ARE THERE INFECTIVITY DIFFERENCES BETWEEN HIV-2 AND HIV-1 RELATED TO APOBEC3?

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REVIEW

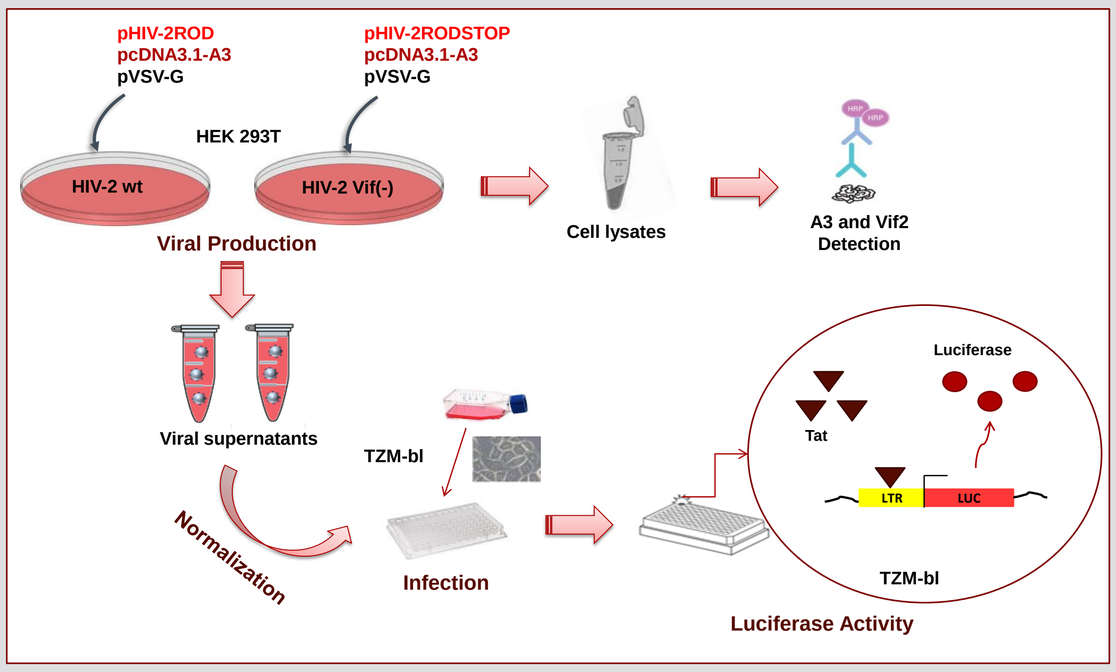
The pathogenicity of the two types of Human Immunodeficiency Virus (HIV) is very different. When compared to HIV-1, HIV-2 exhibits lower plasma viral loads, causes asymptomatic infection, and infected individuals can survive longer. It is possible that differential cellular restriction factor recognition could account for the epidemic HIV-2 versus pandemic HIV-1. One of the restriction factors known is the deaminase APOBEC3G (A3G). This enzyme has antiviral activity against HIV1 that is suppressed by the viral protein Vif.

Our previous studies have shown that A3G is less active in inhibition of HIV-2 than HIV-1 [1]. Viral proteins HIV-2Vif and HIV-1Vif share only 30% of identity and these viruses show differential replication and productive infection capacity in several cell lines [1,2], suggesting either different threshold requirements for the same cellular factor or the involvement of different factors counteracting Vif1 and Vif2 functions.

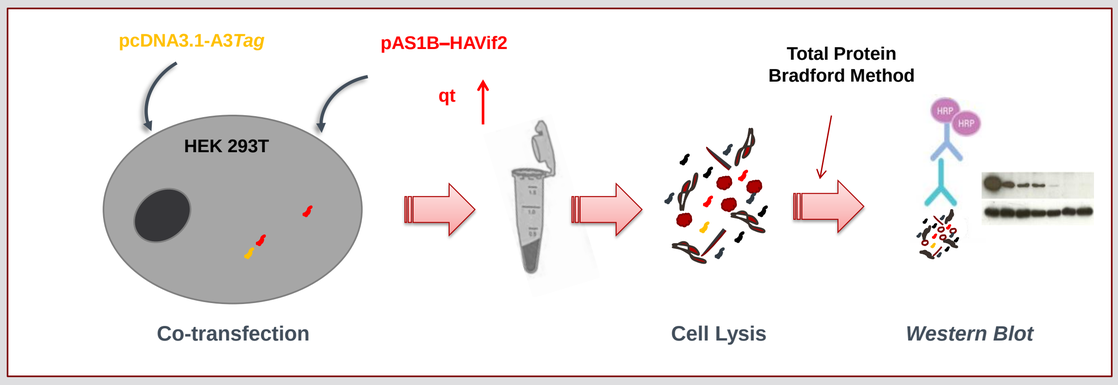
Aim: Understand the role of the A3 family members in HIV-2 infection, compare to HIV-1 and characterize the Vif2-APOBEC3 protein interaction

METODOLOGY AND RESULTS

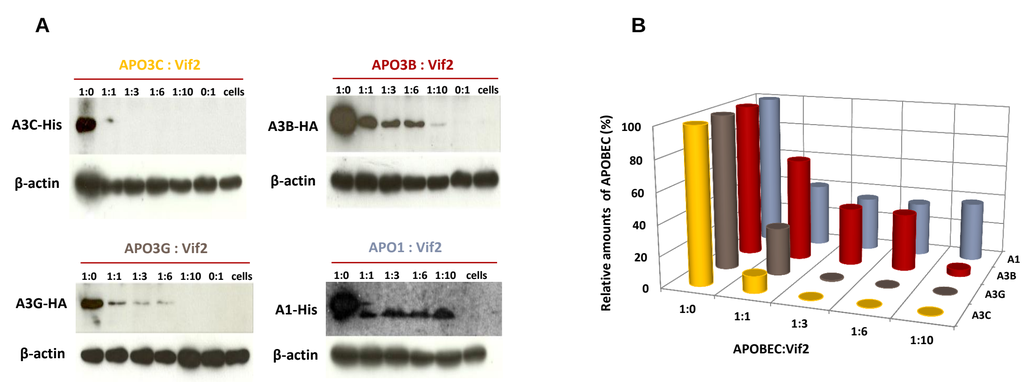
Antiviral effects of APOBEC3 members on HIV-2 infectivity



