Dear editor of PlosOne

We are pleased to submit the manuscript entitled, “*Is the tryptophan codon of gene vif the Achilles’ heel of HIV-1?*”, we present in this study results of the relationship between the hypermutation in the HIV gene *vif* and levels of CD4+ lymphocytes and levels of viral RNA.

We used 7072 proviral sequences HIV-1 gene *vif* from public databank to evaluate the impact of Apobec3 to the evolution of HIV in a population level.

First we found that tryptophan codons (TGG) of the gene *vif* targeted exclusively by RT have lower mutation rates than TGG codons target by Apobec3.

Then we used a subset of 857 sequences (sequences with information of CD+4 counts and viral loads) and found that patients harboring hypermutated viruses tend to have lower mRNA levels and higher counts of CD4+ cells

Overall our findings indicate that at individual level Apobec3-induced hypermutation a subtle effect the HIV replication. However, at the population level Apobec3 activity is minimal to restrain HIV spread because it is rare (only 0.6% of all sequence in the genbank were hypermutated).

Sincerely yours

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(Nucleotide context) codon position

Mutation rates

0.000 0.001 0.002 0.003

Other
Stop codons

Figure#1

Figure#2

Figure#3