Medical Xpress

Study finds that ketone bodies, as alternative cellular fuels, boost immunity

July 28 2023

Credit: Van Andel Research Institute

A metabolic by-product that is more prevalent during fasting may supercharge immune cells as they fight infection and disease, reports an early stage study by Van Andel Institute scientists and collaborators.

The findings, published July 28 in *Immunity*, may pave the way for

future personalized dietary recommendations to augment treatments for infection, cancer and other diseases.

"This study helps us better understand how nutrition affects the immune system," said VAI Professor Russell Jones, Ph.D., the study's corresponding author. "This is an exciting first step and we look forward to one day translating this knowledge into dietary recommendations to boost immune function."

The findings center on ketone bodies, which are regularly produced by the liver but become more numerous when glucose, a sugar that acts as the main power source for cells, is in short supply. This can occur during exertion such as exercise, when cells are rapidly burning through fuel, or during fasting, when there is little food available to be broken down into glucose.

To compensate, the liver steps up production of ketone bodies to feed the brain and other organs. The study shows that ketone bodies also power immune cells, a surprise finding that illuminates new connections between diet and immunity.

Like other cells in the body, T cells—the soldiers of the immune system—absorb nutrients like glucose from our diets to generate the energy required to do their jobs. Jones and colleagues demonstrated that T cells prefer ketone bodies over glucose as a fuel source. They also found that ketone bodies improve T cell function by reprogramming them to better neutralize threats. Conversely, loss of the ability to process ketone bodies causes defects in T cell function and hampers their ability to combat infection.

The authors hypothesize that ketone bodies may be an evolutionary failsafe that boosts the immune system when nutrient resources are limited, such as when one's appetite is suppressed during illness.

"This work underscores how different nutrient fuels source distinct cellular functions," said Peter Crawford, M.D., Ph.D., Vice Dean for Research and Professor of Medicine at University of Minnesota Medical School and study co-author. "It also fosters future interest in considering the diversity of nutrient fuel utilization patterns among different immune cell types in varying infectious disease or cancer contexts."

Although the study suggests increasing ketone bodies through fasting or intermittent fasting regimens may enhance T cell function in certain circumstances, other studies suggest that fasting may suppress immune function. Rather than being at odds with one another, these studies illuminate the intricate interactions between diet and the immune system and underscore the need for further research into this complex relationship.

Going forward, Jones and colleagues will explore how fasting and ketone body supplementation impacts immune function, with a focus on T cells' ability to fight cancer.

More information: Russell G Jones, Ketolysis drives CD8+ T cell effector function through effects on histone acetylation, *Immunity* (2023). DOI: 10.1016/j.immuni.2023.07.002.
www.cell.com/immunity/fulltext … 1074-7613(23)00314-X

Provided by Van Andel Research Institute