AI helps create better, simpler hepatitis and COVID-19 tests

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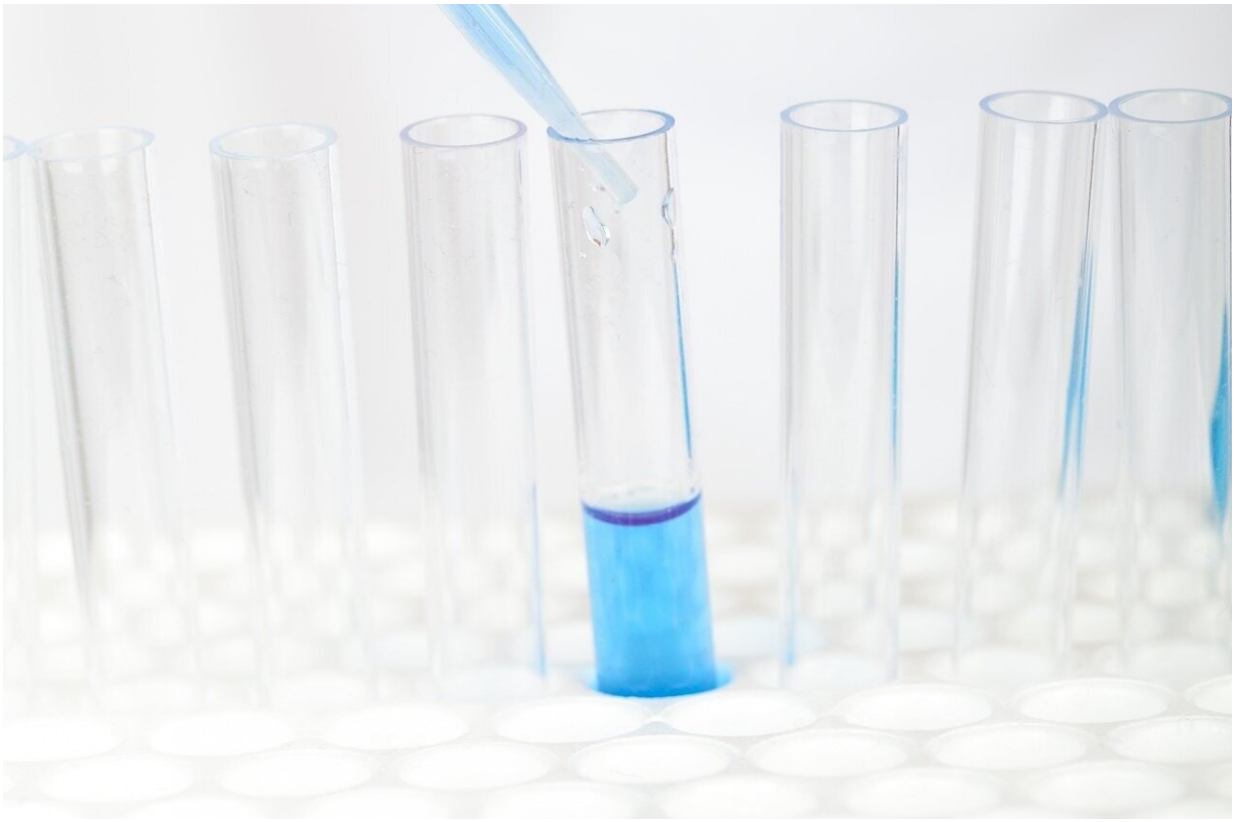

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Going beyond pregnancy and COVID-19, the world could someday soon come to rely on at-home tests for many diseases thanks in part to AI-fueled improvements.

University of Florida scientists have used artificial intelligence tools to simplify a test that works for both hepatitis C and SARS-CoV-2, the virus that causes COVID-19. The simplified test happens in one small test tube in just a few minutes. With further refinement, it could come to doctor's offices soon and, one day, even home tests that are as easy as a pregnancy test.

"We are trying to build a home-based test that is as reliable as a lab-based test," said Piyush Jain, a UF professor of chemical engineering who led the latest research. "We are trying to make the test simple, eliminate the need for expensive equipment and provide results in just 10 to 20 minutes."

To accomplish those goals, Jain's group is innovating on a system known as a one-pot reaction, because the entire test happens in one small test tube. These tests, based on a technology known as RT-LAMP, can amplify small portions of a virus's genome and produce a visible signal when it detects the virus. Reading these tests can be as simple as looking for a blue color or using a small device that detects a change in the test tube.

The FDA has approved some at-home, one-pot tests for COVID-19, as a part of the emergency use authorization, but they have a relatively high false positive rate, meaning they aren't as reliable as they could be.

"We are combining another technology called CRISPR to determine the difference between a false positive and a true positive," Jain said.

CRISPR has become known in the biotech world for its ability to drive rapid genetic engineering improvements, which have the potential to one day cure inherited diseases by repairing genomes. Jain's group relies on the CRISPR system's ability to home in on particular genetic sequences. Only if the sequence for, say, the hepatitis virus is really present will the

test show a positive result.

The only problem? The RT-LAMP technology requires a temperature of 150 degrees F, while CRISPR works best at 100 degrees. That difference makes tests far more complicated requiring two separate reactions—too complicated for at-home use. Jain's team has been trying to bridge this gap by developing a CRISPR system that can withstand higher temperatures.

From a heat-loving species of bacteria, the researchers recently discovered a CRISPR enzyme that thrives at 140 degrees. In their latest work, Jain's group turned to AI tools to analyze this enzyme and discover how they could make it survive at 150 degrees. The AI programs suggested a few dozen changes to the enzyme, which Jain's group tested in the lab. They eventually found four changes to the enzyme that let it work at 150 degrees.

"It's very challenging for any human to do this kind of analysis on an enzyme. We didn't have to spend years, we could make these improvements in months," Jain said. "With everything working at the same temperature, now we are able to combine everything in a true one-pot reaction, we call SPLENDID."

The team verified their simplified SPLENDID test on clinical samples from patients with hepatitis C or COVID-19. The test was 97% accurate for SARS-CoV-2 and 95% accurate for the most prevalent version of the hepatitis C virus found globally. Although it didn't work well against all other less predominant versions of the hepatitis C virus, straightforward changes to the test should quickly improve its accuracy, Jain says. His team published their findings May 8 in the journal *Cell Reports Medicine*.

More information: Piyush K. Jain, Engineering Highly Thermostable Cas12b via De Novo Structural Analyses for One-Pot Detection of

Nucleic Acids, *Cell Reports Medicine* (2023). DOI: 10.1016/j.xcrm.2023.101037. www.cell.com/cell-reports-medi … 2666-3791(23)00151-9