

**P056** The EBV transcription factor EBNA 3C disrupts the cell cycle by up-regulating RGC-32

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The EBNA 3C protein encoded by the cancer-associated virus Epstein-Barr virus (EBV) deregulates the cell cycle and promotes inappropriate progression through the G1/S, G2/M and M-phase checkpoints through multiple potential mechanisms. We have shown that the novel cell-cycle regulator RGC-32 is upregulated in EBNA 3C-expressing B-cell-lines and that over-expression of RGC-32 alone is sufficient to disrupt the G2/M checkpoint activated by DNA damage in a B-cell line. We have also confirmed that recombinant RGC-32 activates CDK1 *in vitro* indicating that inappropriate CDK1 activation through RGC-32 upregulation by EBNA 3C may represent part of the mechanism through which EBNA 3C disrupts the block at G2/M. EBNA 3C can only directly activate the RGC-32 promoter at low levels and EBNA 3C does not appear to be targeted to the promoter through a potential binding site for its DNA binding cofactor, RBP-J kappa. Other direct or indirect pathways may contribute to the RGC-32 mRNA upregulation, although we have not detected an increase in RGC-32 mRNA half-life in EBNA 3C-positive cells. RGC-32 has been shown to be upregulated in other cancer tissues and the EBV-mediated upregulation described here could therefore contribute to the development of EBV associated malignancies.