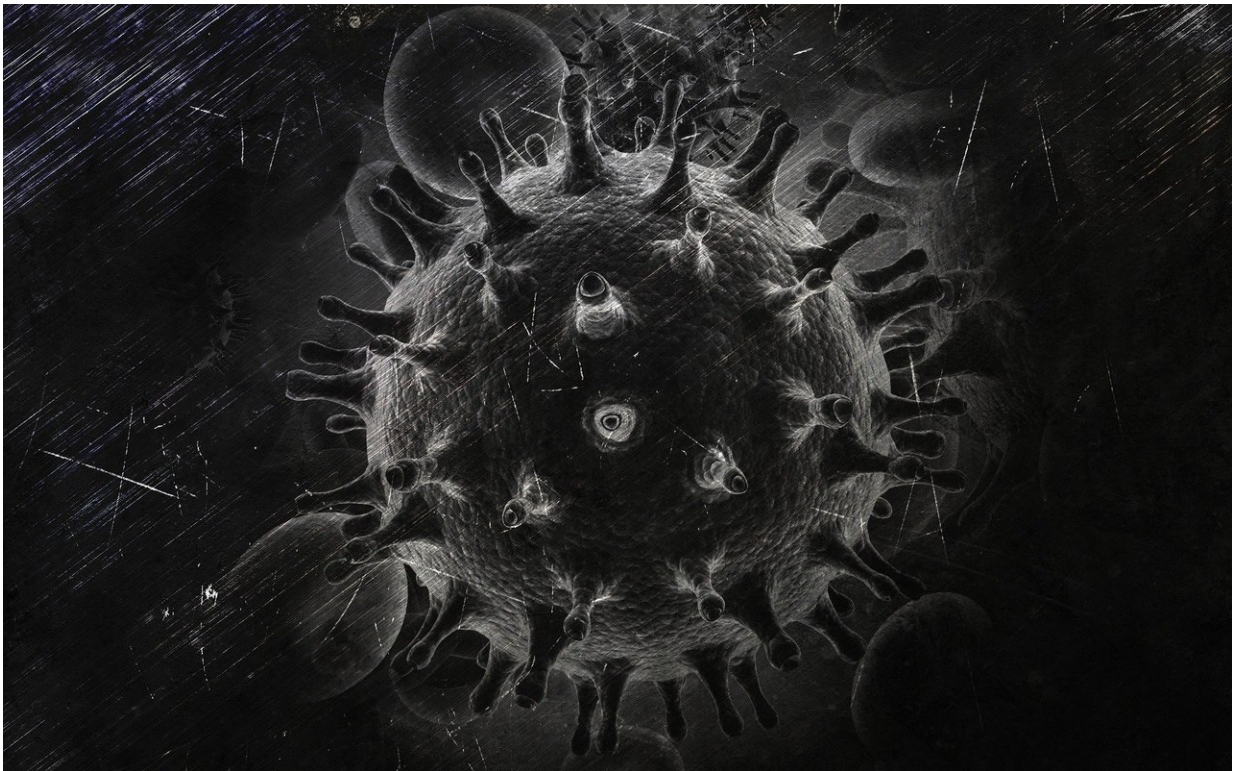


Breakthrough discovery in HIV research opens path to new, better therapies

April 23 2020



Credit: CC0 Public Domain

New research on the structure of the human immunodeficiency virus (HIV) has revealed a promising novel drug target for treating HIV infection, which affects more than 1 million Americans and 40 million people worldwide. The findings, published today in *Science*, show that

the virus's genetic code can be read in two different ways by cells the virus has infected. The result is that infected cells make two different forms of the virus's RNA.

"This functional diversity is essential for the virus to replicate in the body. The virus has to have a proper balance between the two forms of RNA," says Joshua Brown, the lead author on the study. "For decades, the scientific community has known that two different structural forms of HIV RNA exist—they just didn't know what controls that balance. We've discovered that a single nucleotide is having a huge effect, which is a [paradigm shift](#) in understanding how HIV works."

