Medical Xpress

Team develops a non-invasive method for profiling a person's unique circadian rhythm

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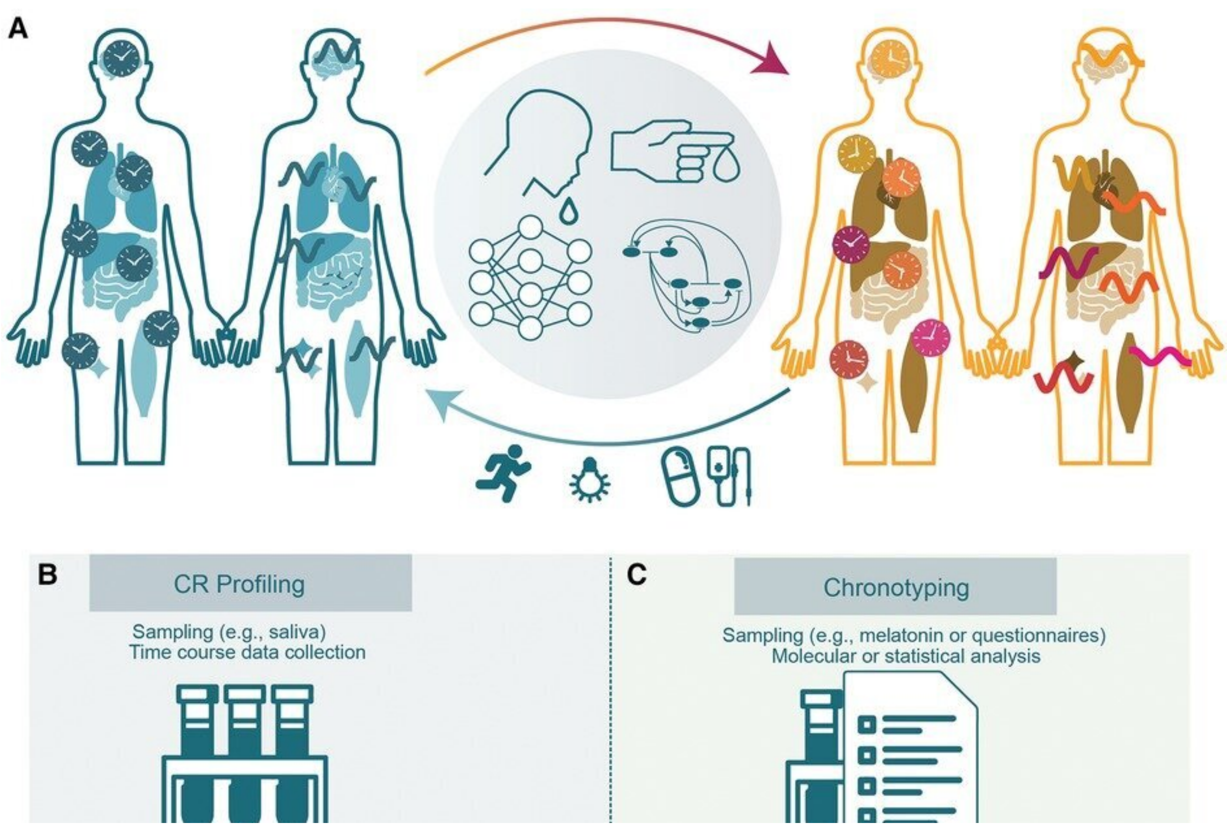

The circadian system and methods for determining CRs and chronotyping. (A) The role of the circadian clock in health and disease. A proper functioning clock ensures correct timing of physiological events such as sleep/wake cycles and contributes to sustain a healthy life (left). The disruption of CRs (right) is associated with numerous diseases including sleep disorders, neurodegenerative diseases, and cancer. Various circadian relevant clinical applications are being studied and implemented to diminish the negative effects of circadian disruption e.g., by the usage of zeitgebers like bright light therapy or physical exercise to reset the clock, and timely administration of drug compounds. For this purpose, methodologies (cetre) using molecular data retrieved from time course collection of biological samples for e.g., from blood or saliva in combination with computational and mathematical modeling of the clock network are needed to generate a personalized profile of the CR. (B) CR profiling by repetitive and representative sampling, molecular and computational analysis to generate a personalized circadian profile. (C) Molecular analysis of biological samples or questionnaires and correlation to populational data for typification of an individual into chronotypes. Credit: *Frontiers in Digital Health* (2023). DOI: 10.3389/fdgth.2023.1157654

An interdisciplinary team led by Prof. Angela Relógio, a scientist at Charité's Molecular Cancer Research Center (MKFZ) and Institute for Theoretical Biology and the MSH Medical School Hamburg, has developed a non-invasive method for profiling a person's unique circadian rhythm. Their research is now published in the journal *Frontiers in Digital Health*.

