Up-regulation of LAG-3 expression on T cells in HIV-1 infection is correlated with disease progression

Xiaoling Tian1, Anli Zhang1, Chenli Qiu1, Songhua Yuan1, Sugan Qiu1, Huiliang Hu1, Wanhai Wang1, Chao Qiu1, Xiaoyan Zhang1,2,3, Jianqing Xu1,2,3*
1. Laboratory of Emerging and Re-emerging Infectious Disease, Shanghai Public Health Clinical Center & Institutes of Biomedical Sciences, Fudan University, Shanghai, China
2. Key Laboratory of Medical Molecular Virology of Ministry of Education/Health, Fudan University, Shanghai, China
3. State Key Laboratory for Infectious Disease Prevention and Control, China CDC, Beijing, China. Jianqingxu2008@gmail.com

ABSTRACT

Lymphocyte activation gene-3 (LAG-3), expressed on activated CD4+ and CD8+ T cells, is known to negatively regulates T-cell responses, but its role in HIV-1 infection in vivo remains unclear. In the present study, we analyzed differences of LAG-3 expression between HIV-uninfected and HIV-infected individuals using quantitative PCR and flow cytometry. We found that LAG-3 expression in PBMC cells was higher in HIV-1 infected individuals than HIV-sero-negative persons. LAG-3 expression was correlated with disease progression: LAG3 expression was up-regulated on both CD4 and CD8 T cells from HIV-1 infected individuals, which was also correlated positively with viral load and inversely with CD4 count. We further characterized Lag-3+CD4 and Lag3+CD8 T cells. In conclusion, LAG-3 is up-regulated concurrently with HIV-1-mediated chronic immune activation in comparison with HIV-sero-negative controls, may represent a novel target for the therapeutic reversal of HIV-1 associated T cell dysfunction. In addition, blockade of Lag-3 enhanced cytokine production such as TNF-γ, IL-2 and IFN-γ.

INTRODUCTION

LAG3, a cell surface molecules, binds to MHC II molecules with higher affinity than CD4 (1-3). It was found negatively regulate T-cell function (1-3). To evaluate the role of LAG3 on T cell exhaustion in HIV-1 infection, we did a comparative analysis of LAG3 expression on PBMC from HIV-1-uninfected individuals and ART free chronically HIV-1-infected subjects by qPCR and flow cytometry.

RESULTS

LAG-3 was expressed at higher levels in HIV-1 infected subjects than in the HIV-1 uninfected subjects (Figure 1). The percentage of LAG-3-expressing HIV-specific CD4+ T cells and CD8+ T cells was significantly greater in HIV-1+ subjects compared with HIV-1 uninfected individuals (Fig 1; Fig 2). The frequency of LAG3+ of T cells correlated positively with HIV-1 viral load and inversely with absolute CD4+ T cell counts in peripheral blood of HIV-1-infected individuals. After gag-b peptide pool stimulation and blockade of Lag-3, we observed an increase in IFN-γ production such as TNF-γ, IL-2 and IFN-γ.

CONCLUSION

In conclusion, Lag-3 is up-regulated concurrently with HIV-1-mediated chronic immune activation in comparison with HIV-1 sero-negative controls, may represent a novel target for the therapeutic reversal of HIV-1 associated T cell dysfunction. In addition, blockade of Lag-3 enhanced cytokine production such as TNF-γ, IL-2 and IFN-γ.

REFERENCES


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