Truncation and Competition Studies of an Anti-HIV-1 capsid lattice RNA aptamer

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The capsid core has become a potential antiviral target in HIV-1 because of its indispensable role in the viral replication cycle. The capsid houses the viral genome and the enzymes required for replication. The capsid is involved in many different stages within the HIV replication cycle, including reverse transcription, uncoating, trafficking to the nucleus, entry into the nucleus, integration, assembly, and maturation. The capsid core is a conical lattice composed of approximately 250 capsid protein (CA) hexamers and 12 CA pentamers.

It is unknown how the different capsid assembly states, such as the assembled lattice or hexamers, contribute to capsid function, and there are currently limited tools available to study the roles of capsid assembly states. Aptamers are structured nucleic acids that bind to a target with high specificity and affinity. Because of their ability to bind to unique epitopes, aptamers could be used to study the roles of the different assembly states during the HIV replication cycle. Previous work identified aptamers that bind to the lattice, including aptamer 15-2. To better understand the sequence and structural requirements for this aptamer to bind capsid assemblies, a series of truncations from the 3' end were generated to identify the simplified functional core of the aptamer. To quantify their results, the truncated aptamers were tested using an electrophoretic mobility shift assay (EMSA) that reveals competition between the full-length aptamer and various truncated versions as compared to competition by non-specific RNAs. In these assays the 80 and 60 nucleotide truncated forms of aptamer 15-2 competed strongly with the full-length aptamer, while the shorter versions were indistinguishable from the non-specific controls. We will extend this analysis to six additional aptamers that also bind lattice as full- length aptamers.