A viral protein that helps EBV-infected B cells to escape human killer T cells

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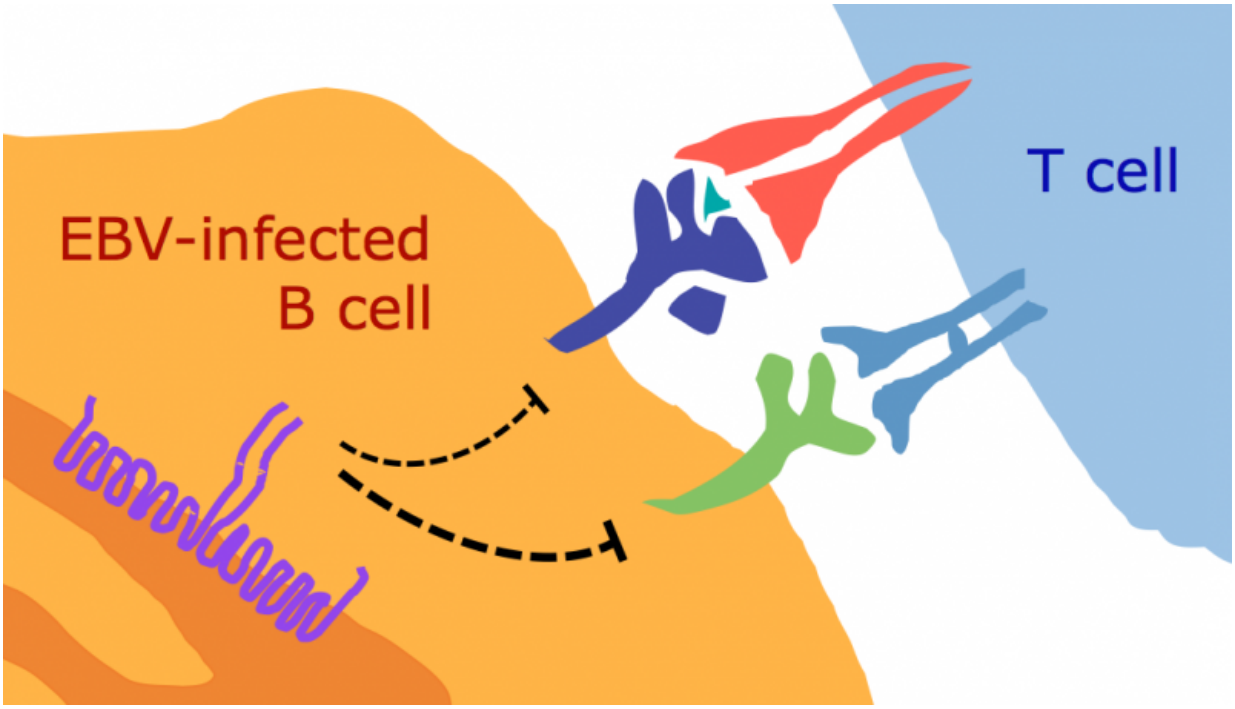

In EBV-infected cells, the viral protein LMP2A (violet) cuts back the number of molecules that activate antiviral T cells. Credit: Rancan, CC-BY

About 90% of adults worldwide are infected with Epstein-Barr virus, or EBV. The virus infects B cells (the white blood cells that make antibodies) and can contribute to B-cell-derived cancers, but in most people it remains dormant—a state scientists refer to as "latent infection"—for the rest of their lives. A study published on June 11th in

PLOS Pathogens sheds new light on why the infected person's immune system cannot eliminate EBV, or the associated cancer risk.

Interested in the immune response against EBV, Andreas Moosmann, from the Helmholtz-Zentrum in Munich, Germany, and colleagues focused in this study on the role of a viral protein called LMP2A, which is present in latently infected B cells and also in many EBV-associated cancers, which have somehow escaped detection and elimination by the immune system. The scientists studied an engineered EBV virus that cannot make LMP2A and compared this mutant virus with the normal one.

They infected human B cells with normal and LMP2A-deficient EBV. Because EBV transforms these cells, meaning that they can be changed to grow indefinitely, the researchers were able to examine so-called lymphoblastic cell lines that contained either virus. They found that LMP2A counteracts the recognition of EBV-infected B cells by EBV-specific immune lymphocytes called CD8+ killer T cells. In contrast, EBV-transformed cells without LMP2A are more efficiently identified, and the ability of these T cells to recognize and kill the EBV-infected B cells is enhanced.

Examining the mechanism underlying the LMP2A-mediated evasion, they found several ways in which it interferes with the recognition of EBV-infected cells. First, LMP2A reduced levels of several EBV proteins whose fragments are recognized by CD8+ T cells on the surface of the cell targeted for killing. Second, LMP2A disturbs expression of cellular molecules on infected B cells that interact with NKG2D, a host molecule on the surface of CD8+ T cells that aids their activation, thereby weakening the immune response against EBV-infected cells.

"Taken together", the researchers conclude, "we describe here a functional immunomodulatory effect for the EBV protein LMP2A, and

show that LMP2A mediates partial escape of infected B cells from recognition by CD8+ T cells." They also suggest that that similar immune evasion mechanisms to the ones revealed may operate in different types of LMP2A-expressing cancers caused by EBV.

More information: Rancan C, Schirrmann L, Hüls C, Zeidler R, Moosmann A (2015) Latent Membrane Protein LMP2A Impairs Recognition of EBV-Infected Cells by CD8+ T Cells. *PLoS Pathog* 11(6): e1004906. DOI: 10.1371/journal.ppat.1004906