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TRF 120B

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An RNA Pseudoknot stimulates HTLV-1 pro-pol Programmed -1 Ribosomal Frameshifting

Programmed -1 ribosomal frameshifts (-1 PRFs) are commonly used by viruses to regulate their enzymatic and structural protein levels. Human T-cell lymphotropic virus type 1 (HTLV-1) is a carcinogenic retrovirus that uses two, independent -1 PRFs to express viral enzymes critical to establishing new HTLV-1 infections. How the *cis*-acting RNA elements in this viral transcript function to induce frameshifting is unknown. The objective of this work was to conclusively define the 3' boundary of and RNA elements within the HTLV-1 *pro-pol* frameshift site. We hypothesized that the frameshift site structure was a pseudoknot and that its 3' boundary would be defined by the pseudoknot's 3' end. To test these hypotheses, the *in vitro* frameshift efficiencies of several HTLV-1 *pro-pol* frameshift sites with different 3' boundaries were quantified. The results indicated that nucleotides included in the longest construct were essential to highly-efficient frameshift stimulation. Interestingly, only this construct could form the putative frameshift site pseudoknot. Next, the secondary structure of this longer frameshift site was determined. The dominant structure was an H-type (Hairpin-type) pseudoknot which, together with the slippery sequence, stimulated frameshifting to 19.4(±0.3)%. The pseudoknot's critical role in frameshift stimulation was directly revealed by examining the impact of structural changes on HTLV-1 *pro-pol* -1 PRF. As predicted, mutations that occluded pseudoknot formation drastically reduced the frameshift efficiency. These results are significant because they demonstrate that a pseudoknot is important to HTLV-1 *pro-pol* -1 PRF and define the frameshift site's 3' boundary.

Hosted by Professor Peter Qin

The scientific community is invited

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