

Diagnostics breakthrough brings viral sequencing to doctors' toolkit

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Scientists at the Center for Infection and Immunity at Columbia University's Mailman School of Public Health report a breakthrough genetic testing method called the Virome-Capture-Sequencing platform for Vertebrate viruses that promises to give clinicians a powerful new tool detect and sequence viruses. Left to right: Thomas Briese, Nischay Mishra, Arvind Kumar, Amit Kapoor, and Ian Lipkin. Credit: Columbia University's Mailman School of Public Health

Until now, there hasn't been a fast, efficient way to broadly screen for viral infections. A breakthrough genetic testing method promises change this situation by giving clinicians a powerful new tool to detect and sequence viruses. Developed by scientists at the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health, the Virome-Capture-Sequencing platform for Vertebrate viruses (VirCapSeq-VERT) is as sensitive as the gold standard polymerase chain reaction (PCR) assays while enabling simultaneous testing for hundreds of different viruses and providing near complete sequence of their genomes.

The system and its capabilities are described for

the first time in a paper in the journal *mBio*.

To use VirCapSeq-VERT, scientists select genetic pieces from among nearly 2 million known [viruses](#), representing all viral taxa known to infect vertebrates. These genetic pieces are used to constitute a probe, which is introduced alongside material taken from the sample being tested. A magnetic process "pulls out" segments from the sample that match the probe; these segments are then analyzed using high-throughput sequencing. In a series of tests detailed in the study, scientists used VirCapSeq-VERT to test for a wide range of viruses in lung tissue, blood, nasal swabs, and feces. In tests of blood or tissue, the method resulted in 100 to 10,000-fold increases in viral matches compared with conventional high-throughput tests.

A Harbinger of Precision Medicine

Ian Lipkin, MD, CII director and John Snow Professor of Epidemiology, explains that heretofore high-throughput screening lacked the necessary sensitivity for detecting viruses. And PCR lacked the ability to test for multiple viruses simultaneously, making screening viruses time consuming and expensive. By contrast, says Lipkin, senior author on the paper, "VirCapSeq-VERT is a specific, sensitive, powerful way of characterizing all of the viruses in a sample. This will be an important tool for [precision medicine](#) as well as basic and clinical research."

A major advantage of VirCapSeq-VERT is that it can collect the entire genome of viruses detected in the sample. By contrast, PCR detects a much smaller segment of the viruses' genome.

Captures Viruses Even After They Mutate

The method's ability to detect a broader swath of the genome is especially useful in screening for viruses, which mutate many times faster than

bacteria. VirCapSeq-VERT is able to detect and collect genetic information about viruses even if the sample doesn't exactly match the probe. According to its developers, VirCapSeq-VERT can detect a novel virus when as much as 60 percent of its sequence doesn't match the probe. When the suspect virus mutates, the technology is still able to catch it.

VirCapSeq-VERT also gives researchers a new tool for efficient viral discovery to help them find all the viruses within a population, or shed light on an emerging infectious disease. CII is already using the tool in its research and is in talks with other labs interested in using it.

But VirCapSeq-VERT's most important contribution, according to Thomas Briese, associate professor and first author, will be in the clinical setting. "If you have patients you suspect has a viral disease, you can now for a very reasonable amount of money, definitively characterize all the viruses present in those individuals in order to figure out how they should be treated," he explains.

VirCapSeq-VERT costs approximately \$40 when testing for 20 viruses, comparing favorably with other procedures like rRNA depletion (approximately \$65 per sample).

Among the world's best-known virus hunters, Ian Lipkin has a long track record of advances in microbiology. In the 1980s, he was the first to use subtractive cloning. A decade later, he used a similar approach to discover the first cases of West Nile virus in the western hemisphere. More recently, Lipkin and colleagues at CII developed mass-tag PCR and the first pan-microbial microarray. CII is also the first to use high-throughput sequencing for the discovery of novel microbes.

Provided by Columbia University's Mailman School of Public Health

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