Control of Epstein-Barr virus infection in vitro by T helper cells specific for virion glycoproteins.

Abstract:
Epstein-Barr virus (EBV) establishes lifelong persistent infections in humans by latently infecting B cells, with occasional cycles of reactivation, virus production, and reinfection. Protective immunity against EBV is mediated by T cells, but the role of EBV-specific T helper (Th) cells is still poorly defined. Here, we study the Th response to the EBV lytic cycle proteins BLLF1 (gp350/220), BALF4 (gp110), and BZLF1 and show that glycoprotein-specific Th cells recognize EBV-positive cells directly; surprisingly, a much higher percentage of target cells than those expressing lytic cycle proteins were recognized. Antigen is efficiently transferred to bystander B cells by receptor-mediated uptake of released virions, resulting in recognition of target cells incubated with <1 virion/cell. T cell recognition does not require productive infection and occurs early after virus entry before latency is established. Glycoprotein-specific Th cells are cytolytic and inhibit proliferation of lymphoblastoid cell lines (LCL) and the outgrowth of LCL after infection of primary B cells with EBV. These results establish a novel role for glycoprotein-specific Th cells in the control of EBV infection and identify virion proteins as important immune targets. These findings have implications for the treatment of diseases associated with EBV and potentially other coated viruses infecting MHC class II-positive cells.