The Future Of COVID-19 Testing

PRESCOUTER

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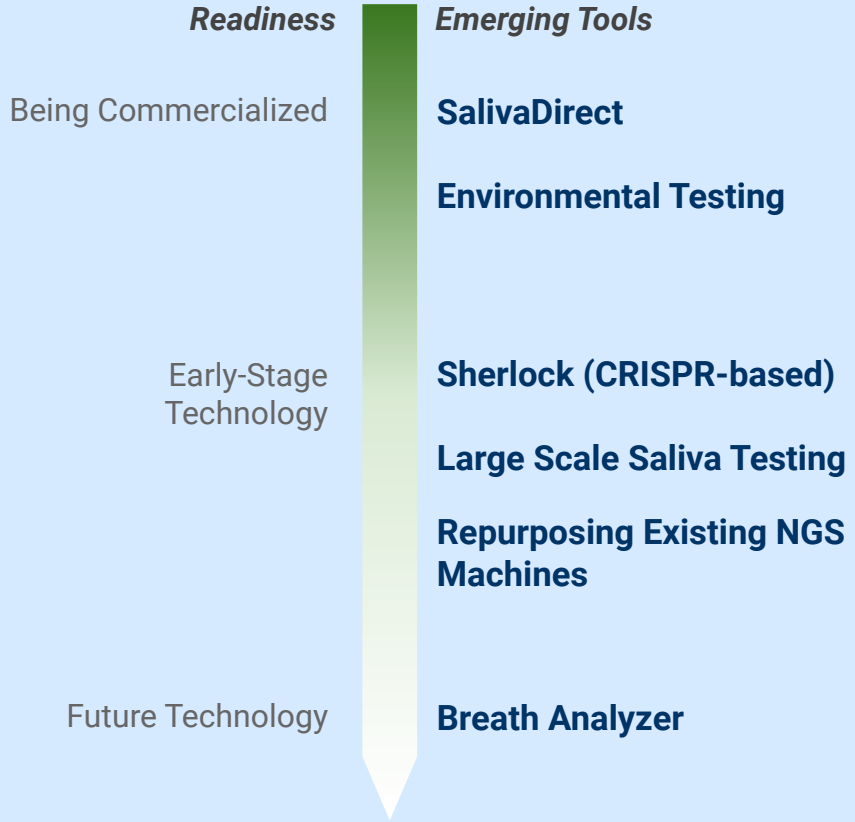
Over the next year, new COVID-19 diagnostic tools are likely to emerge.

Innovators are continuing to make strides towards a test that is rapid, reliable and easy-to-use. Such testing technologies could supplement existing RT-PCR-based strategies.



During this pandemic, PreScouter is leveraging its network of 4000+ experts, lab partners and prototyping firms to provide clients with the testing expertise and resources they need to safeguard their workplaces. While this report provides general recommendations, we welcome inquiries to help determine what may be best for your specific situation.

Contact us at covid19@prescouter.com or (708) 613-7132

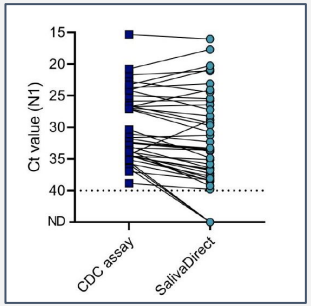
SalivaDirect: Rapid, low-cost saliva-based RT-PCR testing.

Status: Being Commercialized

Typically, with RT-PCR testing, the genetic viral material (RNA) in a sample is isolated and undergoes a series of purification steps before performing RT-PCR. A recent study from Yale found that saliva samples can be used directly without the need for isolation of RNA. This method, called SalivaDirect, reduces costs normally associated with the RT-PCR testing process. It was used by the NBA to test all the players and staff in the Disney Bubble for the NBA finals.

- ✔ SalivaDirect saves time and is far less expensive because the viral RNA isolation step is removed.
- ✔ SalivaDirect retains all the benefits of regular RT-PCR. For instance, the method can detect very low amounts of virus.
- ✔ Collection of saliva is minimally invasive and can reliably be self-administered. This makes it ideal for on-site testing.

SalivaDirect at a Glance



SalivaDirect is an FDA-EUA approved RT-PCR technique that uses saliva instead of respiratory swabs. SalivaDirect is highly sensitive with a limit of detection of 6-12 SARS-CoV-2 copies/µL. When compared to a traditional RT-PCR test recommended by the CDC, using nasopharyngeal swabs, high agreement was found in testing outcomes (>94% overlap, see figure above). The technique is inexpensive and easy to implement. It was first piloted in the NBA during the Spring of 2020. *(Source: SalivaDirect Publication)*

PRESCOUTER EXPERT NOTE:

"SalivaDirect is a game-changer and will allow for low-cost, rapid RT-PCR testing for workplaces and schools"

- Anne Wyllie - Developed SalivaDirect, Scientist at Yale University

Environmental Sampling: A proxy for measuring SARS-CoV-2 infections in a community.

