

POSTER PRESENTATION

Open Access

Global expression analysis of EBV-infected B cells early and late after infection reveals a dynamic interplay between growth and survival signals

Alexander Price, Jason Tourigny, Eleonora Forte, Micah Luftig*

From 13th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies (ICMAOI)
Bethesda, MD, USA. 7-8 November 2011

Epstein-Barr virus (EBV) is a member of the γ -herpesvirus family estimated to infect 90% of the world's adult population. Despite the high prevalence of infection, EBV-associated malignancies are largely kept in check by a strong cytotoxic T cell immune response. However, EBV causes lymphoproliferative disease in immunodeficient individuals following transplant and CNS and other lymphomas in HIV-infected individuals. EBV also plays a role in the pathogenesis of endemic African Burkitt's lymphoma, Hodgkin's disease, and nasopharyngeal carcinoma. *In vitro*, EBV infection of primary human B cells results in proliferation and outgrowth of indefinitely proliferating lymphoblastoid cell lines, or LCLs, which represent a viable model for the pathogenesis of EBV-associated malignancies.

Ongoing studies in our group have shown that the earliest EBV-infected proliferating B cells differ greatly from LCLs phenotypically. Using CFSE staining and flow cytometry-based sorting, we have isolated these early proliferating B cells and analyzed genome-wide exon level mRNA expression relative to uninfected resting B cells and LCLs. Gene ontology analysis of these expression data identified enrichment of genes associated with proliferation and the DNA damage response in early proliferation. Furthermore, *c-Myc* mRNA and activity, as inferred from its genome-wide expression signature, were also highly induced early.

Most interestingly, however, analysis of changes from early proliferating to final LCL outgrowth revealed striking attenuation of proliferative gene sets and *c-Myc*, along with delayed induction kinetics of NF κ B activation. Specifically, genes with NF κ B motifs in their promoters were

highly expressed from early proliferating B cells to LCL and many canonical NF κ B targets and pathway components were induced at late times after infection. These results suggest a novel, dynamic EBV-driven growth pattern and expression program that relies on mutually exclusive signals from *c-Myc* and NF κ B. Furthermore, our data suggest that the earliest stages of EBV-driven B cell immortalization may provide unique insight into the pathogenesis of EBV-associated malignancies.

Published: 19 April 2012

doi:10.1186/1750-9378-7-S1-P34

Cite this article as: Price et al.: Global expression analysis of EBV-infected B cells early and late after infection reveals a dynamic interplay between growth and survival signals. *Infectious Agents and Cancer* 2012 **7**(Suppl 1):P34.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



* Correspondence: micah.luftig@duke.edu
Department of Molecular Genetics and Microbiology, Duke University,
Durham, NC, USA