ABSTRACT

TITLE:	Ribosomal Frameshifting in HTLV-1: Examining the Pro-Pol Frameshift Site
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ABSTRACT: Human t-cell lymphotropic 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 as a programmed change in the ribosome's reading frame during translation. HTLV-1 has been observed to have ribosomal frameshifting at two difference sites. The frameshift sites gag-pro and pro-pol have been established but the efficiencies and structures of these two frameshift sites has not yet been determined. The HTLV-1 pro-pol site consists of three RNA elements: a slippery sequence (UUUAAAC), a spacer, and a downstream structure. In this work, the HTLV pro-pol -1PRF mechanism is investigated. A pseudoknot structure is predicted downstream of the slippery sequence. We hypothesize 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 was utilized to determine the frameshift efficiencies for the wild-type and variant frameshift sites.