Fatty acid oxidation is important for immune cell function:

The NIH MINI Study receives additional funding to study immune function in FAODs

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The immune system is a complex collection of cells, tissues and organs that serves to protect individuals against disease. Although scientists have learned a great deal about the immune system and how it functions, many questions still remain regarding the development of an immune response. *Specifically, what metabolic pathways are present in immune cells and how do these pathways contribute to the immune response to keep us healthy?*

Over the past few years, the immunology community has become increasingly interested in the metabolism of immune cells like T-cells and B-cells. Recently, fatty acid oxidation has emerged as a process that is critical for the development of T-cell responses.

T-cells are a type of white blood cell that constantly circulates via the blood throughout the body, poised to fight off infection. Interestingly, there are many different types of T-cells, each of which have their own job to do. One specific type is the memory T-cell. Memory T-cells are a subset of infection fighting T-cells that have previously encountered and responded to an infection (or vaccination). Memory T-cells travel around in the blood, actively searching for the same infection again in organs and tissues. This surveillance by memory T-cells allows the immune system to respond much more quickly and robustly when the infection shows up again.

Recent work has demonstrated some unique properties of the memory T-cell; it requires fatty acid oxidation to function properly. Long chain fatty acid oxidation is normally increased in memory T-cells, providing energy for their day-to-day functioning. When CPT1a, the gene involved in sticking long chain fatty acids onto carnitine for transport into the mitochondria, is knocked down or inhibited by drugs in T-cells, there is a reduction in the development of functional memory T-cells. Overall, these data suggest that long chain fats are critical for memory T-cell formation.

What does this mean for patients with fatty acid oxidation disorders? Since memory T-cells thrive on fatty acid oxidation, this suggests that individuals with enzyme deficiencies in the pathway of long chain fatty acid oxidation may have altered memory T-cell functioning. This has implications for infections as well as childhood vaccinations. Examples of disorders in the pathway of long chain fatty acid oxidation include CPT1a deficiency,

CPT2 deficiency, CACT deficiency, VLCAD deficiency, LCHAD deficiency, and MAD deficiency (glutaric aciduria type 2).

The NIH MINI Study: Metabolism Infection and Immunity in Inborn Errors of Metabolism (www.genome.gov/mini) is an exciting new study at the NIH Clinical Center (clinicalcenter.nih.gov). The main goal of the study is to learn about the function of the immune system in metabolic disorders. As many patients, caregivers and providers know, infection can be problematic in FAODs by causing low blood sugar (hypoglycemia), liver problems or rapid muscle breakdown (rhabdomyolysis). Therefore, understanding immune function in patients with FAODs is important for their overall health and well-being. *In light of the recent research findings mentioned above, The NIH MINI Study has partnered with the Center for Human Immunology at the NIH to receive additional funding to* ***specifically study patients with FAODs*** *to better serve this important group of patients.* Study participants are screened by phone and invited to the NIH Clinical Center in Bethesda, Maryland for an evaluation. All types of FAODs are evaluated for immune function. Travel costs are provided in advance for patients and their families. The NIH MINI team is available to discuss eligibility for this protocol with anyone that may be interested in participating and welcomes all inquiries.

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