In response to the COVID-19 outbreak, Clinical Reference Laboratory, Inc. (CRL) identified an urgent need to mitigate current limitations to sample collection methods involving nasopharyngeal (NP), oropharyngeal (OP), and interior nasal swabs. This includes the shortage of swabs, inherent difficulty in the proper self-collection of swabs which could lead to false negative test results, shortage of PPE, and the patient experience. CRL's scientific team performed extensive R&D efforts on COVID-19 in effort to use sample matrices more amenable to reliable self-collection, including saliva, dried blood spot, and urine. Such collection methods could be deployed by individuals in self-isolation in an effort to lessen the impact on healthcare providers for initial COVID-19 testing requests, thus enabling greater healthcare access for critical patients. Further, these self-collection devices could be distributed to employees at home in effort to test an entire company to enable them to return safely to work. Also, this alternative provides an attractive method for public health collected samples from both rural and metropolitan areas.

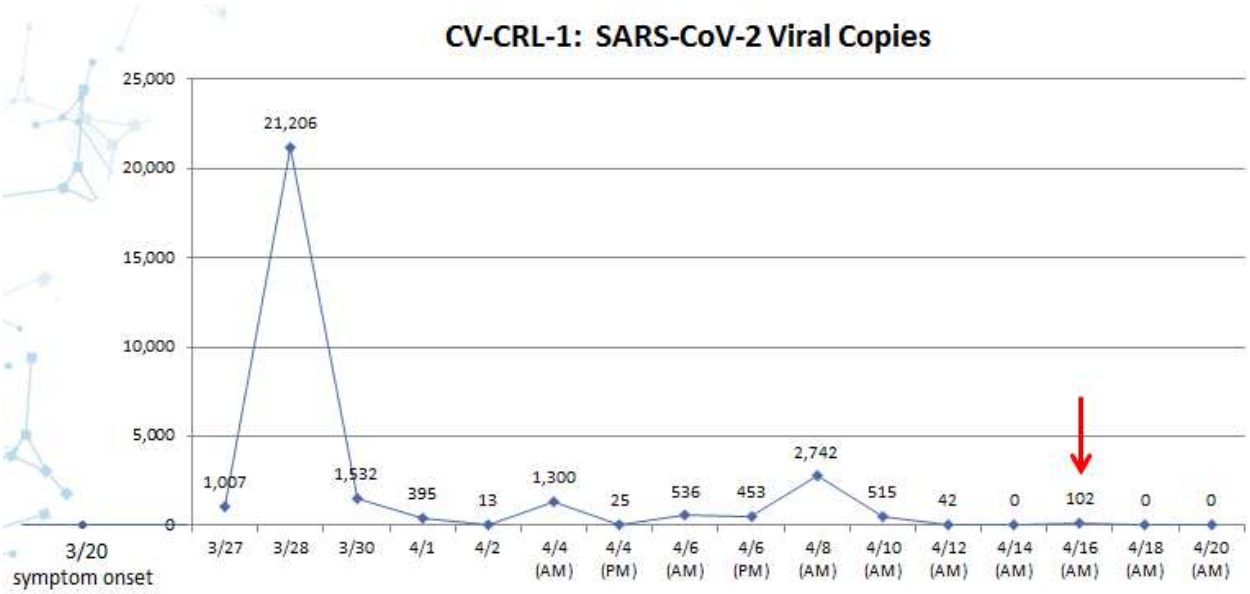
There are two main types of tests for COVID-19, molecular and serological. The molecular test detects the genetic material from SARS-CoV-2, which is the virus that causes COVID-19. The serological test identifies individuals who have developed an immune response to the virus. Serological tests detect antibodies to SARS-CoV-2 to help identify people who are currently infected with SARS-CoV-2 virus or who have recovered from the COVID-19 infection.

