EBNA1 EXPRESSION DOWN-REGULATES MYC AND RESCUES FROM SERUM STARVATION'S DEATH. FROM MICROARRAYS PROFILING TO FUNCTIONAL BIOASSAY (Well, not a viral oncogene but a survival molecule!)

Epstein-Barr virus (EBV) is associated with several types of lymphomas and epithelial tumors including Burkitt's lymphoma (BL), HIV-associated lymphoma, post-transplant lymphoproliferative disorder and nasopharyngeal carcinoma. EBV nuclear antigen 1 (EBNA1) is expressed in all EBV associated tumors and is required for latency and transformation. EBNA1 initiates latent viral replication in B cells, maintains the viral genome copy number, and regulates transcription of other EBV-encoded latent genes. B cell-specific expression of EBNA1 in a transgenic mouse model results in the appearance of lymphoma, clearly implicating EBNA1 directly in B cell transformation. To further elucidate the role of EBNA1 in transformation of B cells and epithelial cells, we have examined the effect of EBNA1 on cellular gene expression by microarray analysis using the B cell BJAB and the epithelial 293 cell lines transfected with EBNA1. Analysis of the data revealed distinct profiles of cellular gene changes in BJAB and 293 cell lines. The MYC gene, however, was down-regulated in the presence of EBNA1 in both cell lines, and Northern analysis confirmed these results. These studies suggest that EBNA1 induces tissue-specific and EBNA1-specific cellular gene expression and contributes to EBV-associated alterations in MYC expression. In addition, under serum deprivation conditions, cell growth and cell death assays suggest that EBNA1 is a survival/rescue molecule.