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Endosomal Toll-Like Receptors (TLRs) mediate enhancement of IL-17A production triggered by Epstein-Barr virus (EBV) DNA in mice

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Abstract

Introduction: EBV has long-been associated with autoimmune disorders. We have previously demonstrated that EBV DNA increases the production of IL-17A in mice. This property may play a role in the association of EBV with autoimmune diseases. The objective of this study was to elucidate mechanisms through which EBV DNA modulates IL-17A levels in mice.

Methodology: To study the potential role of endosomal receptors in detecting EBV DNA, chloroquine, an endosomal maturation inhibitor, was used to treat mouse peripheral blood mononuclear cells (PBMCs) in the presence or absence of EBV DNA. IL-17A levels were then assessed by ELISA. Subsequently, to determine whether TLR3, 7 or 9 played a role in this pathway, specific inhibitors were used for these TLRs both in mouse PBMCs and *in vivo* in BALB/c mice treated with the viral DNA; IL-17A levels were then similarly assessed.

Results: IL-17A production was enhanced from mouse PBMCs cultured with EBV DNA; pre-incubation of PBMCs with chloroquine significantly reduced its production. When cells were cultured with EBV DNA and a TLR3, 7 or 9 inhibitor, a significant decrease in IL-17A levels was detected. A similar decrease in the EBV DNA-triggered IL-17A production in mice was observed when animals were treated with the TLR inhibitors.

Conclusion: Endosomal TLRs appear to be involved in recognizing EBV DNA and subsequently triggering IL-17A production in mice. Targeting these receptors in EBV positive subjects with autoimmunity may be useful pending investigations assessing whether they play a similar role in humans.

Key words: Toll-like receptors; EBV DNA; IL-17; chloroquine.

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