At the foundation of a quality COVID-19 test is the methodology. For the molecular COVID-19 test, CRL Rapid Response®, CRL's Molecular Diagnostics team thoroughly investigated numerous technologies that could be leveraged for test design. Ultimately, the Co-Diagnostics Logix Smart Coronavirus COVID-19 RT-PCR assay was selected for the detection of the virus. This reverse-transcriptase quantitative PCR assay (RT-qPCR) uses proprietary Co-Primer technology that improves the specificity of the test compared to others. The test targets the RdRp gene of the SARS-CoV-2 virus which has a low mutation rate compared to other regions of the viral genome.

Using this test, the research team investigated a variety of sample types (urine, blood, urine) that were obtained using collection devices from various manufacturers. The team successfully identified SARS-CoV-2 in the saliva of confirmed COVID-19 positive individuals. CRL studies as well as others in the literature support the detection of SARS-CoV-2 in saliva samples[1,2].

To further validate these findings, CRL initiated a formal research study (WIRB Protocol #20201072) to compare the use of nasal swabs and saliva for the detection of SARS-CoV-2. The clinical evaluation guideline established by the FDA for COVID-19 Molecular Diagnostic Emergency Use Authorization (EUA) requires 30 patient samples. As presented in CRL's EUA documentation, 100% of known COVID-19 positive patients tested (n=31) were successfully identified in this study using the saliva-based CRL Rapid Response® test. In comparison, concurrently collected anterior nasal swabs identified the presence of the virus in only 55% of the samples. Since EUA submission, CRL has conducted additional studies using paired nasopharyngeal swabs and saliva samples collected from COVID-19 positive patients. In all cases (n=15), the CRL Rapid Response® test accurately detected the presence of the virus.

CRL uncovered interesting findings in the course of research and development on the Rapid Response® molecular COVID-19 test. Using saliva samples collected from confirmed COVID-19 positive individuals, CRL serially tracked SARS-CoV-2 viral levels. The results demonstrated detectable virus nearly 4 weeks post symptom onset in some patients. In these individuals, often the viral level would drop to zero, and then reappear days later at a low viral count. This finding has been documented by other studies as well [3,4]. Another key discovery was that viral levels varied by time of day with morning collections yielding higher viral copy number. As a result, the recommendation of a morning collection was incorporated into CRL's Rapid Response® collection instructions to ensure accurate results.



For serological COVID-19 testing, CRL partnered with several leading industry manufacturers to explore and validate tests. The Roche Elecsys Anti-SARS-CoV-2 serology test offers a high quality and high throughput testing option. Per the manufacturer, this test has a specificity of >99.8% (ability to correctly identify non-infected individuals), and a sensitivity of 100% (ability to successfully identify infected individuals) (14 days post-PCR confirmation)[5]. Using a blood sample, collected either using venipuncture or fingerstick, the test can detect total antibodies to COVID-19 which could signal whether a person has been already infected and potentially developed immunity to the virus. To add further insight into the antibody results, CRL is using a separate serology test that can discern active infection (IgM) from past infection/exposure (IgG).

CRL is leveraging both the molecular and serology tests in a product offering for clients. Our team has developed a COVID-19 workflow which identifies individuals who should be tested using the serology test and/or molecular test based on CDC Guidelines[6]. Low risk individuals can use a finger stick collection kit to provide a sample for the serology test. Should antibodies suggesting an active infection the molecular test to identify the SARS-CoV-2 virus would be suggested as a reflex test. Those

individuals with high risk for COVID-19 infection can use a saliva collection kit for the Rapid Response® molecular test as an initial test.

Through this testing effort, CRL is actively collecting population level data to help our clients, and the community better understand the virus. Our main goals are to help patients and stop the spread of COVID-19 by providing highly accurate, timely test results using patient-friendly self-collection methods.

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4. Wall Street Journal, South Korea's New Coronavirus Twist: Recovered Patients Test Positive Again, April 24, 2020 https://www.wsj.com/articles/south-koreas-new-coronavirus-twist-recovered-patients-test-positive-again-11587145248
5. Full specifications of Roche's Elecsys® Anti-SARS-CoV-2 antibody test and immunoassay systems, including throughput diagnostics.roche
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