A blood test for your body clock? It's on the horizon

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What time is your body clock set on?

The answer, mounting research suggests, can influence everything from

your predisposition to diabetes, heart disease and depression to the optimal time for you to take medication. But unlike routine blood tests for cholesterol and hormone levels, there's no easy way to precisely measure a person's individual circadian rhythm.

At least not yet.

New CU Boulder research, published in the *Journal of Biological Rhythms*, suggests that day could come in the not-too-distant future. The study found that it's possible to determine the timing of a person's internal circadian or biological clock by analyzing a combination of molecules in a single blood draw.

"If we can understand each individual person's circadian clock, we can potentially prescribe the optimal time of day for them to be eating or exercising or taking medication," said senior author Christopher Depner, who conducted the study while an assistant professor of integrative physiology at CU Boulder. "From a personalized medicine perspective, it could be groundbreaking."

Syncing our life with our clock

For decades, researchers have known that a central 'master clock' in a region of the brain called the hypothalamus helps to regulate the body's 24-hour cycle, including when we naturally feel sleepy at night and have the urge to wake up in the morning.

More recently, studies reveal that nearly every tissue or organ in the body also has an internal timing device, synced with that master clock, dictating when we secrete certain hormones, how our heart and lungs function throughout the day, the cadence of our metabolism of fats and sugars, and more.

As many as 82% of protein-coding genes that are drug targets show 24-hour time-of-day patterns, suggesting many medications could work better and yield fewer side effects if administration was timed appropriately.

And when our internal rhythm is at odds with our sleep-wake cycle, that can boost risk of an array of diseases, said study co-author Ken Wright, a professor of integrative physiology and director of the Sleep and Chronobiology Laboratory at CU Boulder.

"If we want to be able to fix the timing of a person's circadian rhythm, we need to know what that timing is," he said. "Right now, we do not have an easy way to do that."

Even among healthy people, sleep-wake cycles can vary by four to six hours.

Simply asking someone, 'are you a morning lark, a night owl or somewhere in-between?' can provide hints to what a person's circadian cycle is.

But the only way to precisely gage the timing of an individual's circadian clock (including where the peaks and troughs of their daily rhythm) is to perform a dim-light melatonin assessment. This involves keeping the person in dim light and drawing blood or saliva hourly for up to 24 hours to measure melatonin—the hormone that naturally increases in the body to signal bedtime and wanes to help wake us up.

A molecular fingerprint for circadian rhythm

In pursuit of a more precise and practical test, Wright and Depner brought 16 volunteers to live in a sleep lab on the Anschutz Medical campus in Aurora for 14 days under tightly controlled conditions.

In addition to testing their blood for melatonin hourly, they also used a method called "metabolomics"—assessing levels of about 4,000 different metabolites (things like amino acids, vitamins and fatty acids that are byproducts of metabolism) in the blood.

They used a machine learning algorithm to determine which collection of metabolites were associated with the circadian clock—creating a sort of molecular fingerprint for individual circadian phases.

When they tried to predict circadian phase based on this fingerprint from a single blood draw, their findings were surprisingly similar to those using the more arduous melatonin test.

"It was within about one hour of the gold standard of taking blood every hour around the clock," said Depner, now an assistant professor of kinesiology at the University of Utah.

He noted that the test was significantly more accurate when people were well rested and hadn't eaten recently—a requirement that could make the test challenging outside of a laboratory setting. And to be feasible and affordable, a commercial test would likely have to narrow down the number of metabolites it's looking for (their test narrowed it down to 65).

But the study is a critical first step, said Wright.

"We are at the very beginning stages of developing these biomarkers for circadian rhythm, but this promising study shows it can be done."

Other research, including some from Wright's lab, is exploring proteomics (looking for proteins in blood) or transcriptomics (measuring the presence of ribonucleic acid, or RNA) to assess circadian phase.

Ultimately, the researchers imagine a day when people can, during a routine physical, get a blood test to precisely determine their circadian phase—so doctors can prescribe not only what to do, but when.

"This is an important step forward in paving the way for circadian medicine—for providing the right treatment to the right individual at the right time of day," said Depner.

More information: D. Cogswell et al, Identification of a Preliminary Plasma Metabolome-based Biomarker for Circadian Phase in Humans, *Journal of Biological Rhythms* (2021). DOI: 10.1177/07487304211025402

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