S1 | EBV latent transcription programs, latent genes and their functions.

EBV latency programs, the cells in which they are expressed and their protein/RNA expression profile

Transcription Program	Cell Type where Found	Latent Genes Expressed
Growth (Latency 3)	Newly infected B cells Immunoblastic lymphoma	EBNA1Cp/Wp, EBNA2, EBNA3A, EBNA3B, EBNA3C, EBNALP, LMP1, LMP2A, LMP2B, EBER1, EBER2, BART
Default (Latency 2)	Germinal center B cells Hodgkin's disease	EBNA1Qp, LMP1, LMP2A, LMP2B, EBER1, EBER2, BART
EBNA1 only (Latency1)	Dividing memory cells Burkitt's lymphoma	EBNA1Qp EBER1(?), EBER2(?), BART(?)
Latency Program (Latency 0)	Resting memory cells	EBER1, EBER2, BART(?)

EBV Latency Genes and their functions

EBNA1 – required for tethering of the viral genome to ensure replication and segregation of the viral DNA. Transactivates the latency control region (LCR) which encompasses Cp and Wp.

EBNA2 – transcription factor necessary for activating the promoters (Cp, Wp, LMP1p and LMP2p) involved in driving gene expression in the growth program. Functional homologue of NotchIC. Down regulates bcl-6, up regulates c-myc expression.

EBNA3A+3C – believed, but not proven, to be involved in transition from growth to default transcription program. Negative regulators of EBNA2. Facilitate epigenetic down regulation of Cp, Wp and bim.

EBNA3B – probably also involved in the negative regulation of Cp.

EBNALP – cooperates in EBNA2-mediated transactivation.

LMP1 – provides constitutive T helper cell signal which together with LMP2A helps rescue infected GC cells and drives them into the memory compartment. Down regulates bcl-6. Induces AID.

LMP2A - provides tonic BCR signal which together with LMP1 rescues infected GC cells. Induces AID.

EBER 1 and 2 – small RNAs believed, but not proven, to be expressed in all cells latently infected with EBV.

BARTs – collection of RNAs that get processed into microRNAs also believed, but not proven, to be expressed in all cells latently infected with EBV.