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Up-regulation of interferon-a/APOBEC3G signal pathway potently inactivates HIV-1 infectivity in resting CD4-T cells

Keyang Chen
Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA, Keyang.Chen@jefferson.edu

Jialing Huang
Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA

Chune Zhang
Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA, Chune.Zhang@jefferson.edu

Sophia Huang
Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA

Giuseppe Nunnari
Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA, Giuseppe.Nunnari@jefferson.edu

See next page for additional authors

Authors
Keyang Chen, Jialing Huang, Chune Zhang, Sophia Huang, Giuseppe Nunnari, Feng-xiang Wang, Xiangrong Tong, Ling Gao, Kristi Nikisher, and Hui Zhang

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Poster presentation

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Keyang Chen, Jialing Huang, Chune Zhang, Sophia Huang, Giuseppe Nunnari, Feng-xiang Wang, Xiangrong Tong, Ling Gao, Kristi Nikisher and Hui Zhang*

Address: Center for Human Virology, Division of Infectious Diseases, Department of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107, USA

* Corresponding author

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Background

Interferon (IFN) system, including various IFNs and IFN-inducible gene products, is well known for its potent innate immunity against wide-range viruses. Recently, a family of cytidine deaminases, functioning as another innate immunity against retroviral infection, has been identified. However, its regulation remains largely unknown.

Methods

IFN-a was added to the culture of resting CD4 T-cells. The expression of APOBEC3G was detected with real time RT-PCR and Western blotting. The promoter of APOBEC3G was analyzed by luciferase expression. The effect of IFN-a/APOBEC3G upon HIV-1 was examined by treating the cells with APOBEC3G-specific siRNA.

Results

We have demonstrated that, through a regular IFN-a signal transduction pathway, IFN-a can significantly enhance the expression of APOBEC3G in human primary resting but not activated CD4 T-cells, and the amounts of APOBEC3G associated with a low molecular mass (LMM). Interestingly, short-time treatments of newly-infected resting CD4 T-cells with IFN-a will significantly inactivate human immunodeficiency virus type 1 (HIV-1) at its early stage. This inhibition can be counteracted by APOBEC3G-specific short interfering RNA (siRNA), indicating that IFN-a-induced APOBEC3G plays a key role to mediate this anti-HIV-1 process.

Conclusion

Our data suggest that APOBEC3G is also a member of IFN system, at least in the resting CD4 T-cells. Given that IFN-a/APOBEC3G pathway has potent anti-HIV-1 capability in resting CD4 T-cells, augmentation of this innate immunity barrier could prevent residual HIV-1 replication in its native reservoir in the post-highly active antiretroviral therapy (HAART) era.