

How the circadian rhythm of the liver is regulated by muscle activity

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The biological clock/circadian rhythm is the mechanism that ensures that a certain physiological process takes place at a specific time of the day or night. It is coordinated by the brain at a general level, but each organ or tissue is also subjected to specific regulation. Adjusting to geophysical time is a way to optimize processes, but how does the liver "know" when it is day or night?

Scientists led by ICREA researcher Dr. Salvador Aznar-Benitah at IRB Barcelona have discovered how skeletal [muscle](#) regulates [liver function](#) and determines [fat metabolism](#). Specifically, a molecule secreted by muscle and that reaches the liver through serum is responsible for modulating around 35% of the metabolic functions of the liver. The remaining basal functions of this organ and others related to [carbohydrate metabolism](#) are

independent of muscle activity and are regulated by the basal circadian rhythm, that is to say, by the brain.

"It's a very nice discovery because it is the first demonstration of the need for communication between the circadian clocks of tissues and organs outside the brain, and we can see that this communication between muscle and liver is altered by aging," says Dr. Aznar-Benitah. "When we get older, cells stop obeying the [biological clock](#) and begin to perform functions in a non-optimal manner, leading to errors that cause tissues to age."

The liver, conductor of sugar and fat metabolisms

The liver's main role is to help the body digest food, mainly fats and sugars. The brain is the main consumer of sugar in our body while [skeletal muscle](#), which allows us to move, run and jump and also allows the heart to pump, is the main consumer of fat.

The mechanism published by the scientists in the journal *Science Advances* reveals that the liver is not autonomous in the metabolism of fats and that it is muscle that sends the message that it is time to switch on fatty acid metabolism and how it should go about this. "We didn't expect to find this connection between the [liver](#) and muscle because it wasn't known previously, but, on second thought, it makes complete sense that fat management is coordinated by one of its main consumers," says Dr. Aznar-Benitah. Carbohydrate metabolism is dependent on the basal coordination exercised by the brain.

Circadian rhythm and aging

Between 2011 and 2019, the Stem Cell and Cancer lab headed by Dr. Aznar-Benitah published several studies that explained how, with age, the circadian rhythm is altered and no longer focuses on

matching processes with the day/night cycle to optimize results but rather on damage repair. This change leads to the "neglect" of physiological processes and causes the accelerated aging of tissues and organs.

The authors also showed that the circadian rhythm is best preserved on a low-calorie diet.

More information: Salvador Aznar-Benitah et al, The circadian rhythm of the liver is regulated by muscle activity, *Science Advances* (2021). [DOI: 10.1126/sciadv.abi7828](https://doi.org/10.1126/sciadv.abi7828)

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