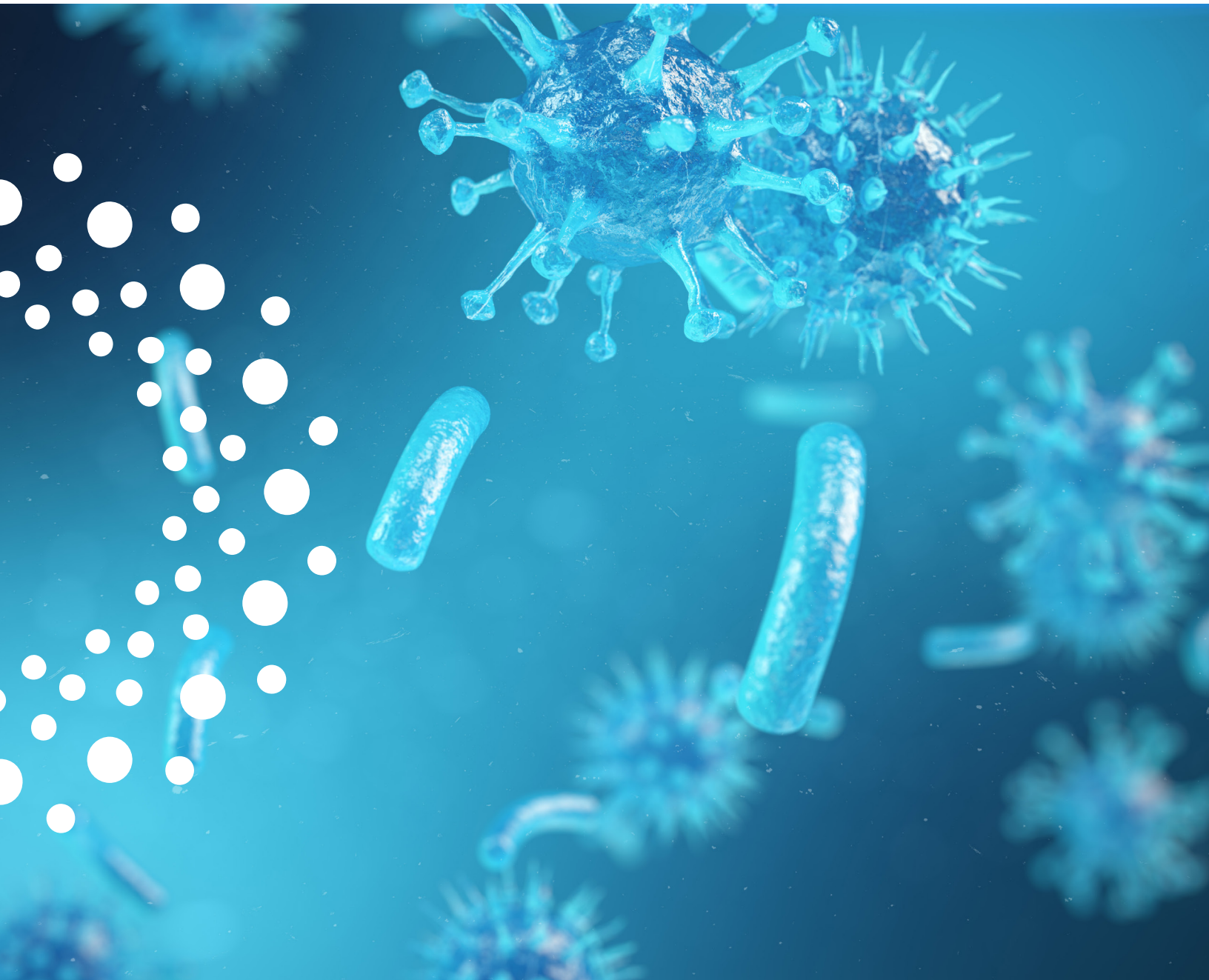
BODYBIO
RESEARCH

The link between short chain fatty acid production & immunity

The immune system is not merely a module that occupies space in the body, though that would open a market for replacement parts. It's composed of mechanisms that enlist the specific talents of several organs, with the overall goal of preventing or limiting infection. A sound immune system can distinguish healthy cells from unhealthy cells by identifying odd molecular patterns that don't match those programmed into the body.

