Abstract for an Invited Paper
for the MAR10 Meeting of
The American Physical Society

Single molecule DNA interaction kinetics of retroviral nucleic acid chaperone proteins

MARK WILLIAMS, Northeastern University

Retroviral nucleocapsid (NC) proteins are essential for several viral replication processes including specific genomic RNA packaging and reverse transcription. The nucleic acid chaperone activity of NC facilitates the latter process. In this study, we use single molecule biophysical methods to quantify the DNA interactions of wild type and mutant human immunodeficiency virus type 1 (HIV-1) NC and Gag and human T-cell leukemia virus type 1 (HTLV-1) NC. We find that the nucleic acid interaction properties of these proteins differ significantly, with HIV-1 NC showing rapid protein binding kinetics, significant duplex destabilization, and strong DNA aggregation, all properties that are critical components of nucleic acid chaperone activity. In contrast, HTLV-1 NC exhibits significant destabilization activity but extremely slow DNA interaction kinetics and poor aggregating capability, which explains why HTLV-1 NC is a poor nucleic acid chaperone. To understand these results, we developed a new single molecule method for quantifying protein dissociation kinetics, and applied this method to probe the DNA interactions of wild type and mutant HIV-1 and HTLV-1 NC. We find that mutations to aromatic and charged residues strongly alter the proteins' nucleic acid interaction kinetics. Finally, in contrast to HIV-1 NC, HIV-1 Gag, the nucleic acid packaging protein that contains NC as a domain, exhibits relatively slow binding kinetics, which may negatively impact its ability to act as a nucleic acid chaperone.