Researchers devise a new way to plot circadian clock

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(Phys.org)—Everyone has an internal clock, that mysterious process which controls sleeping and hunger patterns, but now researchers are finding out that because the internal clock also controls metabolism, it would be helpful to be able to easily chart out a person's personal rhythm because it appears many drugs work better or worse at certain stages of their cycle. Until now, charting out a person's clock has involved taking blood samples every twenty minutes or so over a twenty four hour period and measuring melatonin levels. Now new research by a team in Japan has found what appears to be an easier way. They measure, as they describe in their paper published in the *Proceedings of the National Academy of Sciences*, certain metabolites using just two blood samples over a 12 hour period to prduce an accurate clock.

The team based their research on an idea by botanist Carolus Linnaeus, who suggested that a bio or flower clock could be made by observing the opening and closing times of different types of flowers and planting them amongst one another. A person could theoretically use the flowers to discern the correct time by noting which were open.

Instead of flowers opening and closing, the researchers focused on metabolite (substances that take part in metabolism) levels which tend to rise and fall throughout the day. To find out which ones could be used to chart a circadian clock, the researchers enlisted six volunteers to live in a controlled environment for two weeks where their metabolites could be closely monitored. In so doing they identified several metabolites they believed would allow for plotting out a person's circadian clock with just

a few samples taken.

To test their idea, they next took just two blood samples from three different male volunteers over a thirty six hour period, and found that in measuring the metabolites they had singled out previously, that they were able to chart out their internal clocks as accurately as could be done using the melatonin level test.

Of course tests with much larger groups of subjects will have to be undertaken before the metabolite method of plotting a person's circadian clock can be proven to be useful, but this study does suggest that there are better and easier ways to get it done with the hope that one day, it will become a routine part of a patient's health care, leading to better results when taking medications and perhaps a better night's sleep.

More information: Human blood metabolite timetable indicates internal body time, *PNAS*, Published online before print August 27, 2012, doi: 10.1073/pnas.1207768109

Abstract
A convenient way to estimate internal body time (BT) is essential for chronotherapy and time-restricted feeding, both of which use body-time information to maximize potency and minimize toxicity during drug administration and feeding, respectively. Previously, we proposed a molecular timetable based on circadian-oscillating substances in multiple mouse organs or blood to estimate internal body time from samples taken at only a few time points. Here we applied this molecular-timetable concept to estimate and evaluate internal body time in humans. We constructed a 1.5-d reference timetable of oscillating metabolites in human blood samples with 2-h sampling frequency while simultaneously controlling for the confounding effects of activity level, light, temperature, sleep, and food intake. By using this metabolite timetable as a reference, we accurately determined internal body time within 3 h

from just two anti-phase blood samples. Our minimally invasive, molecular-timetable method with human blood enables highly optimized and personalized medicine.