Does lactate, the bane of athletes, help drive cancer?

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Credit: Pixabay

For decades, lactate has been studied largely in the context of exercise, painted as a nagging metabolic byproduct that accumulates in the tissues

and blood during workouts, stiffening muscles and hindering performance.

Now a provocative new paper, published in February in the journal Carcinogenesis, paints the complex, often misunderstood molecule in a more sinister light—as a key driver in the development and spread of cancer.

Its authors say the paper could help explain why people who exercise tend to have lower rates of cancer – because their bodies are able to more effectively process the lactate we all produce when we metabolize sugar. It also could lead to new treatments.

"With this paper, we open a whole new door for understanding cancer, showing for the first time that lactate is not only present, but mandatory for every step in its development," said lead author Inigo San Millan, director of the sports performance department and physiology laboratory at the CU Sports Medicine and Performance Center at CU Boulder.

San Millan, also an assistant professor in the Department of Physical Medicine and Rehabilitation at the CU School of Medicine, spent two years working on the paper with University of California Berkeley professor and renown lactate researcher George Brooks. The team applied lessons learned from dozens of exercise physiology and muscle metabolism studies conducted at CU Boulder, the CU Anschutz Medical Campus in Aurora, the University of California and elsewhere to try to answer a century-old question: How does a normal cell become a cancer cell and then what happens?

As far back as 1923, German Nobel laureate Otto Warburg observed that cancer cells take in exponentially more sugar, or glucose, than normal cells. They also inefficiently convert far less of it into ATP, or energy, converting about 70 percent of it to lactate as a byproduct. The

phenomenon—the first sign of a normal cell turning cancerous through abnormal cell metabolism—is known as the "Warburg effect." The paper seeks to explain why it happens.

With a heightened focus on genetics in recent decades, most researchers moved away from studying cancer metabolism, and the role of lactate became overshadowed, San Millan said. He hopes to help swing the pendulum back.

The paper illuminates the role lactate plays in fueling angiogenesis (the formation of new blood vessels in tumors); how it interferes with the body's immune response to cancer; and how it creates an acidic microenvironment (the space outside the cancer cell) supportive of cancer metastases, or spread. The paper also theorizes how three major transcription factors, or proteins, involved in most cancers (HIF-1,cMYC, and p53) kick-start and perpetuate lactate deregulation in cancer.

Inigo San Milan uses a new hand-held ultrasound technology for a study involving pro cyclist Chris Winn. Credit: Glenn Asakawa/University of Colorado

The paper draws parallels between what happens in the muscles of an athlete in training, and what happens in a developing cancer.

"During high-intensity exercise, working muscles display many of the same metabolic characteristics as cancer cells," explains San Millan, a former pro cyclist and physiologist to Tour de France cyclists. Muscles take up large amounts of glucose, turning it to energy inside the mitochondria and churning out more lactate than the body can immediately clear.

In a healthy person, Brooks' research has shown, the body then recycles that lactate for beneficial use – turning it into a key source of fuel for the brain, muscles, and organs, preventing it from building up.

In cancer, the authors suggest, that recycling system breaks down.

San Millan hypothesizes that while people who exercise regularly are at less risk of cancer—in part due to their body's ability to clear lactate more efficiently—a sedentary lifestyle, combined with excess sugar intake may fuel lactate accumulation and kick-start the metabolic misfiring that can lead to cancer.

The authors hope cancer researchers will use the paper as a starting point for further studies. Already, San Millan is studying breast cancer cell lines, and this summer he will team up with University of Colorado Hospital to study the impact of personalized exercise programs on cancer patients.

Ultimately, he hopes the paper could lead to new exercise and dietary prescriptions for cancer patients, new diagnostic tools that could use deregulated lactate signaling as a marker of a brewing cancer, or new drugs which target MCT Transporters, which are responsible for transporting lactate from cell to cell.

"We hope to sound the alarm for the research community that to stop cancer you have to stop lactate," he said. "There are many ways to do that."

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