Exposure to HIV-1-encoded Toll-like receptor 8 ligands enhances monocyte response to microbial encoded Toll-like receptor 2/4 ligands

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\textbf{Background:} Chronic HIV-1 infection is characterized by high levels of persistent immune activation. Both HIV-1-encoded Toll-like receptor 7/8 (TLR7/8) ligands and TLR ligands encoded by products of microbial translocation have been implicated in inducing and sustaining immune activation in infected individuals, but the consequences of simultaneous exposure to different TLR ligands are not well understood.

\textbf{Objective:} To examine the impact of preexposure of monocytes to HIV-1-encoded TLR8 ligands on their ability to respond to subsequent stimulation with microbial TLR2/4 ligands.

\textbf{Method:} Stable monocytic cell lines (THP-1-Blue-CD14 cells) or primary monocytes were stimulated with ligands for TLR2, TLR4, and TLR8, including chemically inactivated HIV-1, alone, or in sequential combinations. Responses by THP-1 cells to TLR stimulation were quantified using Quanti-Blue colometric assay, and TLR-induced tumor necrosis factor-\(\alpha\) production of primary monocytes was quantified by intracellular cytokine staining using flow cytometry.

\textbf{Results:} The exposure of monocytes to HIV-1 or HIV-1-derived TLR8 ligands sensitized these cells for TLR4 stimulation, resulting in a significantly higher response to lipopolysaccharide compared to cells that were not prestimulated with TLR8 ligands or HIV-1.

\textbf{Conclusion:} TLR crosstalk can enhance the pro-inflammatory monocytes response to products of microbial translocation and might play an important role in the modulation of immune function in HIV-1 infection.

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\textbf{Introduction}

Chronic HIV-1 infection is characterized by strong persistent immune activation, and the level of immune activation has been identified as a significant predictor of HIV-1-disease progression [1,2]. One widely accepted model of HIV-1 immunopathogenesis postulates that heightened immune activation results in accelerated