# Researchers are using RNA in a new approach to fight HIV

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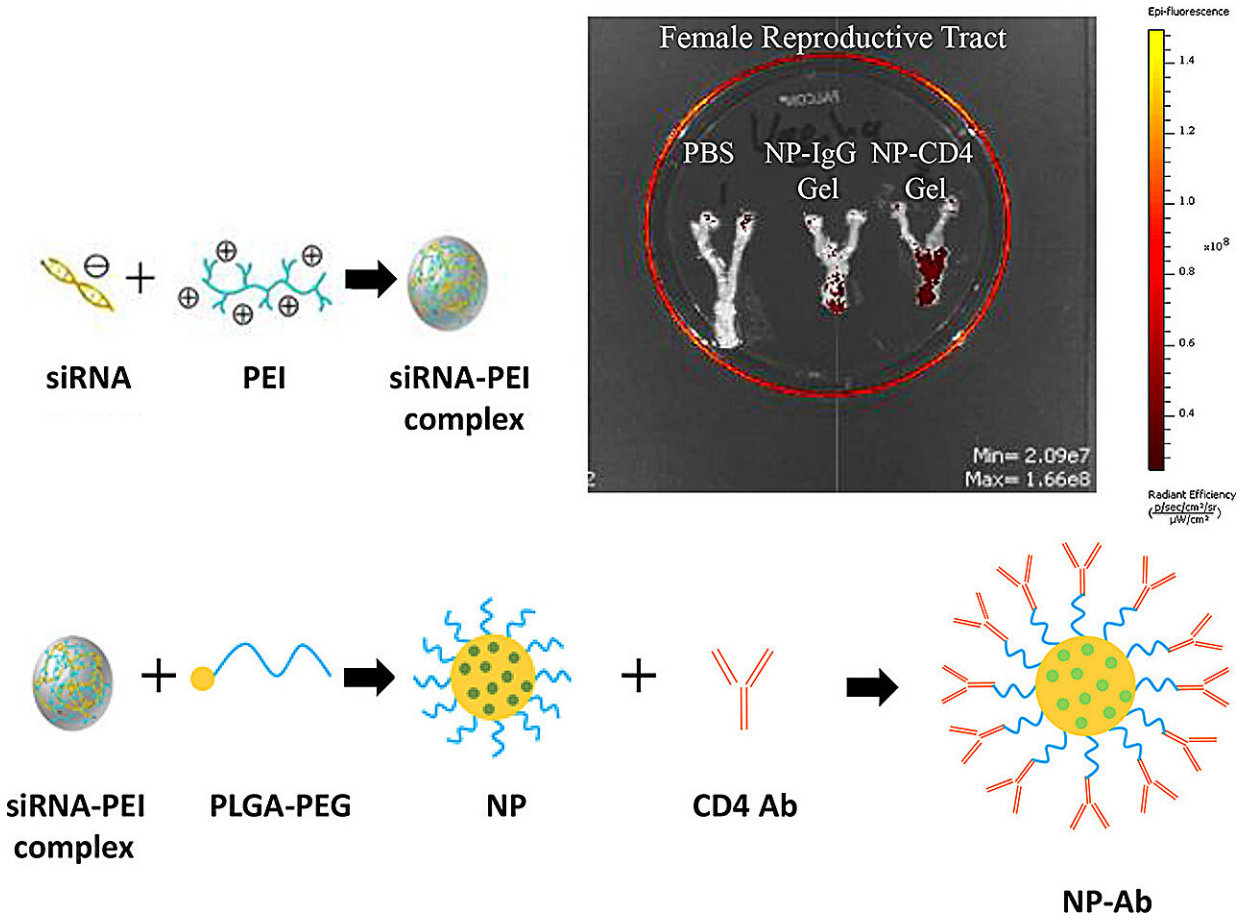


Graphical abstract. Credit: *Journal of Controlled Release* (2024). DOI: 10.1016/j.jconrel.2023.12.043

Society learned about the value of mRNA during the COVID-19

pandemic when we saw scientists and medical professionals harness its power to deliver a vaccine for the virus within a year.

Now, University of Waterloo pharmacy associate professor Emmanuel Ho has developed a novel nanomedicine loaded with genetic material called small interfering RNAs (siRNA) to fight human immunodeficiency virus (HIV) using gene therapy. These siRNAs regulate which genes or proteins are turned on or off in our cells and showed a 73% reduction in HIV replication.

The study, "pH-sensitive dual-preventive siRNA-based nanomicrobicide reactivates autophagy and inhibits HIV infection in vaginal $CD4^+$ cells," was published in the *Journal of Controlled Release.*

"This opens the door for new therapeutics in the fight against HIV," said Dr. Ho, who is among Waterloo's researchers and entrepreneurs leading health innovation in Canada.

Autophagy, also known as the body's recycling process, plays an important role in our body to eliminate microbes such as viruses and bacteria inside cells. HIV is quite smart and produces a protein, Nef, that prevents cells from activating autophagy.

This is the first research to develop a combination nanomedicine that can reactivate autophagy and prevent HIV entry into cells, allowing our body to re-initiate its defense system.

Additionally, HIV has a gene, CCR5, that allows the virus to enter a cell. The siRNAs target both Nef and CCR5 to reduce HIV infection.

This nanomedicine is intended to be applied vaginally to protect against sexual transmission of HIV. As a result, the nanomedicine is designed to be stable without leakage of siRNAs in the acidic vaginal environment

but release the siRNA once inside cells.

"Viruses are smart. They produce Nef proteins to prevent autophagy from occurring," Ho said. "Our process allows our body to fight the viral infection without needing additional drugs,"

Ho confirms that the next steps include further optimizing the process and improving our understanding of how autophagy plays a role in how our cells protect us from viruses.

"We also hope this will shed some light to develop more alternative approaches to effectively reduce antimicrobial resistance," Ho said.

**More information:** Sidi Yang et al, pH-sensitive dual-preventive siRNA-based nanomicrobicide reactivates autophagy and inhibits HIV infection in vaginal CD4+ cells, *Journal of Controlled Release* (2024). DOI: 10.1016/j.jconrel.2023.12.043

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