

Lentiviral genomes present a strong nucleotide bias, with extremely high frequencies of the A nucleotide in HIV/SIV RNAs. Combining genomics, experimental and clinical data, we show a correlation between this bias and the pathogenicity of HIV-1. To study the effect of viral nucleotide composition on innate immunity stimulation, we developed an algorithm which uses the degeneracy of the genetic code to modulate the nucleotidic composition of genomic sequences without altering their regulatory elements or amino acid sequences. Then, we designed two artificial simian immunodeficiency viruses (SIV), whose genome sequences were optimized towards the macaque genome mean nucleotide composition. The first synthetic virus (SIVopt1) was optimized in gag and pol genomic regions and showed a dramatic decrease in replicativity. The second virus (SIVopt2) optimized only in pol, presented a similar replicative capacity to wild-type virus but its capacity to stimulate type-I interferon (IFN-I) in vitro was reduced. This synthetic virus with attenuated pathogenic potential open perspectives in HIV vaccine studies, particularly in regard to recent studies concerning codon-based immunity in HIV infections.

lentivirus; SIV; HIV; nucleotide; composition; interferon; IFN; vaccine