Stanford engineers have developed a genetic microlab that can detect COVID-19 in minutes

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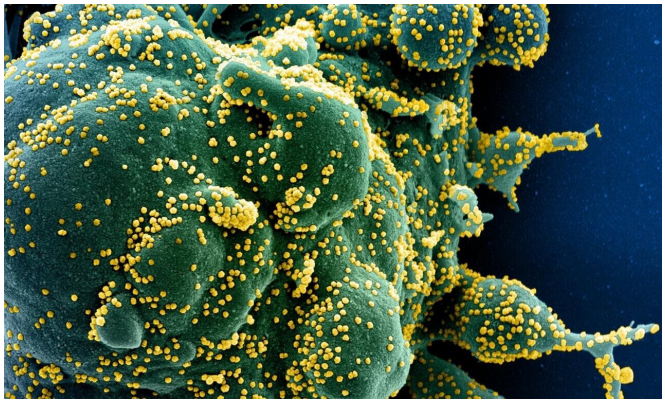

Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-COV-2 virus particles (yellow), isolated from a patient sample. Image captured at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIH/NIAID

Throughout the pandemic, infectious disease experts and frontline medical workers have asked for a faster, cheaper and more reliable COVID-19 test. Now, leveraging the so-called "lab on a chip" technology and the cutting-edge genetic editing technique known as CRISPR, researchers at Stanford have created a highly automated device that can identify the presence of the novel coronavirus in just a half-hour.

"The microlab is a microfluidic chip just half the size of a credit card containing a complex network of channels smaller than the width of a human hair," said the study's senior author, Juan G. Santiago, the Charles Lee Powell Foundation Professor of mechanical engineering at Stanford and an expert in microfluidics, a field devoted to controlling fluids and molecules at the microscale using chips.

The new COVID-19 test is detailed in a study published on Nov. 4 in the journal *Proceedings of the National Academy of Sciences*. "Our test can identify an active infection relatively quickly and cheaply. It's also not reliant on antibodies like many tests, which only indicates if someone has had the disease, and not whether they are currently infected and therefore contagious," explained Ashwin Ramachandran, a Stanford graduate student and the study's first author.

The microlab test takes advantage of the fact that coronaviruses like SARS-COV-2, the virus that causes COVID-19, leaves behind tiny genetic fingerprints wherever they go in the form of strands of RNA, the genetic precursor of DNA. If the coronavirus's RNA is present in a swab sample, the person from whom the sample was taken is infected.

To initiate a test, liquid from a nasal swab sample is dropped into the microlab, which uses electric fields to extract and purify any nucleic acids like RNA that it might contain. The purified RNA is then converted into DNA and then replicated many times over using a technique known as isothermal amplification.

Next, the team used an enzyme called CRISPR-Cas12—a sibling of the CRISPR-Cas9 enzyme associated with this year's Nobel Prize in Chemistry—to determine if any of the amplified DNA came from the coronavirus.

If so, the activated enzyme triggers fluorescent probes that cause the sample to glow. Here also, electric fields play a crucial role by helping concentrate all of the important ingredients—the target DNA, the CRISPR enzyme and the fluorescent probes—together into a tiny space smaller than the width of a human hair, dramatically

increasing the chances they will interact.

"Our chip is unique in that it uses electric fields to both purify nucleic acids from the sample and to speed up chemical reactions that let us know they are present," Santiago said.

The team created its device on a shoestring budget of about $5,000. For now, the DNA amplification step must be performed outside of the chip, but Santiago expects that within months his lab will integrate all the steps into a single chip.

Several human-scale diagnostic tests use similar gene amplification and enzyme techniques, but they are slower and more expensive than the new test, which provides results in just 30 minutes. Other tests can require more manual steps and can take several hours.

The researchers say their approach is not specific to COVID-19 and could be adapted to detect the presence of other harmful microbes, such as E. coli in food or water samples, or tuberculosis and other diseases in the blood.

"If we want to look for a different disease, we simply design the appropriate nucleic acid sequence on a computer and send it over email to a commercial maker of synthetic RNA. They mail back a vial with the molecule that completely reconfigures our assay for a new disease," Ramachandran said.

The researchers are working with the Ford Motor Company to further integrate the steps and develop their prototype into a marketable product.

More information: Ashwin Ramachandran et al, Electric field-driven microfluidics for rapid CRISPR-based diagnostics and its application to detection of SARS-CoV-2, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2010254117