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Research Paper

Codon usage limitation in the expression of HIV-1 envelope glycoprotein

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Abstract

Background: The expression of both the *env* and *gag* gene products of human immunodeficiency virus type 1 (HIV-1) is known to be limited by *cis* elements in the viral RNA that impede egress from the nucleus and reduce the efficiency of translation. Identifying these elements has proven difficult, as they appear to be disseminated throughout the viral genome.

Results Here, we report that selective codon usage appears to account for a substantial fraction of the inefficiency of viral protein synthesis, independent of any effect on improved nuclear export. The codon usage effect is not specific to transcripts of HIV-1 origin. Re-engineering the coding sequence of a model protein (Thy-1) with

the most prevalent HIV-1 codons significantly impairs HIV-1 expression, whereas altering the coding sequence of the jellyfish green fluorescent protein gene to conform to the favored codons of highly expressed human proteins results in a substantial increase in expression efficiency.

Conclusion Codon-usage effects are a major impediment to the efficient expression of HIV-1 genes. Although mammalian genes do not show as profound a bias as do *Escherichia coli* genes, other proteins that are poorly expressed in mammalian cells can benefit from codon re-engineering.



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