What Happens When Our Immune System Becomes Imbalanced

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Welcome to Issue 128 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and CIS0 research news that our team of doctors, scientists, and experts are most excited about--without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

Something's been awry with our immune responses

After a whirlwind first 2 weeks of *The Longevity Nutrient's* launch, we are excited to share that the book has become an instant Best Seller on USA Today's Booklist and Amazon! ❤️🍓

In this series of *Science Says!*, we have been providing a behind-the-scenes science peek relevant to each of the book's chapters. This week, let's talk about how our immune system both helps and hurts us - and studies showing how CIS0 can help keep our immune responses balanced.

What is our immune system, exactly?

If you took a class in college on Immunity 101, you may remember getting through a big, heavy book detailing all the ins and outs of our immune system. And after a couple of years, that book would become outdated... and need to be even bigger and heavier. Bottom line: As summarized by Sa-Nunes, our immune system is complex.

In general, our immune system is like our very own military guard of white blood cells and pro-inflammatory chemicals (called cytokines or chemokines) that help protect our bodies and brains against invaders. This includes, but is in no way limited to:

- **T cells** that are on the front line, ready to jump on anything they see as a foreign threat. Like, bacteria.
- **B cells** that learn from first viral infections (or vaccines) and adapt to fight that virus when it comes back.
- **Eosinophils, mast cells and basal cells**, which help to fight off parasitic infections, in part by releasing histamine.
- **Kupffer cells** that help to take out bad players in our blood as they pass through the ultimate filter: our liver.
- **Microglial cells** that patiently await the unlikely, but possible, chance that invaders make it to our brain.
- **Cytokines (like IL-6 and TNFα,) and chemokines (like MCP-1)** which serve as loud signalers to the body saying, "Hurry up immune cells! There's an invader in Section 4 of the Liver, and we need you here, now!"

Thus, we are fortunate to have a complex immune system that is ready to take on just about any pathogens that come our way (for those viruses, we're ready at least the second time they come our way). While talk about the immune system is often focused on when it goes awry, it is important to remember that it really is there for a good reason. Thus, it is all about keeping our immune system balanced.

When our immune system goes awry.

There is a good reason that imbalanced immune systems have become a giant topic in the fields of science and medicine, and the issue here is the definition of "invader".

Let's use our dog as an example. We have a multipoo who barks at any person who comes to the door. Delivery person, grandma, friends from the neighborhood, and yes, ill-intended invaders. Similarly, when our immune system is unable to properly differentiate a neutral threat from a real threat, you get a whole lotta barking, which translates to an unbalanced immune system that can lead to conditions like:

- **Allergies,** when overeager mast cells improperly release histamine when exposed to neutral threats - like pollen.
- **Autoimmune diseases,** when our immune army accidentally turns on us and goes after our joints, our gut lining, and other tissues.
- **Chronic inflammation,** which happens as our cells break down with age and our cellular signaling is not as good as it used to be.

Many of these conditions have been on the rise. Warren et al. discuss the growing epidemic of food allergy in children and adults across the globe. In their review, Punzi et al. share how autoimmune conditions, including rheumatoid arthritis, are on the rise. Meanwhile, Li et al. share how aging plays a role in chronic inflammation - and how an overactive immune system speeds up our aging.

Where the CIS0 science comes into play.

As covered in *The Longevity Nutrient*, there is evidence that CIS0, as an essential fatty acid, plays a role in ***keeping our immune responses balanced***. This includes the demonstrated ability in cell-based and animal studies for CIS0 to do following:

- **Activate PPARα/δ and inhibit JAK-STAT,** which are mechanisms demonstrated by Venn-Watson et al. and To et al. that help to balance and calm our immune responses.
- **Lower 18+ pro-inflammatory cytokines and chemokines (including IL-6, TNFα, and MCP-1)** in cell systems and animal models mimicking imbalanced immune system responses in joints, the gut, and the liver.
- **Strengthen cell membranes against lipid peroxidation,** a key instigator in aging-related cellular breakdown and subsequent imbalanced immune responses.

Additionally, as we published in *Nature's Scientific Reports*, our body uses CIS0 to make a second molecule, called pentadecanoylcarnitine (aka PDC). In cell-based studies, PDC surprisingly showed that it is both an H1 and H2 receptor *inhibitor*, where the "H" stands for histamine.

These functions of CIS0 may explain why Matthan et al. found that adults with higher CIS0 had more balanced immune responses. And why Stravik et al. found that moms with higher dietary intake of CIS0 translated to babies with more balanced immune responses.

We'll keep you updated on the latest science around CIS0, including its emerging role in supporting a healthy and balanced immune system. In the meantime, have a great week, everyone!

Dive deeper into the science

READ THESE STUDIES

- Sa-Nunes, A. Overview of immune responses.
- Warren et al. Epidemiology and the growing epidemic of food allergy in children and adults across the globe.
- Punzi et al. Why are autoimmune rheumatic diseases on the rise? Role of sex and gender among many players: a narrative review.
- Li et al. From biological aging to functional decline: Insights into chronic inflammation and intrinsic capacity.
- Venn-Watson et al. Efficacy of dietary odd-chain saturated fatty acid pentadecanoic acid parallels broad associated health benefits in humans: could it be essential?
- To et al. Pentadecanoic acid, an odd-chain fatty acid, suppresses JAK2-STAT3 signaling.
- Venn-Watson et al. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.
- Wu et al. Serum and synovial fluid lipidomic profiles predict obesity-associated osteoarthritis, synovitis, and wound repair.
- Singh et al. Anti-Inflammatory Effect of Dietary Pentadecanoic Acid Supplementation on Inflammatory Bowel Disease in Mice.
- Wei et al. Parabacteroides distasonis Uses Dietary Inulin to Suppress NASH via Its Metabolite Pentadecanoic Acid.
- Venn-Watson S. The Cellular Stability Hypothesis: Evidence of Ferroptosis and Accelerated Aging-Associated Diseases as Newly Identified Nutritional Pentadecanoic Acid (C15:0) Deficiency Syndrome.
- Venn-Watson et al, Pentadecanoylcarnitine is a newly discovered endocannabinoid with pleiotropic activities relevant to supporting physical and mental health.
- Matthan et al. Spillover effects of a family-based childhood weight-management intervention on parental nutrient biomarkers and cardiometabolic risk factors.
- Stravik et al., Maternal intake of cow's milk during lactation is associated with lower prevalence of food allergy in offspring.

- Nerd out on all the C15:0 science at DiscoverC15.com