBV+ cells presented less Endoplasmic Reticulum than EBV- cells. Finally, EBNA-1 siRNAs caused an increase in the expression of Bcl-xL (protein and mRNA levels).

EBV is related to Bcl-xL downregulation in Akata EBV+ cells and to increased sensitivity to etoposide.


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