Tulane researchers design nanotechnology blood test to find hidden COVID-19 infections

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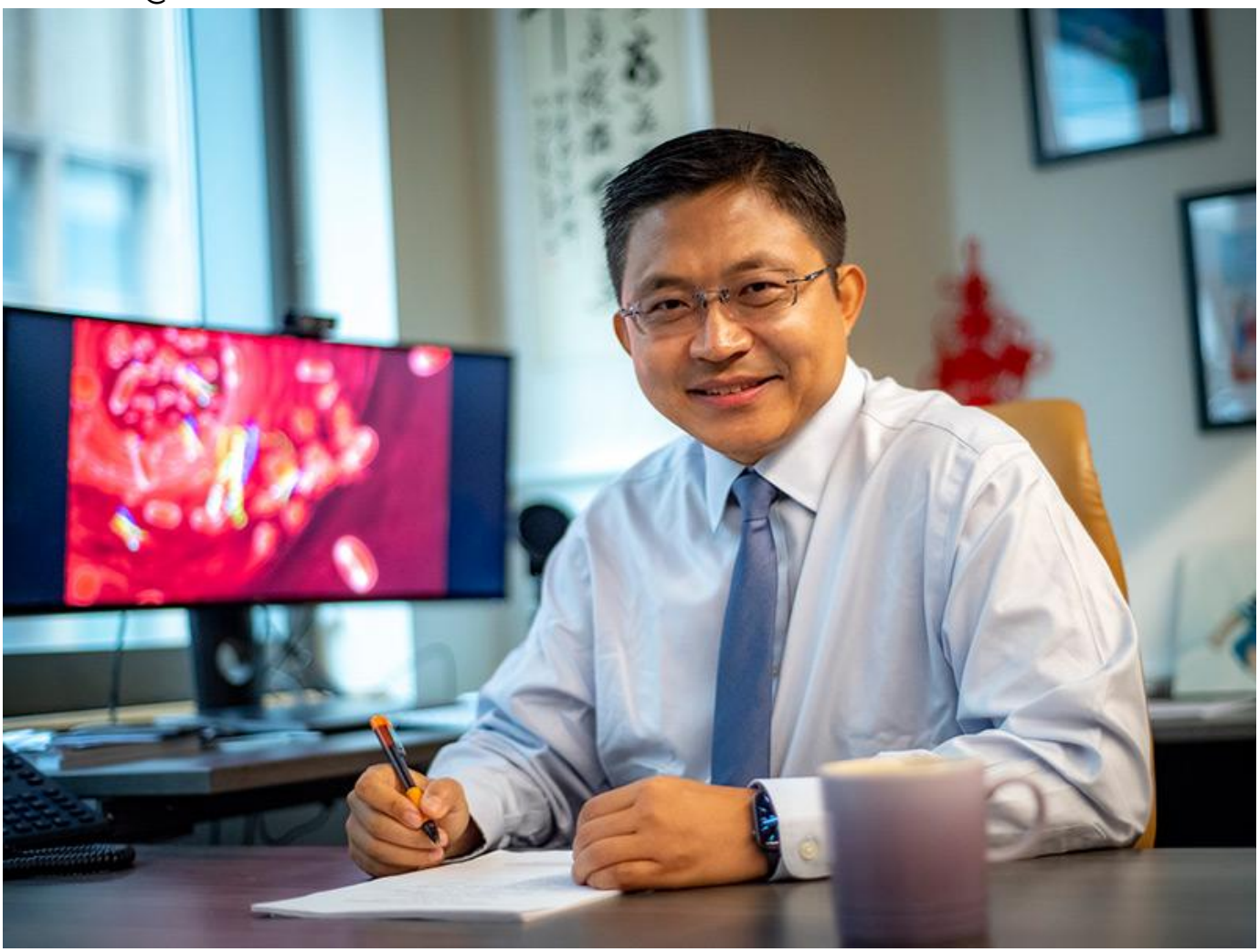

Tony Hu, PhD, Weatherhead Presidential Chair in Biotechnology Innovation at Tulane University School of Medicine, is lead author of a recent study in Nature Nanotechnology that outlines the design of a new blood test to detect SARS-COV-2 using extracellular vesicles. Photo by Paula Burch-Celentano.

Nasal swab PCR tests are the gold standard for diagnosing COVID-19. But sometimes these tests miss cases when patients are swabbed later in the course of their infection as viral levels decline in the upper respiratory tract yet remain in the lungs, gut or other parts of the body.

Tulane University researchers have developed a new type of blood test to find these hidden infections using nanoparticles to detect fragments of the virus released by infected cells anywhere in the body. Because the test uses a screening target that remains stable in the blood, it can detect COVID-19 weeks after initial infection, according to a new study published in the journal *Nature Nanotechnology*.

The test analyzes small lipid-enclosed bubbles of cell material called extracellular vesicles (EVs). These vesicles accumulate in the blood and protect their contents from being destroyed by enzymes. Cells infected by SARS-CoV-2 secrete EVs that contain RNA from the virus. Researchers captured these EVs using an antibody and then fused them with synthetic lipid vesicles loaded with a testing reagent. The blood test uses reverse transcription PCR to amplify the RNA target region and CRISPR to amplify the signal produced by this target to detect an infection.

“We believe the major utility of our approach is its ability to detect plasma EV-derived SARS-CoV-2 RNA as an early and durable sign of systemic infection,” said lead study author Tony Hu, PhD, Weatherhead Presidential Chair in Biotechnology Innovation at Tulane University School of Medicine.

Hu’s lab team compared the new test with standard nasal swab PCR tests in controlled infection models using non-human primates. Viral levels in the upper respiratory tract caught by nasal PCR tests tended to peak between days one and 13 post-infection and decreased rapidly after peak expression. The blood test found lower extracellular vesicle viral RNA levels early in infection, but these consistently increased after day six and remained stable a month after infection.

The EV test was able to detect SARS-COV-2 RNA in blood samples from hospitalized adults who had one or more negative nasal swab tests but who were ultimately diagnosed with COVID-19. It also detected positive results in children who had multiple negative nasal swab PCR test results or a single positive test followed by multiple negative results.

The technology could give doctors a secondary screening tool for suspected COVID-19 cases that are negative via traditional PCR testing, Hu said.

“It may be particularly valuable for individuals with long-term evidence of infection where transient upper respiratory tract PCR results may not reflect virus levels circulating elsewhere in the body,” Hu said. “This includes individuals with compromised immune systems, such as transplant recipients and others receiving

immunosuppressive therapies. It may also be relevant during organ donation to reduce the risk of virus transfer.”

The study was co-authored by Bo Ning, Zhen Huang, Brady M. Youngquist, John W. Scott, Alex Niu, Christine M. Bojanowski, Kevin J. Zwezdaryk, Nakhle S. Saba, Jia Fan, Xiao-Ming Yin, Christopher J. Lyon and Chen-zhong Li of Tulane University School of Medicine; Chad Roy of the Tulane National Primate Research Center and Jing Cao of the University of Texas Southwestern Medical Center.