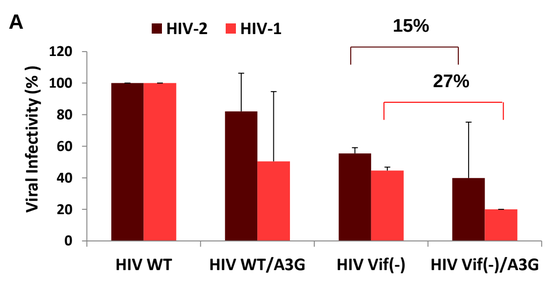
Vif2 effects on APOBECs intracellular levels



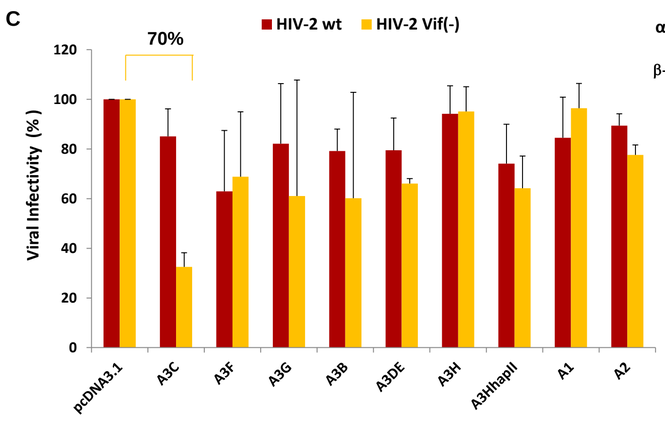
A3C protein is the most sensitive to Vif2-mediated degradation



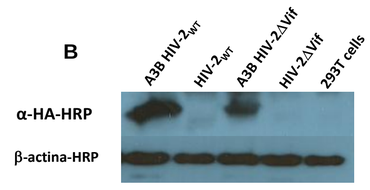
A3G is more efficient at inhibiting HIV-1 than HIV-2



A3C is the most effective inhibitor of HIV-2



A3B levels are not affected by Vif2



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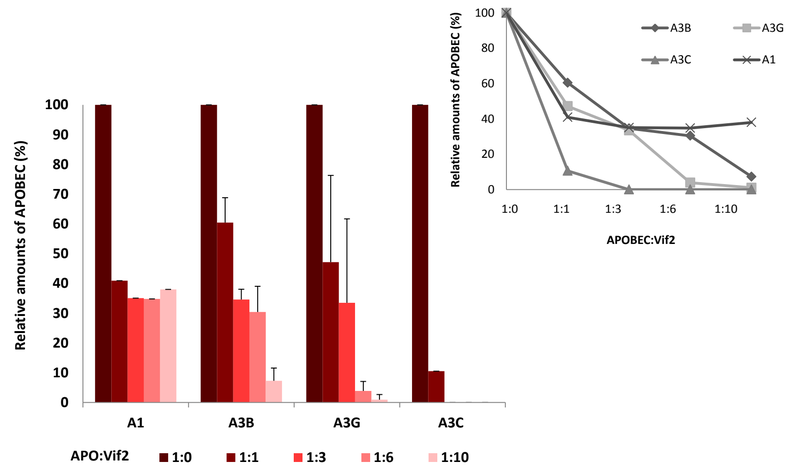

Fig. 1 A) Viral infectivity of HIV-2wt , HIV-1wt, HIV-2ΔVif and HIV-1ΔVif produced in the presence or absence of APOBEC3G. Values are presented as % of infectivity relative to respective wild type viruses produced in the absence of A3G, defined as 100% (n ≥ 2). **B)** Western blot of A3B protein expression in virus-producing cells lysates. **C)** Viral infectivity of HIV-2 wt and HIV-2ΔVif produced in the presence of different APOBEC. The viral infectivity of HIV-2wt and HIV-2ΔVif produced in the presence of pcDNA3.1 (as control) was defined as 100%. Columns and error bars represent average ± SD, respectively, from n ≥ 2 independent experiments.

Fig. 2 Effect of increasing amounts of Vif2 with constant amounts of APOBEC (A3B, A3G, A3C, and A1, in ratios from 1:1 to 1:10 APO/Vif2) in transfected HEK 293T cells. **A) R**epresentative Western blot for each analyzed APOBEC. **B)** 3D plot of Western blots shown in A, analyzed with Image J software, version 1.47v. Background was removed and normalized to β-actin expression levels (internal control). APOBEC expression in the absence of Vif2 (1:0) was defined as 100% **C)** Average values of relative amounts of APOBEC in 293T cell lysates from several assays (A3B and A3G n ≥ 3;. A1 and A3C n = 1).

CONCLUSION

Among several tested APOBEC3:
A3C seems to be the cellular factor specifically inhibiting HIV-2 as opposed to HIV-1, what is mainly inhibited by A3G

[1] Ribeiro, A.C. et al., (2005) Journal of Virology, 79, p.823-833.
[2] Reddy, T.R., et al., (1995) Journal of Virology, 69(6): p. 3549-3553.

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