Crucially, "You can imagine that if you could come up with a [drug](#) that would target the [genetic code](#) at that one specific spot, and shift it to one form only, then it could prevent further infection, theoretically," says Brown, who earned his Ph.D. from UMBC in 2018 and continues to conduct research there while completing his M.D.

A new trajectory

"One of the things we're working on now is testing different molecules that could shift the equilibrium between the two forms, so that it could potentially be used as a treatment for HIV," says Issac Chaudry, a junior at UMBC and an author on the paper.

This exciting work comes from a research group led by Michael Summers, Robert E. Meyerhoff Chair for Excellence in Research and Mentoring and Distinguished University Professor at UMBC. Summers has been conducting groundbreaking research on HIV for decades. Typically, the group's focus is on basic science.

"Drug discovery isn't the direction that the Summers lab usually goes, but this was such an impactful finding in a very attractive area, we took

the initiative to start looking into it," Brown says. "But we're still in the very early stages."

More effective treatments for more patients

Thanks to significant research on HIV over the last few decades, today AIDS is a manageable disease. Still, therapies can come with side effects, medication regimens can be complex, and treatment options can be limited for patients with other conditions, such as liver or kidney problems.

Many therapies, even if they come in the form of a single pill, contain several drugs targeting different parts of the virus's replication cycle. That's necessary because the HIV genetic code, which is made of RNA, mutates rapidly. This allows the virus to adapt and become resistant to current HIV therapies. If a drug targets an area that has mutated in a given patient, the drug may no longer work for them. By using several drugs at once, it's more likely that the regimen will continue to work for longer.

But the area of the HIV RNA genome that this new research focuses on is "highly conserved." This means the rate of mutation is less than other places in the genome, explains Ghazal Becker, a 2019 UMBC alumna and an author on the paper. The result is "there's more chance of a drug that targets that region being effective for longer," she says.

It might also mean that one drug would be enough, rather than patients needing several drugs to get the job done. "If you're targeting a conserved region, you can potentially come up with a treatment plan that uses only one drug," says Aishwarya Iyer, a 2018 UMBC alumna, current M.D./Ph.D. at the University of Maryland School of Medicine, and an author on the paper. "It might have fewer side effects and could offer more treatment options to people with different health conditions."

Expanding the research horizon

This new research opens up a range of opportunities for Brown's research group and others. "We're very interested to see how other labs will interpret our results, expand upon them, and possibly find other applications for this type of RNA function," Brown says.

Those future results and any new therapies they enable could have a major impact. "Every time we get a new drug in HIV, we exponentially improve the chances of individuals finding a drug that works for them, where resistance is a little less likely," says Hannah Carter, a 2017 UMBC alumna, current M.D./Ph.D. student at University of Michigan, and an author on the paper. "Every time a new drug can get on the scene, that's a significant improvement for the lives of HIV patients."

The research could have effects beyond HIV, too. "Some HIV research [has laid the groundwork](#) in how we understand coronaviruses," Carter adds. "All basic science in HIV ends up having a ripple effect throughout all of virology."

The ripple effect might go even farther. "The idea that a single nucleotide difference is changing the structure and function of RNA that is thousands of nucleotides long could open up a whole new aspect of cell biology," Chaudry says. "It could be possible that there are mammalian genes that operate in a similar manner, and the entire mechanism might be something that's applicable to other human genes as well. I think that whole paradigm could provide a new perspective for RNA biology."

More information: "Structural basis for transcriptional start site control of HIV-1 RNA fate" *Science* (2020).

[science.sciencemag.org/cgi/doi ... 1126/science.aaz7959](https://science.sciencemag.org/cgi/doi/10.1126/science.aaz7959)

Provided by University of Maryland Baltimore County

Citation: Breakthrough discovery in HIV research opens path to new, better therapies (2020, April 23) retrieved 25 April 2024 from <https://medicalxpress.com/news/2020-04-breakthrough-discovery-hiv-path-therapies.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.