'Cell food' gives insight into T cell metabolism

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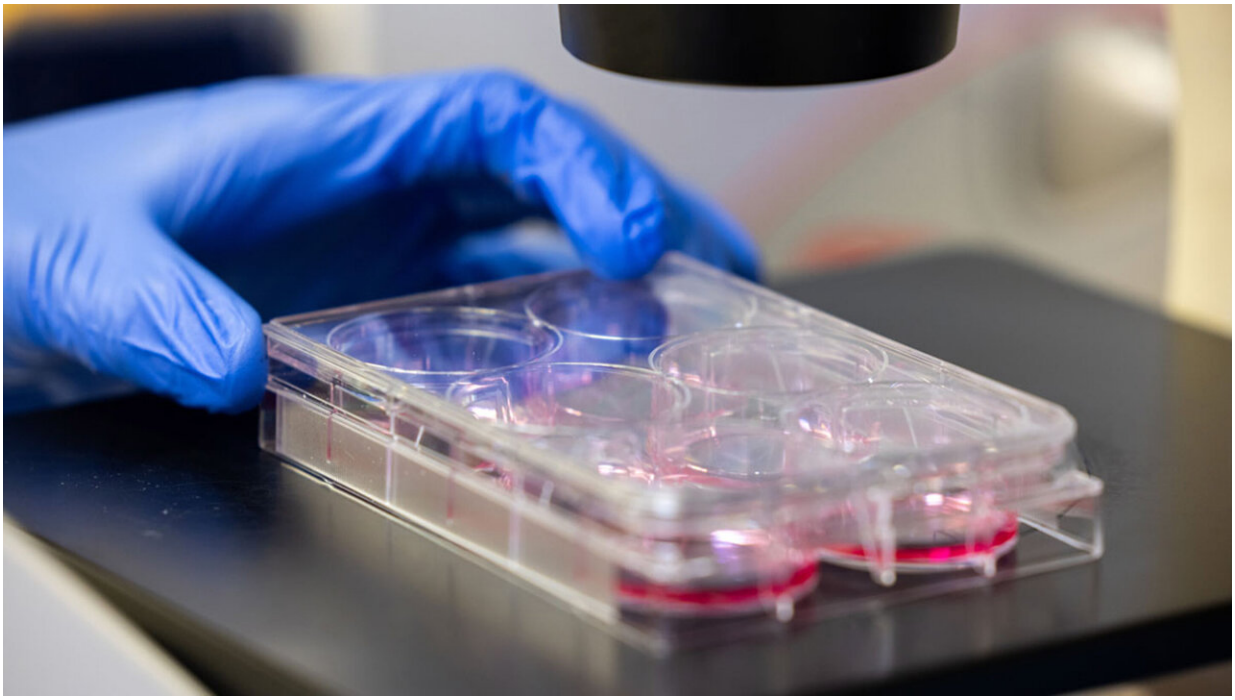

“A T cell's specific identity and function are ruled by metabolic pathways, so each type of T cell's inner workings are distinct,” Hanna Hong explained. Credit: Bryan McCullough

New research from the University of Michigan Rogel Cancer Center reveals that the metabolic pathways that make a specific type of T cell function are different than previously believed. The key to this discovery lies in a new methodology developed by Hanna Hong, graduate student

in immunology and first author of this study. The findings appear in *Science Immunology*.

T cells are critical players of adaptive immunity that protect against infections and cancers. Metabolic pathways produce the energy and building blocks required for them to carry out their jobs. "A T cell's specific identity and function are ruled by metabolic pathways, so each type of T cell's inner workings are distinct," Hong explained.

For this study, Hong developed a type of "cell food" to grow T cells in culture that look and behave like the T cells in an organism.

Previous research from the lab established that the way cells make energy through metabolism inside a living organism is very different from how the field previously modeled metabolism in the lab, a disparity that had led to problems translating previous findings.

This new approach enabled Hong to observe in the lab how different metabolic programs regulate T cell persistence in an organism. Too much T cell persistence equals autoimmunity, or the body misinterpreting and attacking healthy cells as if they were sick cells, and too little persistence means a weakened immune system.

They focused on a specific type of T cell called TH17, which act in the body's immune response to pathogens.

"Because TH17 cells can have different metabolic pathways, they have the capacity to take on properties of other types of T cells that are associated with autoimmunity and immune suppression," Hong said. "We're dedicating more effort to understanding the underlying mechanisms that cause TH17 cells to transition from those that protect against infections to those that promote autoimmunity. Ultimately, the hope is that targeting these pathways can reverse disease."

"T cells play a critical role in protecting us from various diseases, like infections and cancer. However, if over-active, these same properties can lead to autoimmunity and harm us. A more detailed understanding of what T cells eat and how this fuels their metabolism provides important inroads to harness the power of the immune system without tipping the balance toward autoimmunity," added Costas Lyssiotis, Ph.D., Maisel Research Professor of Oncology at the Rogel Cancer Center and principal investigator of this study.

More information: Hanna S. Hong et al, OXPHOS promotes apoptotic resistance and cellular persistence in T H 17 cells in the periphery and tumor microenvironment, *Science Immunology* (2022). DOI: 10.1126/sciimmunol.abm8182

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