Immune cells come from precursors in bone marrow and develop into mature cells through a series of changes that can occur in different parts of the body. Believe it or not, there are immune cells even in the skin, where antimicrobial proteins exist in different layers. In the marrow are several types of stem cells that generate the first responders of the innate immune system—neutrophils, eosinophils, basophils, mast cells, monocytes, dendritic cells and macrophages. These arise from the common myeloid progenitors. Common lymphoid progenitor stem cells lead to adaptive immune cells—B cells and T cells—that mount responses to specific microbes based on previous encounters. Natural killer cells fall into this platoon, sharing features of both innate and adaptive immune cells, as they provide immediate defenses like the innate cells, but also may be retained as memory cells, called lymphocytes.

In the bloodstream, particular status of immunity may be determined by the quality and quantity of immune cells in circulation. T cells are the lymphatic variety that mature in the thymus gland, a small organ located behind the upper sternum. The thymus begins to involute after puberty and is largely replaced by fat in old age. The lymphatic system is a type of conduit for travel and communication between tissues and the bloodstream. Immune cells that are carried here converge in the lymph nodes, which appear in a few places around the body. Here, adaptive cells might recognize pieces of a microbe carried from a distant area, then activate and replicate, and leave the node to address the pathogen. If swollen, lymph nodes may indicate an active immune respose. Let's not forget the spleen, an organ that processes information from the bloodstream while enriching immune cells. Mucosal surfaces of the body are prime entry areas for pathogens, but house specialized immune hubs to intercept them. It is especially so in the respiratory and GI tracts, making mucus stability an important endeavor.



Short Chain Fatty Acids & T-regs Production

Considering all this intricate operation, how do we strengthen the immune system? Healthy living strategies and protection from environmental assaults is a first step. But there is one substance, natural to the body, made in the colon from the fermentation of resistant starches, that holds considerable sway over the immune system—butyrate. This short-chain fatty acid is food for the cells of the intestinal lining, helping to maintain the integrity of this one-cell thick layer that separates the digestive system from the rest of the body. A study reported in the journal Nature found that butyrate acts as a switch that programs the immune system to produce regulatory T cells (T-regs), which help to balance the immune system by helping it to tolerate specific foreign bodies rather than mounting a full-blown immune response that could result in an autoimmune state, where the immune system views the body's own tissues as the enemy. Inflammatory bowel disease is an autoimmune condition that often presents with a shortage of butyrate-producing bacteria in the gut. In laboratory animals bred to display a similar pathology, the administration of butyrate increased T-reg cells and improved symptoms of colitis. This demonstrated butyrate's value as an immune booster in addition to its role in themantenance of the gut lining.

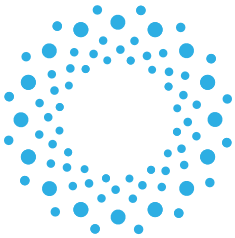
Butyrate as a Histone Deacetylase Inhibitor

Butyrate exerts its activity by acting as a histone deacetylase inhibitor, or by signaling through G protein-coupled receptors. These receptors are located in the cell membrane and bind extracellular substances and transmit signals from these substances to intracellular molecules called G proteins (Guanine nucleotide-binding proteins). There are about a thousand of these encoded in the human genome. As a group, they respond to a host of diverse substances, including light, hormones, amines, neurotransmitters and lipids. These proteins have been called the choreographers of innate immunity by some scientists. And they rely on butyrate.

Butyrate & Inflammation

Butyrate-modulated immunity does not stop at colds and flu. When we think of immunity, we fail to consider its activity outside the contagion box. An immune response in colorectal cancer and its metastasis has been identified as part of the butyrate repertoire. Here, the gut microbiome plays a role, as demonstrated in animal models of colorectal cancer and liver metastasis, wherein supplementation with sodium butyrate decreased both pathologies (Ma, 2020) while increasing natural killer cells. Not only the enhancement of the immune system, but also the attenuation of inflammation is in butyrate's bag of tricks. Regulation of cytokines (TNF-a, IL-2, IL-6) and eicosanoids speaks of butyrate's future in the amelioraton of inflammatory pathologies.

The simple, 4-carbon butyrate molecule has an impressive array of virtues, one we might consider adopting. In an animal model of obesity, butyrate improves insulin sensitivity, increases energy expenditure and reduces adiposity, while inceasing the number of mitochondria in skeletal muscle and brown fat. It keeps the gut mucus layers intact, making sure that the thick inner layer remains devoid of dangerous, even commensal, microbes, and that the loose outer layer plays cordial host to its bacterial occupants, those that have the capacity to direct the immune reasponse.



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