HIV Vpu interferes with NF-κB but not with IRF3 activity

187

Lara Manganaro[1], Elisa deCastro[1], Ana M. Maestre[1], Kevin Olivieri[2], Adolfo García-Sastre[1,3,4], Ana Fernandez-Sesma[1] and Viviana Simon[1,3,4]

[1] Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[2] Sanford-Burnham Medical Research Institute, La Jolla, California, USA
[3] Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA
[4] Global Health and Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Abstract: The accessory HIV protein Vpu antagonizes a number of different host innate restriction mechanisms by inducing degradation of key cellular proteins. Vpu can also directly down regulate IFNβ expression. We investigated the possibility the Vpu induces the degradation of the transcription IRF3. Here we report that HIV Vpu failed to degrade IRF3 in infected primary cells and has no effect on IRF3 dependent gene expression. On the other hand, Vpu is able to down-modulate NF-κB dependent transcription causing an inhibition of IFNβ expression. Taken together, these results suggest that HIV Vpu regulates antiviral innate response by acting on the NF-κB pathway.

Fig. 1: HIV Vpu reduces IFNβ expression

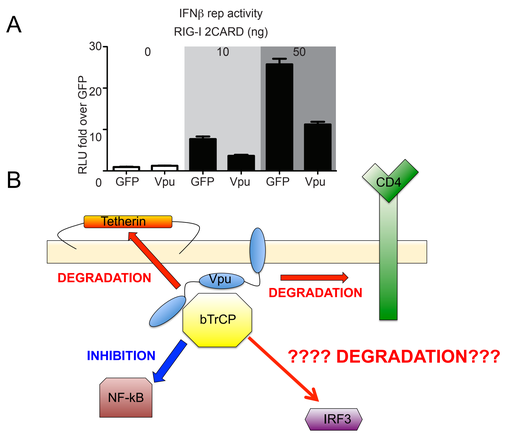


Fig. 2: IRF3 levels are comparable in infected and uninfected CD4⁺ T cells

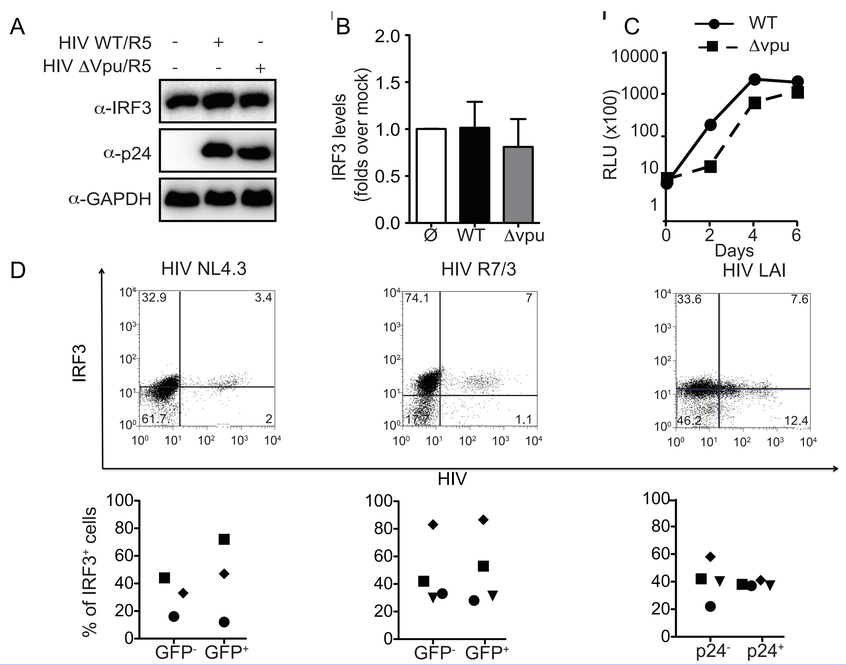


Fig. 3: IRF3 levels in macrophages are not affected by HIV infection

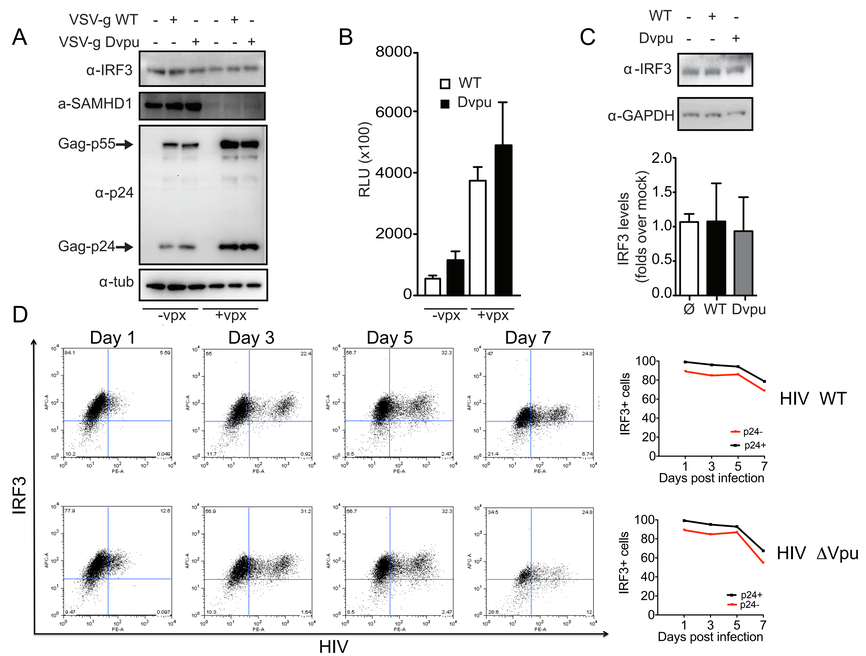


Fig. 4: Vpu inhibits only the NF-κB pathway

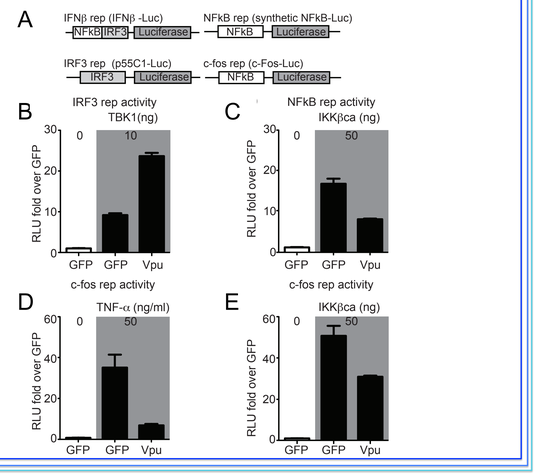


Fig. 5 Vpu-βTRCP binding is required for NF-κB and IFNβ inhibition

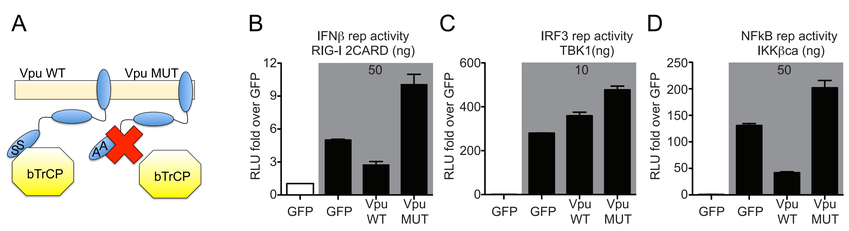


Fig. 6 Different HIV Vpu alleles inhibit NF-κB activation