Starting with a simple saliva sample, the team of experts can create a detailed description of the body's internal clock by combining molecular analysis and computational modeling. The goal is to provide personalized recommendations for adjusting lifestyle factors or treatment timing to the circadian rhythm.

"The biological clock, also known as the circadian clock, ticks in virtually every cell of the body," explains Prof. Angela Relógio. "It regulates the timing of many cellular and molecular mechanisms, such as cell division or metabolic processes, and plays a vital role in maintaining human health. If the circadian rhythm is disrupted, diseases can develop including sleep disorders, depression, diabetes, neurodegenerative diseases, obesity and cancer."

Personal rhythm influences health and well-being

Prof. Relógio directs the Circadian Medicine and Systems Biology Group at Charité's Molecular Cancer Research Center and Institute for Theoretical Biology as well as the Institute for Systems Medicine at the MSH Medical School Hamburg. In addition to having a background in physical-technological engineering, she also has a doctorate in cell and molecular biology. This rare combination enables her to develop and lead the TimeTeller project.

"Circadian rhythms and thus the timing of molecular processes differ from person to person," she reports. "Knowing your personal circadian rhythm and adjusting activities like sleep, exercise and medication intake accordingly can improve your general health and well-being. In cancer patients, for example, we suspect that we could optimize treatment efficacy and reduce side effects by adjusting the timing of medical treatment to the individual patient's circadian rhythm. This could improve patients' quality of life during treatment, while also lowering costs for healthcare systems."

But how do you read the circadian clock? "We know that every cell in the human body regularly increases and decreases the activity of many genes," explains Prof. Relógio. "For example, the genes that control cell division or metabolism are more or less active during certain parts of the 24-hour cycle. Since we assume that all cells in the body work synchronously, we can infer the internal circadian clock by analyzing gene activity in cells in the saliva."

Clock in cells in the saliva ticks individually and synchronously with other cells' clocks

So, Prof. Relógio and her team of scientists determined the activity of at least two genes in cells from saliva samples, collected from subjects at different times of the day, using mRNA: the more mRNA-molecules are present, the more frequently the gene was transcribed.

"We then developed a mathematical model that uses the gene activities to calculate when is the best time to exercise, sleep or take medicine," reports Prof. Relógio. For example, the scientists were able to successfully predict the optimal time for athletes to train. They also worked with cancer patients, calculating when drugs should best be administered to cause cancer cells to die while minimizing the side effects on healthy cells.

Technology to be validated in clinical trials

"So far, we have retrospectively tested our technology in order to find out whether it could have predicted the observed effects," explains Prof. Relógio. "But currently we are involved in different clinical trials to validate our method further. Our goal is to help physicians choose the best time for treatment and to help healthy people adjust their daily activities to their internal clock in order to get or stay healthy."

"The successful transfer of Prof. Relógio's research results into a company is a tangible example of the potential that can be unleashed by translational medicine," says Prof. Christopher Baum, Chair of the BIH Board of Directors and Charité's Chief Translational Research Officer. "This requires well-designed partnerships, in this case with Stiftung Charité, and appropriate tools such as the I4H pilot and our DHA program to support motivated and committed innovators."

"We are extremely pleased for the TimeTeller team," say Tim Huse and Dorothée Marie-Louise Döpfer of the BIH's DHA program. "Their vision, perseverance, and commitment to improving patients' health and quality of life have really impressed us. We wish the team all the very best and success, and look forward to following their progress."

More information: Benjamin Dose et al, TimeTeller for timing health: The potential of circadian medicine to improve performance, prevent disease and optimize treatment, *Frontiers in Digital Health* (2023). DOI: 10.3389/fdgth.2023.1157654

Provided by BIH at Charité

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