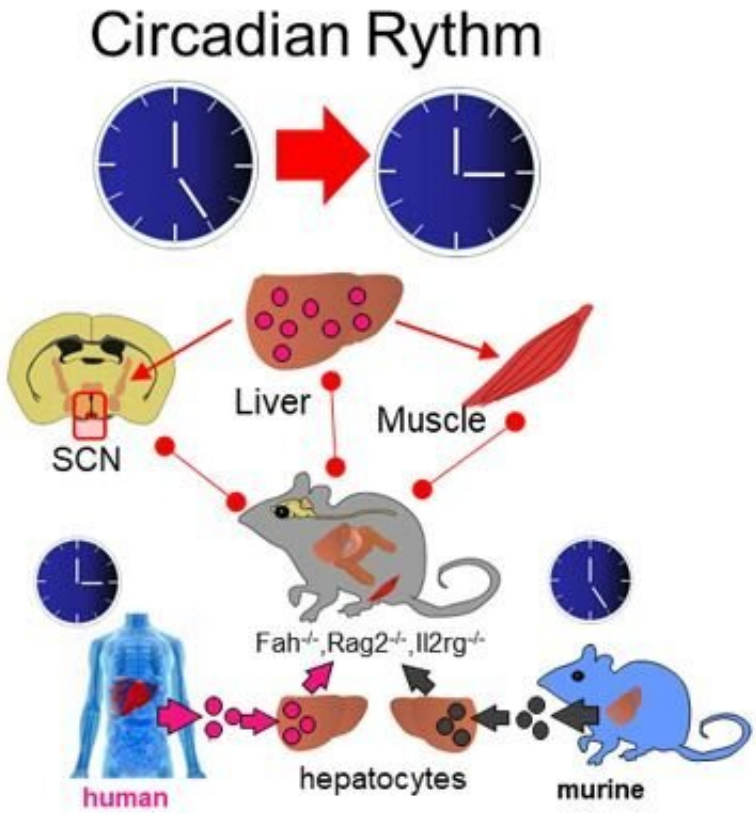
Researchers find that liver cells influence the circadian clock

May 17 2023



A "humanized" mouse model receives liver cells from healthy mice (control group) or human liver cells (humanized mice). The presence of human liver cells leads to a modification in the circadian clock of the liver and muscle and affects the central clock (the suprachiasmatic nuclei). This results in a phase advance in circadian rhythm in the humanized animal, the metabolism and behavior of which shifts forward by a few hours. Credit: *Science Advances* (2023). DOI: 10.1126/sciadv.adf2982

University of Queensland-led research has revealed liver cells influence the body's internal circadian clock, which was previously believed to be solely controlled by the brain.

Associate Professor Frédéric Gachon from UQ's Institute for Molecular Bioscience and Dr. Serge Luquet from Université Paris Cité/CNRS in France and their collaborators have demonstrated that mice with transplanted human liver cells had modified circadian rhythms. The research was published in *Science Advances*.

Dr. Gachon said the circadian internal body clock controls most biological functions including sleep, hormone secretion, body temperature and metabolism.

"Mice are nocturnal but when their liver cells were replaced with human cells, their circadian clock advanced by two hours—they ate and slept at different times to mice without those transplanted cells," Dr. Gachon said.

"The mice in our study started to eat and be active before night-time began, which is very unusual for a nocturnal animal."

Until now, the synchronization of the mammalian circadian rhythm was thought to be controlled exclusively by a central circadian clock composed of a group of brain cells called the suprachiasmatic nucleus.

Dr. Gachon says this study shows human liver cells in a mouse can act on the central clock and modify circadian behavior.

"Liver disease and metabolic diseases such as diabetes and obesity are associated with disrupted sleep, irregular eating and a disturbance of the circadian clock," Dr. Gachon said.

"This study suggests that the abnormal liver function is likely driving this disturbed rhythm.

"Our study deepens our understanding of the hormonal and neuronal mechanisms involved in the role of the liver in controlling circadian rhythms.

"It suggests that restoring liver physiology could benefit the health and well-being of patients.

"It also shows that the regulation of circadian rhythms is more complex than we suspected and presents avenues for investigating potential new treatments for metabolic diseases."

More information: Anne-Sophie Delbès et al, Mice with humanized livers reveal the role of hepatocyte clocks in rhythmic behavior, *Science Advances* (2023). DOI: 10.1126/sciadv.adf2982. www.science.org/doi/10.1126/sciadv.adf2982

Provided by University of Queensland