Breakthrough CRISPR-based test offers faster, more accurate diagnosis for fungal pneumonia

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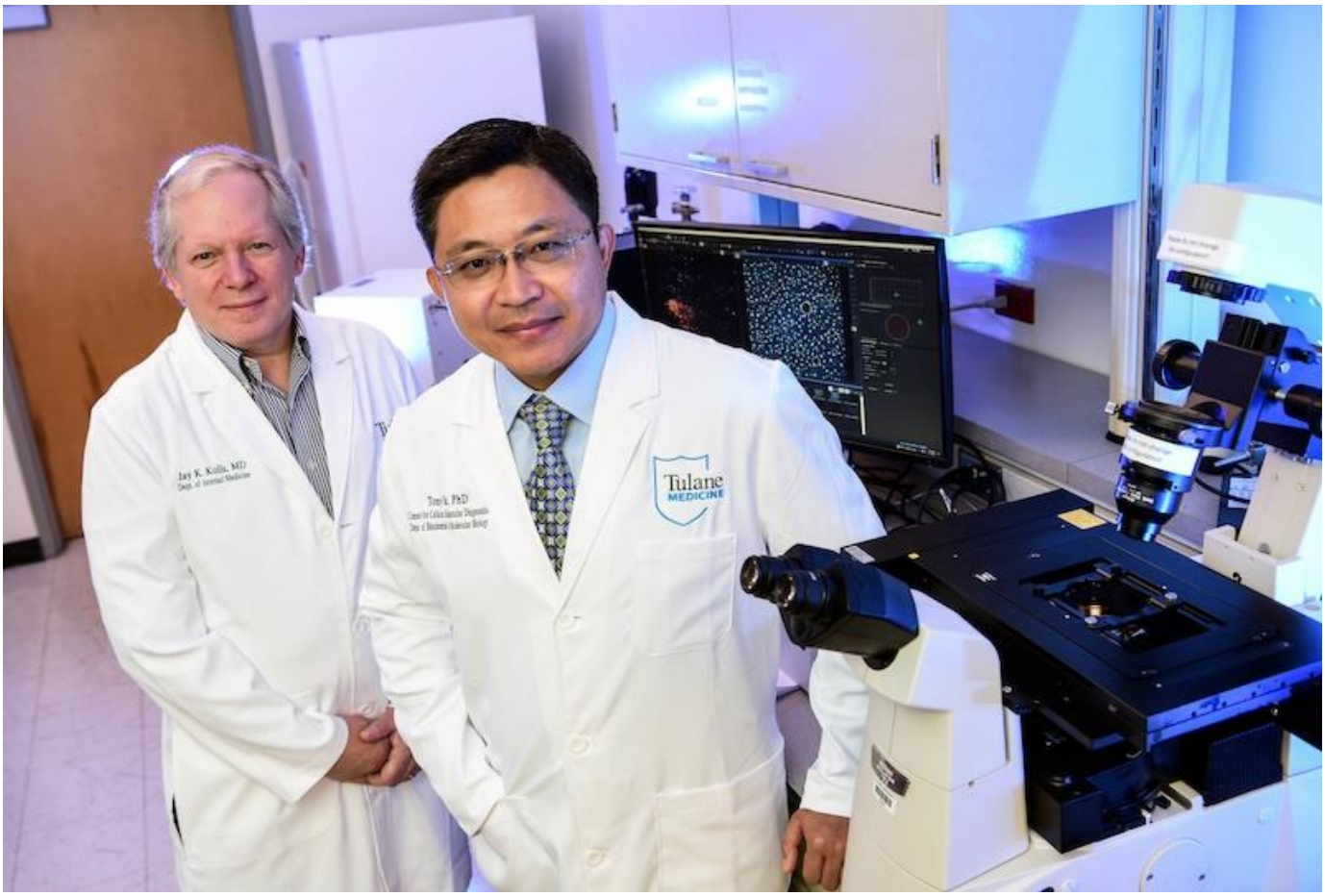

The new diagnostic tool was developed by Dr. Jay Kolls, the John W. Deming Endowed Chair in Internal Medicine at Tulane University School of Medicine (left), and Tony Hu, PhD, the Weatherhead Presidential Chair in Biotechnology Innovation and director of the Tulane Center for Cellular & Molecular Diagnostics (right).

Tulane University researchers have developed a CRISPR-based test that diagnoses *Pneumocystis jirovecii* pneumonia (PJP) — a life-threatening fungal infection primarily affecting children and immunocompromised patients — more quickly and less invasively, according to a new study published in the *Journal of Clinical Investigation*.

The highly accurate test detects RNA from live fungi in blood samples and throat swabs, eliminating the need for invasive bronchoscopy procedures currently used for diagnosis.

"Current diagnostic methods haven't evolved in decades, leaving many patients without timely or definitive answers," said study co-author Dr. Jay Kolls, the John W. Deming Endowed Chair in Internal Medicine at Tulane University School of Medicine. “Having a non-invasive throat swab test or a blood test really allows us to get a faster, but also more specific, diagnostic than we’re able to get right now.”

Kolls and study co-author Tony Hu, PhD, the Weatherhead Presidential Chair in Biotechnology Innovation and director of the Tulane Center for Cellular & Molecular Diagnostics, led a multidisciplinary team to develop the new tool, combining engineering innovation with clinical and biomedical expertise.

The fungus that causes PCP rarely harms healthy people but can trigger dangerous lung infections in those with compromised immune systems, including cancer patients, transplant recipients, people with HIV/AIDS and patients on immune-suppressing drugs.

Traditional diagnostic methods for PJP rely on a bronchoscopy in which a tube is inserted into the patient’s airways to collect samples, an expensive and invasive procedure.

“It can take until the next day, sometimes two days, to receive bronchoscopy results,” Hu said. “With the CRISPR-based assay, we can go from samples to results in 45 minutes.”

PCR swab tests, like those used for rapid COVID testing, often fail to detect active *P. jirovecii* infections. Using the CRISPR-based detection tool alongside PCR testing significantly boosted diagnostic accuracy, correctly identifying 96% of infected infants (compared to 66% with PCR alone) and 93% of infected adults (compared to just 26% with PCR alone).

CRISPR, an acronym for “clustered regularly interspaced short palindromic repeats,” is a gene editing technology that allows scientists to precisely modify DNA. For the PJP diagnostic test, CRISPR is used to detect RNA of the fungus causing PJP.

“That’s novel,” Kolls said. “And we have data that shows PJP may be more prevalent than thought. Better diagnosis can help us prove that.”

In addition to diagnosing patients, the test can be used on throat swabs already gathered in clinics to improve epidemiology and mapping of pneumocystis in the United States.

This study also shows the growing use of CRISPR as a way to streamline disease detection. Looking ahead, the research team sees potential for the CRISPR diagnostic platform to detect other respiratory infections.

“This tool is an example of the collaborative spirit at Tulane University, where cutting edge engineering can work alongside extensive clinical practice to address a very critical issue,” Hu said. “Hopefully we can soon deploy this as a clinical test and improve outcomes for patients.”

The tool developed at Tulane was tested in collaboration with samples from University Health Network/University of Toronto, the Pneumonia Etiology Research for Child Health (PERCH) study, and the International Mycoses Prevention, Research, Implementation, Networks and Training (IMPRINT) consortium at the University of Cape Town. The research was supported by the National Institutes of Health, the Gates Foundation, and the National Institute for Health and Care Research.

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