New coronavirus mass test up to 100 times more sensitive than rapid antigen tests

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Blue-stained swab material from corona tests is prepared for analysis in a sequencing device with the help of a laboratory robot. Credit: Felix Heyder / University Hospital Bonn

A new coronavirus test developed at the University Hospital Bonn can analyze a large number of swabs simultaneously using sequencing

technology and has a sensitivity comperable to the common qPCR test. The innovative method offers great potential, especially for systematic testing in daycare centers, schools or companies. Today, the results of the study on the new coronavirus test have been published in the renowned journal *Nature Biotechnology*.

In addition to vaccination, systematic testing of the population remains of central importance in order to effectively monitor and contain the spread of infections during the coronavirus pandemic. Only in this way can the spread of the virus be effectively monitored and contained through targeted measures.

The innovative coronavirus test 'LAMP-Seq', which has been developed at the University Hospital Bonn (UKB), offers the possibility to test many people regularly for the SARS-CoV-2 virus. In this way, infections can be detected at an early stage and corresponding chains of infection can be interrupted quickly. "Our coronavirus test 'LAMP-Seq' can detect about 100 times lower amounts of virus than current rapid antigen tests and is almost as sensitive and specific as the common qPCR test" describes Prof. Dr. Jonathan Schmid-Burgk from the Institute of Clinical Chemistry and Clinical Pharmacology of the UKB the characteristics of the test procedure, which was developed with other researchers at the UKB.

"Added to this is the high scalability of the test. By using sequencing machines, thousands of samples can be analyzed simultaneously," said Schmid-Burgk, who was appointed to the University of Bonn from the Broad Institute of MIT and Harvard in early 2020. The LAMP-Seq method detects not only coronavirus infections with the original SARS-CoV-2 virus, but also the novel variants of concern alpha to delta.

A microreaction vessel (often referred to as an "eppi") filled with 1 milliliter of liquid contains the amplified swab material from up to 10,000 corona tests, which are analyzed with a sequencer. Credit: Felix Heyder / University Hospital Bonn

Members of the ImmunoSensation2 cluster of excellence, the Institute of Hygiene and Public Health, Life&Brain GmbH and Bundeswehr Central Hospital Koblenz were among those involved in the project.

For the 'LAMP-Seq' test, the Bonn scientists have adapted the already established LAMP method ("Loop-mediated Isothermal Amplification"—propagation of the viral genome at a constant temperature) and made it compatible with sequencing machines used for biomedical research. As a result, many samples can be analyzed

simultaneously in a high-throughput procedure. Before thousands of samples are analyzed together in a sequencing run, each individual sample is linked to a molecular barcode. This barcode ensures that each sample can be assigned without doubt, even after thousands of samples have been pooled. "Retesting of the entire pool in case of a positive test result is therefore no longer necessary" says Dr. Kerstin Ludwig, Emmy-Noether group leader at the Institute of Human Genetics. This technology significantly reduces the cost per test in comparison to the qPCR test and makes the 'LAMP-Seq' procedure a scalable mass test.

"With its high throughput and sensitivity, the 'LAMP-Seq' test can make a significant contribution to the screening of undetected infections. Especially in schools or companies, where many people regularly meet, the coronavirus test is ideal to systematically and preventively monitor the occurrence of infections" describes Ludwig, the co-developer of the test procedure, the possible application scenarios of the 'LAMP-Seq' test.

Prof. Wolfgang Holzgreve, Medical Director and CEO of the UKB, explains the benefits of the new test for coronavirus surveillance as follows: "In order to effectively contain a pandemic, infected people must be found before they infect others. To achieve this goal, we need mass screenings with the highest sensitivity that can give us a detailed picture of existing chains of infection. This is exactly what the coronavirus test 'LAMP-Seq' developed at UKB is suited for."

Prof. Dr. Jonathan Schmid-Burgk is pipetting in a laboratory on the campus of the University Hospital Bonn. Credit: Felix Heyder / University Hospital Bonn

Even smaller models of the sequencing machines used are capable of analyzing around 10,000 samples in a single run (duration: around ten to twelve hours). This virtually eliminates laboratory capacity as a limiting factor in testing.

In several large studies (including school and employee testing) with a total of around 20,000 tests, the Bonn scientists have extensively tested, optimized and successfully validated the entire upstream and downstream logistics, from sample collection by throat swabs to fully digital feedback of the test results. The documentation of the study

results recently passed an independent peer review process and was published today in the renowned journal *Nature Biotechnology*.

While the Bonn scientists have currently focused their innovative method entirely on SARS-CoV-2 testing, 'LAMP-Seq' can also be used in the future for differential diagnostics in testing for other viruses such as influenza A and can also be quickly adapted to other viruses.

The scientists are currently working on CE certification in order to make the 'LAMP-Seq' test available internationally in the near future. Until this approval is obtained, the technically and scientifically fully validated 'LAMP-Seq' method will continue to be used for pilot testing.

More information: Kerstin U. Ludwig et al, LAMP-Seq enables sensitive, multiplexed COVID-19 diagnostics using molecular barcoding, *Nature Biotechnology* (2021). DOI: 10.1038/s41587-021-00966-9

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