Status: Being Commercialized

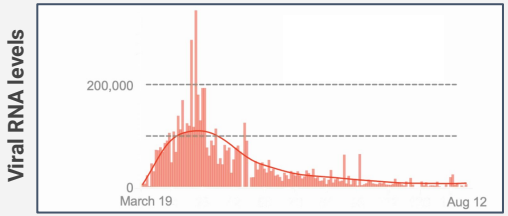
Monitoring the amount of virus in environmental samples, such as wastewater, is a powerful tool that can track COVID-19 outbreaks in a community. People with an active infection excrete the virus in their stool. The presence of the virus in stool can be measured with representative sampling of wastewater and consecutive RT-PCR testing. There are several advantages of environmental sampling over other diagnostic techniques.

- ✔ Environmental samples test a community as a whole with one test.
- ✔ Environmental samples have been shown to detect outbreaks early on and detect asymptomatic individuals as well.
- ✔ Besides wastewater, it is also possible to take samples from surfaces and centralized air ducts.

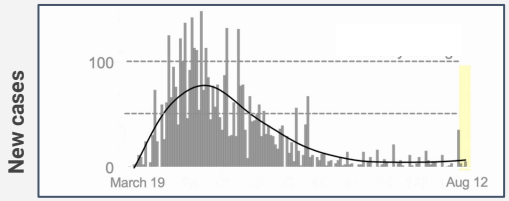
Case Study: Wastewater Sampling in New Haven (CT) Tracks Community Infections

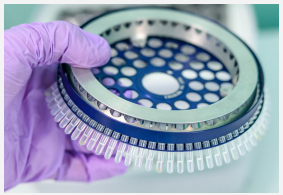
In this study, wastewater samples were acquired between March and June 2020. Samples were analyzed for SARS-CoV-2 with RT-PCR. Wastewater screening correlated with the rise and fall of clinically confirmed cases. In addition, the study showed that monitoring the wastewater revealed an outbreak about 6–8 days ahead of positive test results acquired in the hospital. This means that wastewater sampling can be an early indicator of COVID-19 outbreaks. (Sources: Nature Microbiology & CT Covid Tracker)

RNA levels in wastewater (CT Covid Tracker)



New Confirmed Cases (CT Government)





The levels of virus detected in wastewater exactly matched the clinically confirmed COVID-19 cases. This indicates that wastewater can be an early indicator of viral outbreaks in communities.

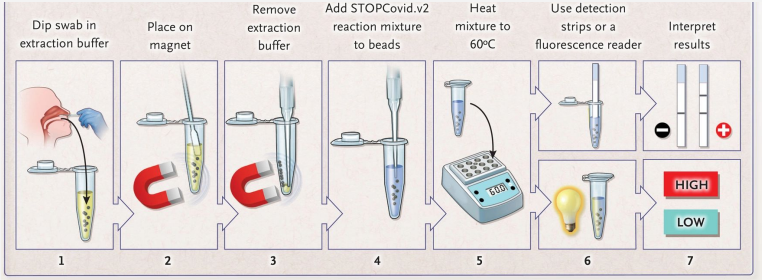
CRISPR-based Diagnostic Testing: Working towards an alternative, point-of-care testing.

Status: Early-Stage Technology

One way of solving testing capacity shortages is to invest in new methods that relieve the pressure on existing techniques and limited reagents. Until recently, CRISPR-based diagnostic testing was not possible in a point-of-care setting. A new research paper published in a leading scientific medical journal shows that simplification steps in the protocol can eliminate the need for viral RNA isolation as well as pipetting steps. The method is called STOP (SHERLOCK Testing in One Pot).

- ✔ STOP has the potential to be used at point-of-care settings.
- ✔ This technology can play a role in future disease diagnostics and has commercial potential.
- ✔ STOP has a lower sensitivity than RT-PCR but can still reliably detect positive samples.

Case Study: The CRISPR-based STOP.Covid Assay



STOP.Covid is a CRISPR-based COVID-19 diagnostic test that can be performed with minimal lab equipment. This allows use of this test in a point-of-care setting. First, a swab is acquired by a healthcare worker (step 1). Afterwards the swab is mixed with an extraction buffer and a magnet is used to capture viral genetic materials (step 2 & 3). After replacing the extraction buffer with a reaction mixture, the sample is heated to 60°C (step 4 & 5) and a dipstick can be used (80 minutes later) to read out the result. Alternatively, a fluorescence reader can be used to read the result after 45 mins at 60°C (step 6 & 7).

PRESCOUTER EXPERT NOTE:

"CRISPR-based testing strategies may not be ready for deployment in COVID-19 diagnostics, but are an incredibly promising tool for future disease diagnostics."

- Ryan LaRanger, PhD, PreScouter Technical Director, PreScouter

Large scale saliva testing could get the US to the levels of testing that are needed.

Status: Early-Stage Technology

Regardless of whether the approach used is PCR or NGS, saliva testing eliminates the need for using trained personnel to acquire accurate samples.

What's needed for large-scale saliva testing?

