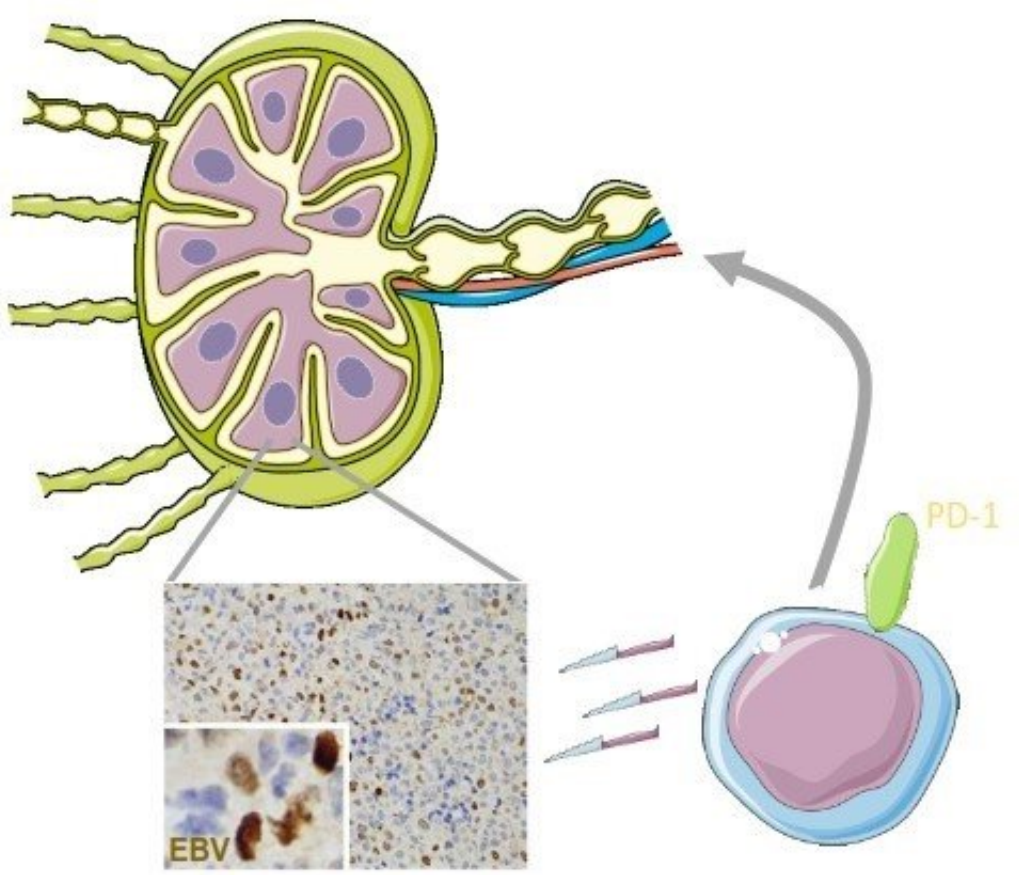
# How the immune system keeps the Epstein-Barr virus in check

May 30 2019




Despite PD-1 expression EBV specific T cells seem to be able to home to lymphoid organs and kill EBV infected B cells at these sites. This figure was created in part with modified Servier Medical Art templates, which are licensed under a Creative Commons Attribution 3.0 Unported license: https://smart.servier.com. Credit: Chatterjee B, et al. (2019)

A protein called PD-1, which is found on immune cells called CD8+ T cells, plays a key role in controlling infection with the Epstein-Barr virus, according to a study published May 30 in the open-access journal *PLOS Pathogens* by Christian Münz of the University of Zurich, and colleagues. The results from this study indicate that monitoring PD-1 signaling during future vaccination and immunotherapy studies may inform patient outcomes.

Since its discovery as a tumor virus by Epstein and colleagues in 1964, the Epstein-Barr virus has been implicated in many serious diseases. This virus is one of the most ubiquitous human pathogens in the world, persistently infecting more than 90% of the adult human population. It drives some of the strongest human CD8+ T cell responses, which can be observed during the initial symptomatic (or primary) stage of infection known as infectious mononucleosis. Despite high viral loads and prolonged CD8+ T cell stimulation during infectious mononucleosis, the Epstein-Barr virus enters latency and is under lifelong immune control in most individuals that experience this disease. Currently, in vivo studies are lacking to understand the comprehensive immune control of the Epstein-Barr virus in most healthy virus carriers, and, in particular, the characteristics of the CD8+ T cells involved in this process.

To address this gap in knowledge, Münz and colleagues examined CD8+ T cells in patients with active infectious mononucleosis, as well as in a well-characterized mouse model for Epstein-Barr virus infection. The researchers found that even though CD8+ T cells express multiple receptors that normally inhibit immune responses, including PD-1, during primary Epstein-Barr virus infection, these T cells appear to retain the ability to produce cytokines, kill infected cells, and proliferate. Importantly, blocking the PD-1 pathway leads to specific defects in controlling the Epstein-Barr virus and increases virus-induced tumor formation in infected animals, indicating that this pathway is important

for viral control. This is in contrast to previous studies showing that PD-1 helps keep the body's immune responses in check, and releasing this inhibitory block is important for reinvigorating immune responses against cancer. Because PD-1 function is required to keep the Epstein-Barr virus in check, this study provides evidence against blocking inhibitory pathways in disease settings that require improved immune control of chronic virus infections.

"Although immune checkpoint blockade constitutes a major breakthrough in cancer therapy, our results suggest that reactivation of persistent virus infections should be monitored as a possible side effect at least during anti-PD-1 treatment." says Bithi Chatterjee, first author of the study.

**More information:** Chatterjee B, Deng Y, Holler A, Nunez N, Azzi T, Vanoaica LD, et al. (2019) CD8+ T cells retain protective functions despite sustained inhibitory receptor expression during Epstein-Barr virus infection in vivo. *PLoS Pathog* 15(5): e1007748. doi.org/10.1371/journal.ppat.1007748

Provided by Public Library of Science