ABSTRACT

TITLE:	Structure and Function of the HTLV-1 Pro-Pol Frameshift Site
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ABSTRACT: Human T-cell leukemia Virus Type I (HTLV-1) was the first identified human retrovirus, identified in 1980. Infection with HTLV-1 results in adult T-cell leukemia with 5-10% incidence. An estimated 15-20 million individuals worldwide are infected with HTLV. Replication of retroviruses, such as HTLV, is dependent upon synthesis of viral structural and enzymatic proteins. Synthesis of HTLV's enzymatic proteins (Protease (PR), Reverse Transcriptase (RT), and Integrase (IN)) is dependent upon programmed ribosomal frameshifting (PRF). PRF is defined by a programmed change in the ribosome's reading frame during translation. In this work, HTLV-1 pro-pol -1 PRF is investigated. The pro-pol frameshift site consists of a heptanucleotide slippery sequence (UUUAAAC) followed by a downstream structure. The frameshift efficiency at this site is ~10%. A pseudoknot structure is predicted downstream of the slippery sequence. We hypothesize that the pseudoknot structure contributes significantly to the frameshift efficiency. To test this hypothesis, we designed four variant frameshift sites to test the importance of the pseudoknot structure to frameshifting. An in vitro dual-luciferase frameshift assay will be utilized to determine the frameshift efficiencies for the wild-type and variant frameshift sites. We report successful cloning of all of the plasmid DNAs, which code for the experimental and control RNAs used in the dual-luciferase frameshift assay. Eight of the ten plasmid DNAs has been successfully linearized and used for RNA synthesis and subsequently purified. Future work will include the synthesis and purification of the remaining RNAs, and final determination of the in vitro frameshift efficiency for each site.