- Multiple, mobile testing locations to collect samples. This includes drive-throughs and walkthroughs.
- Organizing manufacturers to aid in production of clinical swabs, saliva test tubes and kit packaging.
- An infrastructure that allows distribution of kits on a national level.
- Large, high-capacity testing facilities (50,000-100,000 samples/day) that perform high-quality testing.

Challenges in establishing large-scale saliva testing

Step 1.  **Increase manufacturing of swabs/kits**

Step 2.  **Build sample collection points**

Step 3.  **Design large, high-capacity testing labs**

Step 4.  **Create an online results platform and integrate with local healthcare**

WHAT TO KEEP AN EYE OUT FOR:

CURATIVE KORVA COVID-19 DETECTION

Curative Inc. is a start-up that is working on scaling up saliva testing to nationwide levels. Their aim is to create new supplies of kits and tests without competing for resources with existing testing approaches.

Repurposing existing NGS machines: making deployment of millions of tests a day possible.

Status: Early-Stage Technology

Next-Generation Sequencing (NGS) technology was originally designed for sequencing the human genome. However, NGS platforms can be repurposed for diagnostic testing.

The US has 400 NGS machines. Illumina, the Broad Institute, Hudson and others are all developing so-called “multiplexing” tests. Multiplexing - a technique unique to NGS - means a single NGS machine could, hypothetically, test as many as 750,000 individual samples daily.

Since NGS uses different reagents and a different supply chain than existing COVID-19 tests, this approach also effectively creates new testing capacity.

Some limitations of this approach are that it would need to pass EUA approval and need a supporting infrastructure to send samples to the existing 400 NGS machines. The complexity of the technology also means retooling them is not trivial.

NGS compared to the current best approach, RT-PCR

	RT-PCR	NGS
Accuracy	High	High
Ability to scale to US needs	Uncertain	Yes
Tests/day - now	200,000	0
Tests/day - in future	<1 million	Tens of millions
Turn-around time	1-2 days	1-2 days
Sample Type	Nasal swab/ Saliva	Nasal swab/ Saliva
Supply chain risk	Medium	Low

An NGS machine from Illumina. Illumina is developing COVID-19 tests for use on their sequencing platforms. Source: Illumina

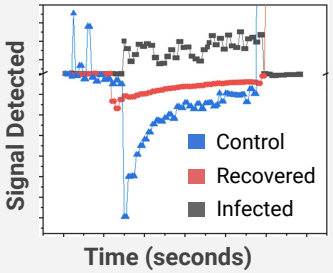
Breath Analyzer: The future of diagnostic screening detects biomarkers in patient breath.

Status: Future Technology

Disruptive technologies that can instantly and accurately diagnose COVID-19 are a holy grail. Whereas the diagnostic testing landscape is evolving rapidly, such a test is still out of reach, for now. However, proof-of-principle testing devices have been gaining traction. One such device is a breathalyzer that detects specific biomarkers that point to infection. Initial results show that such a breathalyzer has the potential to detect disease. Major advantages of a breath test include:

- ✔ Potentially instant results.
- ✔ Non-invasive method of analysis.
- ✔ Could be used anywhere, for instance at airports, events and shops.

Case Study: Nanomaterial-based breath analyzer can be used for COVID-19 screening



The graph above shows the signal that was detected using the breathalyzer from a single patient during his infection (grey line) and shortly after he was infected (red line). A control is used in the experiment to measure background signal. The device clearly shows a higher signal for the infected patient's breath. The training and test set data used in the paper shows a 76-94% accuracy in differentiating patients from controls as well as 90%-95% accuracy in differentiating between patients with COVID-19 and patients with other lung infections. Figure adapted from: Breath Analyzer Paper.

ABOUT PRESCOUTER

DURING THIS PANDEMIC, PRESCOUTER IS LEVERAGING ITS NETWORK OF 4000+ EXPERTS, LAB PARTNERS AND PROTOTYPING FIRMS TO PROVIDE CLIENTS WITH THE TESTING EXPERTISE AND RESOURCES THEY NEED.

PreScouter traditionally provides corporate innovation and R&D leaders with expertise on emerging technologies and markets. During this pandemic, PreScouter is vetting, selecting and promoting *best in class* testing solutions from lab partners, to provide clients with the unbiased expertise and the resources they need to deploy testing to safeguard their workplaces.

To learn more, contact us at covid19@prescouter.com or (708) 613-7132.

EXAMPLES OF OTHER PRESCOUTER PROJECTS:

Technologies and tactics for reducing disinfection time: What tools can companies use to automate disinfection and other safety practices.

Supply Chain Disruption: When traditional resources or raw materials are not available during a pandemic, PreScouter helps clients find alternative solutions - uncovering connections around the world.

Driving Consumer Confidence: Tactics that give workers and consumers confidence that they are in a safe environment, to ultimately drive their re-engagement in economic activity.

Important Disclaimer: The information provided in this briefing report is based on advice from public health authorities, other regulatory agencies and vendors, as well as news reports and scientific publications. This information has been analyzed, reviewed, and summarized by PreScouter. It is not a substitute for medical or legal advice about your employees, workplace, or obligations.

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