Genetic patterns found in the nuclear localization signals (Nlss) associated with ebv-1 and ebv-2 provide new insights into their contribution to different cell-type specificities

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Abstract
The Epstein–Barr virus (EBV) is a globally dispersed pathogen involved in several human cancers of B-cell and non-B-cell origin. EBV has been classified into EBV-1 and EBV-2, which have differences in their transformative ability. EBV-1 can transform B-cells into LCL more efficiently than EBV-2, and EBV-2 preferentially infects T-cell lymphocytes. The EBNA3A oncoprotein is a transcriptional regulator of virus and host cell genes, and is required in order to transform B-cells. EBNA3A has six peptide motifs called nuclear localization signals (NLSs) that ensure nucleocyto-plasmic protein trafficking. The presence of multiple NLSs has been suggested to enhance EBNA3 function or different specificities in different cell types. However, studies about the NLS variability associated with EBV types are scarce. Based on a systematic sequence analysis considering more than a thousand EBNA3A sequences of EBV from different human clinical manifestations and geographic locations, we found differences in NLSs' nucleotide structures among EBV types. Compared with the EBNA3A EBV-1, EBNA3A EBV-2 has two of the six NLSs altered, and these mutations were possibly acquired by recombination. These genetic patterns in the NLSs associated with EBV-1 and EBV-2 provide new information about the traits of EBNA3A in EBV biology.

Author keywords
EBV classification; EBV nuclear antigen EBNA 3A (EBNA3A); Epstein–Barr virus (EBV); Nuclear localization signal (NLS); Phylogeny; Recombination