Statistical Folding Used to Predict HIV-1 5′ Leader’s Primer Binding Site (PBS)

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The human immunodeficiency virus (HIV) is a retrovirus that weakens a person's immune system by attacking the T-cells. Although treatments exist, there is currently no cure for HIV. One potential approach to developing better therapeutics is to target an area on the virus that has a low mutation rate. Because of this, HIV-1’s 5′ Leader could be a potential location to further investigate via NMR. This project aims to investigate HIV’s 5′ Leader, which plays important roles, such as RNA packaging and reverse transcription. The primer binding site (PBS) stem-loop will be the primary location highlighted for this particular project. While there are limitations that have to be met with this location, its centralized location could provide insight into the overall 3D structure of the 5′ Leader. Using a paramagnetic labeled M8-DOTA-SPy tagged U1A protein, we will be able to induce long-range pseudocontact shifts (PCS) in an NMR spectrum. These PCS will allow us to view information about the location of domains in the 5′ Leader when running the NMR. By placing the U1A binding sequence on the PBS-B stem-loop, our lab can elucidate structural information about the angle of domains in the 5′ Leader. This project proposes a location on the PBS (primer binding site) where the U1A binding sequence is added to view information about different regions of the PBS, the SD (splice donor), and the DIS (dimer initiation site).

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