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HIV-1 specifically encapsidates other nucleic acids than its genomic RNA

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Background

HIV particles include two-copies of full-length genomic RNA (gRNA) that is selectively incorporated into the viral particles as a non-covalent dimer. RNA packaging into virus particles is dependent upon specific interaction between gRNA and the nucleocapsid protein (NC) domain of the Gag precursor. Selection of the HIV-1 genomic RNA involves the so-called Psi region located immediately upstream of the *gag* start codon and folded into three stem-loops important for genome packaging (SL1 to SL3). In particular, SL1 mediates RNA dimerization, presumably a prerequisite for gRNA packaging. SL2 and SL3 both bind HIV-1 NC, while SL3 seems to act as the major signal of encapsidation [1]. Little is know about the mechanism by which Gag selects gRNA for incorporation into the nascent virions. In addition, the selection appears weaker than previously thought, since HIV-1 particles also package cellular and spliced viral RNAs in addition to gRNA [2]. The determinants and mechanisms involved in the encapsidation of such non-genomic RNAs remain undefined.

Results

In order to unravel the mechanisms conferring RNA packaging specificity, we undertook a detailed quantitative analysis of the RNA content of HIV-1 particles by RT-qPCR. We determined the relative packaging efficiencies of all singly- and fully-spliced viral mRNAs and of few distinct host RNA species (7SL, U6, and GAPDH RNAs) relative to that of gRNA [3]. We also evaluated the importance of the different regions of HIV-1 RNA and of the RNA export pathway on the packaging efficiency. Although the spliced viral RNA lacks the SL2-SL3 motifs, they were found selectively packaged into virions. Moreover, the persistence of SL1 signal in spliced RNA sequences did not confer packaging ability to these subgenomic RNAs. We found that packaging of cellular RNAs greatly varied from one species to another. 7SL RNA was packaged in wt HIV-1 particles as efficiently as singly- and fully-spliced viral RNAs, whereas packaging of U6 snRNA was less efficient. At the opposite, GADPH mRNA was not detectably encapsidated into virions. Furthermore, our results showed that host and viral RNAs were packaged through independent mechanisms [3].

Conclusion

Recently, we showed that spliced viral RNAs are present in infectious particles and consequently participate, along with the unspliced gRNA, to some of the early steps of infection such as the reverse transcription step [4]. Similarly, packaging of host RNAs could lead to their reverse transcription in an infected cell. These non-genomic reverse transcripts may recombine with the viral genome

and integrate together into the host cell genome leading to defective viruses or oncogenes production.

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