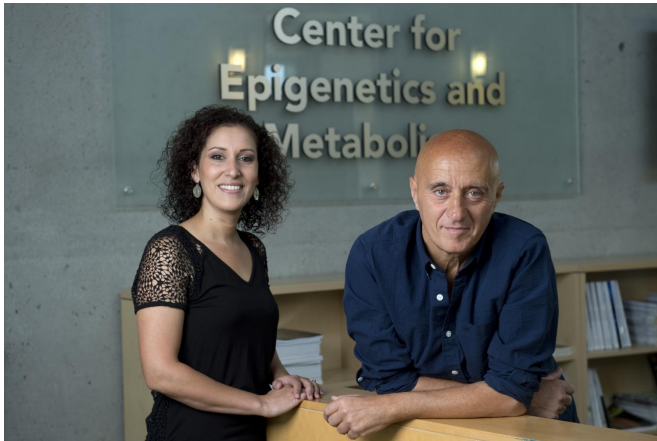


Lung tumors hijack metabolic processes in the liver, study finds

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A study by UCI's Selma Masri (left) and Paolo Sassone-Corsi reveals the unsuspected capacity of a tumor to rewire circadian metabolism. Credit: Steve Zylius / UCI

University of California, Irvine scientists who study how circadian rhythms—our own body clocks—control liver function have discovered that cancerous lung tumors can hijack this process and profoundly alter metabolism.

Their research, published online in *Cell*, is the first showing that [lung adenocarcinoma](#) can affect the [body clock](#)'s sway over [lipid metabolism](#) and [sensitivity](#) to [insulin](#) and glucose.

Paolo Sassone-Corsi and Selma Masri of UCI's Center for Epigenetics & Metabolism and colleagues found in rodent studies that lung adenocarcinoma sends signals to the [liver](#) through an inflammatory response, which rewires the circadian mechanisms that manage metabolic pathways. As a result of this inflammation, the insulin signaling pathway is inhibited in the liver, leading to decreased [glucose](#) tolerance and reorganization of lipid metabolism.

"It seems that lung tumors take control of circadian

metabolic function in the liver, potentially to support the heightened metabolic demands of cancer cells," said Masri, a research scientist in the Sassone-Corsi lab. "We believe that this distal rewiring of metabolic tissues does not occur only in the liver, suggesting a systemic shake-up of metabolism."

Circadian rhythms of 24 hours govern fundamental physiological processes in virtually all organisms. The circadian clocks are intrinsic time-tracking systems in our bodies that anticipate environmental fluctuations and adapt to suit the time of day. Changes to these rhythms can profoundly influence human health. Up to 15 percent of people's genes are regulated by the day-night pattern of circadian rhythms; nearly 50 percent of those involved with metabolic pathways in the liver are affected by these rhythms.

For the past decade, Sassone-Corsi—one of the world's foremost researchers on circadian rhythms—has investigated how the body clock controls various liver functions through the influence of external factors, such as day-night patterns and nutrition. That path has led him and his colleagues to explore how diseases such as cancer can impact these elegant regulators.

Despite numerous remarkable advances in research over the last 40 years, cancer remains a major unsolved problem. For many cancer patients, the deterioration of normal physiology and organismal function is the actual cause of death.

In the *Cell* study, tumor-derived inflammation was found to inhibit insulin signal transduction pathways in the liver, leading to hyperglycemia in mice with lung tumors. Fatty acid synthesis was also suppressed, while total cholesterol levels were elevated.

The Sassone-Corsi lab is currently analyzing the factors secreted by the [lung tumors](#) in an effort to fully map the metabolic effects of cancer and to

better understand lung adenocarcinoma's ability to act as an organizer of the circadian clocks in metabolic tissues.

"It's important to continue learning more about the processes of circadian rhythms and how diseases like cancer can alter them," said Sassone-Corsi, the Donald Bren Professor of Biological Chemistry at UCI. "With increased knowledge, we can begin to develop interventions—both behavioral and pharmaceutical—that can help maintain and restore good human health."

More information: *Cell*, DOI: [10.1016/j.cell.2016.04.039](https://doi.org/10.1016/j.cell.2016.04.039)

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