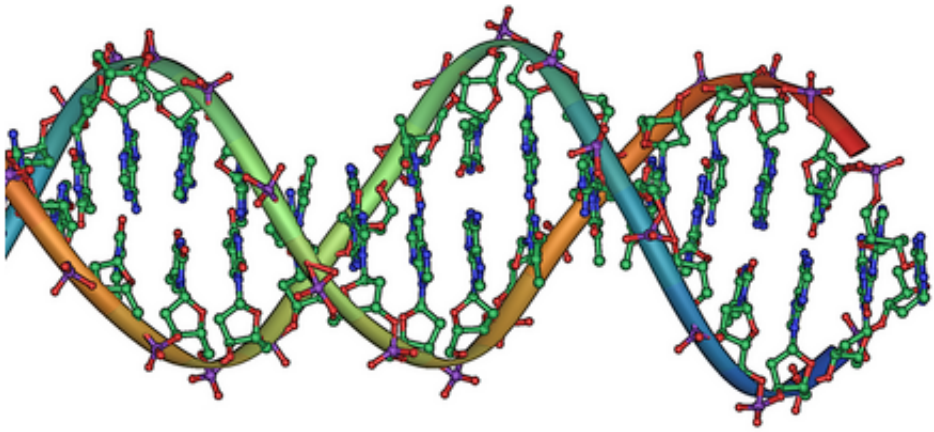
Retroviral DNA needs time to find its home, but insertion happens in a blink

April 26 2016, by Darrell Ward



DNA double helix. Credit: public domain

When retroviruses such as HIV infect a cell, they first make a copy of their RNA genome in the form of DNA. The relatively short viral DNA strand then moves to the cell nucleus, where it inserts itself into the host cell's DNA.

A new study led by researchers at The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James) reveals details

about how such viral DNA insertion complexes hunt for a suitable spot and how quickly insertion happens at the chosen site.

The findings could help improve treatments for HIV infection and make gene therapy safer and more efficient.

The researchers used Prototype Foamy Virus integrase as a model and two molecular microscopy techniques to record viral integration complexes traveling along stretches of target DNA in search of insertion points. (Integration complexes consist of viral DNA plus the enzymes that insert it into the host DNA.)

The integration complexes moved along the target DNA for distances of 1,500 DNA base pairs for periods of 2-3 seconds. When they found a sweet spot, insertion of the viral DNA happened in less than a half second - 0.470 second to be precise.

The study is published in the journal *Nature Communications*.

"We were surprised that the enzyme complex does so much searching," says co-corresponding author Kristine Yoder, PhD, assistant professor of molecular virology, immunology and medical genetics.

"Searching 1.5 kilobases of DNA is quite a distance, and 2-3 seconds is a long time in molecular terms to remain associated with the DNA."

Their data also showed that the viral integration complexes move along DNA like a nut on a bolt rather than sliding along like a washer.

The findings are important, Yoder explains. "The integration of retroviral DNA is a relatively uncommon event compared with the number of viral DNA copies found in infected cells. If we can understand why insertion doesn't occur more often, it might lead to new

drugs that prevent retroviral infection.

"Our study suggests that the problem lies in the search for an insertion site and not the insertion itself," she says. "In addition, gene therapy involves searching and insertion events, so our findings might help make that process more efficient."

Provided by Ohio State University Medical Center