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# Researcher refining synthetic molecules to prevent HIV resistance

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Evolving HIV viral strains and the adverse side effects associated with long-term exposure to current treatments propel scientists to continue exploring alternative HIV treatments. In a new study, a University of Missouri researcher has identified broad-spectrum aptamers. Aptamers are synthetic molecules that prevent the HIV virus from reproducing. In lab tests, aptamers known as RT5, RT6, RT47 and some variants of those were recently identified to be broad-spectrum, which would allow them to treat many subtypes of HIV-1. Now, researchers are gaining a better understanding of the biochemical characteristics that make aptamers broad-spectrum.

"Aptamers are promising candidates as anti-HIV and anti-cancer therapeutic agents for reducing virus infectivity," said Donald Burke-Aguero, an associate professor in the Department of Molecular Microbiology and Immunology in the Christopher S. Bond Life Sciences Center. "They also might be beneficial in developing gene therapy applications."

In cell cultures, aptamers have suppressed viral replication by inhibiting important enzymes in the HIV-1 virus. One important enzyme is reverse transciptase (RT), which copies genetic material and generates new viruses. Scientists hope to create aptamers that will disrupt RT and suppress the virus's growth. Aptamers can reduce viral infectivity by blocking the normal action of RT.

"Successful aptamers get in the way of the virus's genetic material,

which it is trying to copy as it invades a cell," Burke-Aguero said. "The structure of the aptamer is very important. Broad-spectrum aptamers must have an adaptable structure, which make it difficult for RT to get around them.

There are several different HIV-1 subtypes around the world, and each subtype has a different amino acid sequence making it difficult to create a single aptamer that will work on every substype. Synthetic molecules must be the right size and shape to bind with HIV proteins, Burke-Aguero said.

"The first batch of aptamers developed were designed for a particular virus and would not work on all strains of HIV," Burke-Aguero said. "Now our goal is to develop broad-spectrum aptamers. If an aptamer has broad-spectrum function, viruses will be less likely to develop resistance to the therapy. We are in the process of refining aptamers and understanding the nature of resistance in order to get multi-year to lifetime protection."

Burke-Aguero's study, "Novel Bimodular DNA Aptamers with Guanosine Quadruplexes Inhibit Phylogenetically Diverse HIV-1 Reverse Transciptases," was published in *Nucleic Acids Research*.

Source: University of Missouri-Columbia