

Simple new blood test reveals your body's precise internal clock to guide treatments, improve health

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The first simple blood test to identify your body's precise internal time clock as compared to the external time has been developed by

Northwestern Medicine scientists.

The test, TimeSignature—which requires only two blood draws—can tell physicians and researchers the time in your body despite the time in the external world. For instance, even if it's 8 a.m. in the external world, it might be 6 a.m. in your body.

"This is a much more precise and sophisticated measurement than identifying whether you are a morning lark or a night owl," said lead author Rosemary Braun, assistant professor of preventive medicine (biostatistics) at Northwestern University Feinberg School of Medicine. "We can assess a person's biological clock to within 1.5 hours.

"Various groups have tried to get at internal circadian time from a [blood test](#), but nothing has been as accurate or as easy to use as TimeSignature," Braun said.

Previously, measurements this precise could only be achieved through a costly and laborious process of taking samples every hour over a span of multiple hours.

The paper will be published Sept. 10 in the journal *PNAS*.

Processes in nearly every tissue and organ system in the body are orchestrated by an internal biological clock, which directs circadian rhythm, such as the sleep-wake cycle. Some individuals' internal clocks are in sync with external time but others are out of sync and considered misaligned.

The new test for the first time will offer researchers the opportunity to easily examine the impact of misaligned circadian clocks in a range of diseases from heart disease to diabetes and Alzheimer's disease. When the blood test eventually becomes clinically available, it also will provide

doctors with a measurement of an individual's [internal biological clock](#) to guide medication dosing at the most effective time for his or her body.

The software and algorithm are available for free to other researchers so they can assess physiological time in a person's body. Northwestern has filed for a patent on the blood test.

"This is really an integral part of personalized medicine," said coauthor Dr. Phyllis Zee, chief of sleep medicine in neurology at Feinberg and a Northwestern Medicine neurologist. "So many drugs have optimal times for dosing. Knowing what time it is in your body is critical to getting the most effective benefits. The best time for you to take the blood pressure drug or the chemotherapy or radiation may be different from somebody else."

Zee also is the Benjamin and Virginia T. Boshes Professor of Neurology.

The test measures 40 different [gene expression](#) markers in the blood and can be taken any time of day, regardless of whether the patient had a good night's sleep or was up all night with a baby. It is based on an algorithm developed by Braun and colleagues by drawing subjects' [blood](#) every two hours and examining which genes were higher or lower at certain times of day. Scientists also used gene expression data from studies conducted at four other centers.

The scientists then developed a novel machine-learning method that was used to train a computer to predict the time of day based on patterns in these gene expression measurements. Out of about 20,000 genes measured, these 40 emerged with the strongest signal.

"Timing is everything," said study coauthor Ravi Allada, a professor of neurobiology at Northwestern's Weinberg College of Arts and Sciences.

"We know if you have disruption of your internal clock, it can predispose you to a range of diseases. Virtually every tissue and organ system are governed by circadian rhythm.

"Before we didn't have a clinically feasible way of assessing the clock in healthy people and people with disease. Now we can see if a disrupted clock correlates with various diseases and, more importantly, if it can predict who is going to get sick."

A link between circadian misalignment and diabetes, obesity, depression, heart disease and asthma has been identified in preclinical research by scientist Joe Bass, chief of endocrinology, metabolism and molecular medicine at Feinberg.

Down the road, Zee envisions improving health and treating disease by aligning people's circadian clocks that are out of sync with external time.

"Circadian timing is a modifiable risk factor for improving cognitive health, but if we can't measure it, it's difficult to know if we've made the right diagnosis," Zee said. "Now we can measure it just like a lipid level."

The paper is titled "A Universal Method for Robust Detection of Circadian State from Gene Expression."

More information: Rosemary Braun et al., "Universal method for robust detection of circadian state from gene expression," *PNAS* (2018). www.pnas.org/cgi/doi/10.1073/pnas.1800314115

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