

Protecting Against Age-Related Immunosenescence

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Welcome to Issue 105 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 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 over 80 peer-reviewed scientific publications, is reading.



HEALTHY AGING

A New Study on How C15:0 Can Both Calm Inflammaging & Boost Good Immunity

It's International Longevity Month, which coincides well with a new study from Kumar et al. that evaluated age-related changes in our metabolome that affect our immune responses. To cut to the chase, this peer-reviewed study published in *Science Advances* showed C15:0 as the strongest fatty acid predictor of healthy immune function among older people. High five, C15:0.

So, how does our immune system change as we age?

Simply put, our immunity becomes unbalanced as we age.

- On one hand, **we experience increased and unwanted production of pro-inflammatory cytokines** (like IL-6) that lead to systemic inflammaging. As reviewed by Choperchini et al. and Tylutka et al., this chronic, low-lying inflammation affects our muscles, vessels, heart, liver, joints, brain and, well, just about everything.
- On the other hand, **aging also results in decreased lymphocytes, especially lymphocytes that help us produce antibodies**. As described by Fulop et al., this is important because antibodies help protect us against specific infections, such as influenza (aka flu). Termed *immunosenescence*, this immune-suppressing effect in older people results in a less robust immune boost response from flu shots compared to younger people.

One big goal to help support our longevity? Keep our overactive pro-inflammatory cytokines at bay, while still allowing our immune system to defend itself effectively against viruses and other pathogens.

Links between inflammaging and immunosenescence.

While this goal may appear like a conflict of immune-interest, there is actually sound science on how taming inflammaging can also boost a proper immune response. Here's one example from Teissier et al.:

- As we age, many pro-inflammatory cytokines go up, including interleukin 15 (aka IL-15).
- IL-15 not only contributes to inflammaging, but it also blocks important production of antibodies against influenza.
- Thus, lowering IL-15 may help our bodies produce antibodies that protect us against the flu.

With that background, we can get to the Kumar et al. study.

Higher C15:0 predicts lower IL-15... with improved flu antibody production.

Kumar et al.'s study included 235 people who were older than 65 years old. This group received flu shots and were evaluated for how well they developed antibodies against influenza. "Poor responders" were those who did not mount a good immune response.

They then used untargeted metabolomics to evaluate hundreds of molecules in the blood to better understand differences between the poor and good responders.

What did they find?

- People with baseline *higher* IL-15 levels had *lower* antibody production post-shot (aka, they were poor responders).
- IL-15 activated natural killer cells that suppressed the production of antibodies.
- People with higher C15:0 levels had lower IL-15 levels. The researchers propose that C15:0's immune calming effect led to healthier antibody production against influenza.
- Among all fatty acids assessed, C15:0 had the most statistically significant association with this benefit.

Based on their study's findings, Kumar et al. suggest that lower C15:0, which naturally occurs as we age, leads to increased IL-15, resulting in poorer immune response to flu shots. Further, the authors propose that increasing C15:0 before vaccination may effectively lower IL-15 and improve flu shot responses, especially among older people.

It is important to note that this study was one of association (not causation), and more studies are needed to test this hypothesis. This study is encouraging, however, on yet another benefit of C15:0 that may support our health with longevity.

Restoring Immune, Muscle & Cognitive Function: XPRIZE Healthspan

Pretty much everyone agrees that optimal healthy aging and longevity will not come from simply waiting for chronic diseases to arise, and then treating each of those diseases with different drugs.

As we shared last week, our ability to truly live longer and healthier as individuals will come from slowing early and core processes of aging that will have broad and meaningful effects, including having a balanced immune system. We're talking about interventions that truly slow the process of aging itself, keeping us strong and resilient.

This is the goal of XPRIZE Healthspan, a whopping \$101M prize purse and global competition for teams who can demonstrate "a proactive, accessible therapeutic that reduces the risk of chronic age-related diseases, increases the human healthspan, and extends quality of life well into our later years."

The specific challenge? A given intervention must restore immune, cognitive and muscle function by a minimum of 10 years, with a goal of 20 years, in persons aged 50-80 years.

Given pure C15:0's demonstrated ability to...

- ✓ Restore healthy C15:0 levels (that naturally decline with aging)
- ✓ Strengthen cell membranes to protect against and reverse Cellular Fragility Syndrome, resulting in greater cellular resilience, lower lipid peroxidation, reversed ferroptosis, and slower cellular aging
- ✓ Activate AMPK, a core and early mechanism to support longevity
- ✓ Have more cellular benefits than leading longevity-enhancing compounds
- ✓ Calm 18+ pro-inflammatory cytokines, including IL-6
- ✓ Restore mitochondrial function
- ✓ Restore healthy red blood cells; and
- ✓ Restore healthy iron metabolism

...which are expected to restore immune, cognitive and muscle function, we say, "Challenge accepted." Stay tuned for more on that front. In the meantime, have a wonderful week!



Dive deeper into the science

READ THESE STUDIES

- ▶ Kumar et al. [Systemic dysregulation and molecular insights into poor influenza vaccine response in the aging population.](#)
- ▶ Coperchini et al. [Inflamm-aging: How cytokines and nutrition shape the trajectory of ageing.](#)
- ▶ Tylutka et al. [Level of IL-6 and age-related conditions: a systematic review and meta-analysis.](#)
- ▶ Fulop et al. [Inflammaging and immunosenescence.](#)
- ▶ Teissier et al. [Interconnections between inflammaging and immunosenescence during ageing.](#)
- ▶ Robinson et al. [C15:0 supplementation in young adults with overweight and obesity: a randomized controlled trial.](#)
- ▶ 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.](#)
- ▶ Wei et al. [Parabacteroides distasonis uses dietary inulin to protect liver health via pentadecanoic acid.](#)
- ▶ Fu, W.C. et al. [Pentadecanoic acid promotes basal and insulin-stimulated glucose uptake in C2C12 myotubes.](#) Food Nutr Res 65:10.29219/fnr.v65.4527 (2021).
- ▶ Venn-Watson & Schork. [Pentadecanoic Acid \(C15:0\), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.](#)
- ▶ 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?](#)
- ▶ Nerd out on all the C15:0 science at [DiscoverC15.com.](#)