

Public Abstract

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Title:The Minimal Primary Structures of RNA Aptamers Selected to Bind HIV-1 Reverse Transcriptase

Human Immunodeficiency Virus (HIV), the virus responsible for causing AIDS, is a world wide epidemic afflicting almost 40 million people. In developed nations, current drug regimens can turn what would be a death sentence into a chronic but manageable disease. Unfortunately, the virus mutates readily and patients must take the drugs on a precise schedule to keep drug resistant strains from developing in the host. These schedules can be hard to maintain due to their frequency and the toxic nature of the drugs. Even if the schedules are adhered to perfectly, it does not guarantee the patient will remain without drug resistant virus. For this reason, innovative therapies are needed for the treatment of HIV.

Nucleic acid aptamers constitute one class of molecules that could lead to new treatments for AIDS.

Nucleic acids normally function as information storage and transfer molecules in organisms, like the DNA and RNA in human cells. Aptamers are small nucleic acids which take on a three dimensional shape and bind targets. Some aptamers have been synthetically produced and selected for binding to an HIV protein called reverse transcriptase (RT), a protein which performs an essential step in the HIV life cycle and is currently the most common target of anti-HIV drugs. It has been proven that many of these aptamers bind to RT tightly, inhibit its function, and even reduce infectivity of the virus in living human cells.

It is important to understand the structure of the aptamers that bind to RT. The three dimensional structure of the aptamer determines how it contacts RT and helps us understand how it inhibits the function of RT. Furthermore, it helps us learn more about the virus and how to better control it. Most RNA structure takes on a form known as a stem-loop. A variation of that form is known as a pseudoknot. A pseudoknot derives its name from the resemblance it bears to a knot when it is drawn on paper, and it is the structure most commonly associated with anti-RT RNA aptamers.

Pseudoknots are often easy to identify when they are the structure responsible for binding RT. In RNA aptamers, other structures are rarely responsible. I have investigated several RNA aptamers with unknown structure that bind RT. I have found that many of these structures are also pseudoknots, but some of them form stem-loop or pseudoknot plus stem-loop structures. The structures I have elucidated are novel in the anti-RT RNA aptamer field and important to pursuing these compounds as future therapeutics.